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A MANUAL OF PHYSIOLOGY

STEWART

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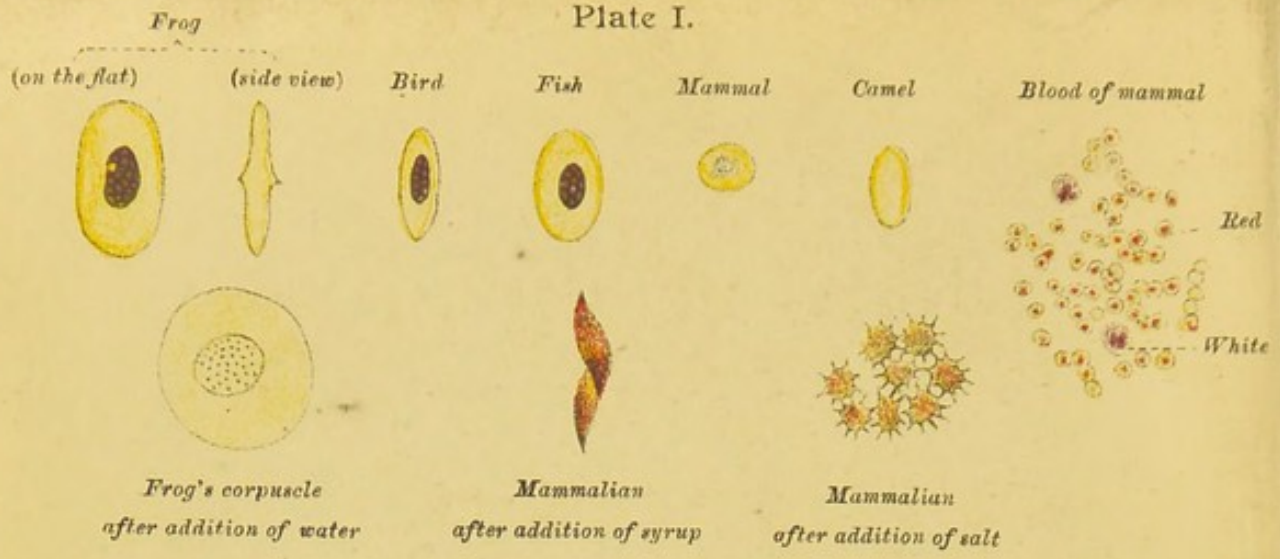
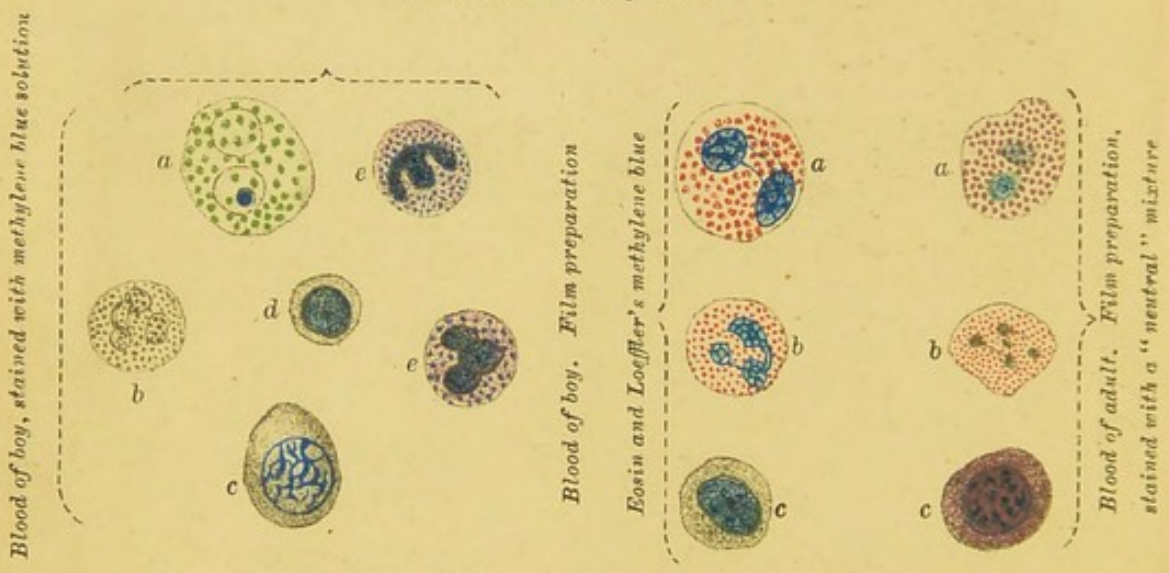
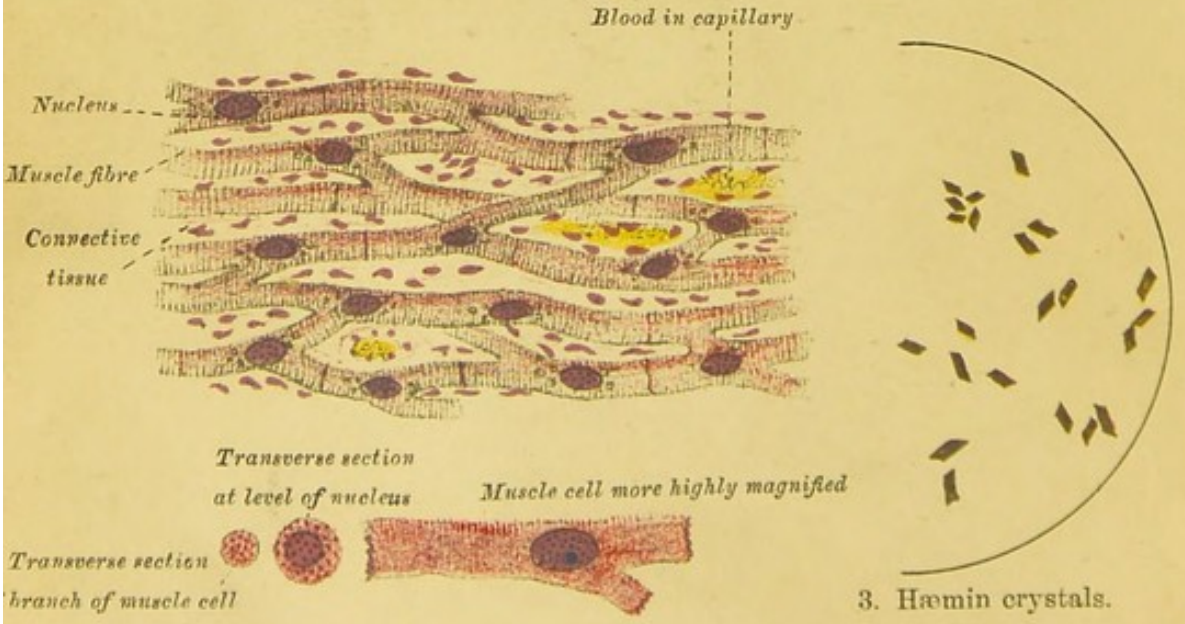
Plate I.



1. Red blood-corpuscles.



2. The colourless corpuscles of human blood, × 1000. *a*, coarsely granular oxyphile cells; *b*, finely granular oxyphile cells; *c*, hyaline cells; *d*, lymphocyte; *e*, finely granular basophile cells (Kanthack and Hardy). The magnification is much greater than in 1.



3. Hæmin crystals.

4. Section of heart, × 300. (Stained with hæmatoxylin.)

GEORGE KENNING, COLOR PRINTER.

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MED-CHIRURGICAL SOCIETY

A MANUAL OF PHYSIOLOGY.

WITH PRACTICAL EXERCISES.

BY

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SENIOR DEMONSTRATOR OF PHYSIOLOGY IN THE OWENS COLLEGE, VICTORIA UNIVERSITY,
ETC.

WITH THREE HUNDRED AND THIRTY-SIX ILLUSTRATIONS, AND FIVE COLOURED PLATES.

FOURTH EDITION.

LONDON:
BAILLIÈRE, TINDALL AND COX,
20 & 21, KING WILLIAM STREET, STRAND.
[PARIS AND MADRID.]
1900.

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602587

FROM THE PREFACE TO THE FIRST EDITION.

In this book an attempt has been made to interweave formal exposition with practical work, according to a programme which I have followed for some time past in teaching Physiology to medical students on the other side of the Atlantic, and which has, it is believed, proved to be well adapted to their needs and opportunities. It ought, however, to be explained that, for various reasons, a somewhat wider range of experiment is open to the student in America than in this country. But as nobody will use this book except in a regular laboratory and under responsible guidance, it has not been thought necessary to mark in any special manner the parts of the exercises which the English student must do by proxy (that is, learn from demonstrations), and the parts he ought to perform for himself.

An arrangement of the exercises with reference to the systematic course has this advantage—that by a little care it is possible to secure that practical work on a given subject shall actually be going on at the time it is being expounded in the lectures. Cross-reference from lecture-room to laboratory, and from laboratory to lecture-room, from the detailed discussion of the relations of a phenomenon to the living fact itself, is thus rendered easy, natural, and fruitful.

As some teachers may wish to know how a course such as that described in the Practical Exercises may be conducted for a fairly large class, a few words on the method we have

followed may not be out of place. It is obvious that many of the exercises require more than one person for their performance; and it may be said that, except in the case of the simpler experiments and the chemical work as a whole, which each student does for himself, it has been found convenient to divide the class into groups of four, each group remaining together throughout the session. It is possible that some may find a group of four too large a unit, and it is certain that three, or perhaps even two, would be better; but in a large school so minute a subdivision is hardly possible, without entailing excessive labour on the teachers.

The systematic portion of the book is so arranged that it can equally well be used independently of the practical work, and aims at being in itself a complete exposition of the subject, adapted to the requirements of the student of medicine.

I am indebted to my friend Dr. Arthur Clarkson for the coloured drawings in Plate I., 1, 3, and 4; Plate II.; Plate III., 1, Plate V., 1 and 2; and to my former pupil, Dr. Kelly, for Plates III., 4, and IV., 4.

As to the matter of the text, it is hardly necessary to say that this book does not aspire to the dubious distinction of originality; and it is literally impossible to acknowledge all the sources from which information has been derived. In many cases names have been quoted, but names no less worthy of mention have often been of necessity omitted.

G. N. STEWART.

CAMBRIDGE, *September*, 1895.

PREFACE TO THE THIRD EDITION.

THE first edition was quickly exhausted, and the second was simply a reprint. In the present edition the book has been revised, and in parts rewritten. A considerable amount of new matter has been added, especially in the Practical Exercises. These additions, however, have in part been balanced by the omission of some passages and the abridgment of others, and the bulk of the volume is only a little increased. I am indebted to my friend Dr. Arthur Clarkson for Fig. 112 and all the coloured drawings, except Plate I., 11-13, taken from a paper by Dr. Kanthack and Mr. Hardy, and Plates III., 4, and IV., 4, supplied by my former pupil, Dr. Kelly. Figs. 2, 94-98, 106, 116, 119, 120, 152, 174, 234, 264, and 277, have been borrowed from Beaunis' 'Physiologie.' Messrs. Jung and Zeiss have lent me several electrotypes of instruments.

G. N. STEWART.

CAMBRIDGE, *August* 15, 1898.

PREFACE TO THE FOURTH EDITION.

In the present edition the book has been revised, and in parts rewritten. A considerable amount of new matter has been added, especially in the chapter on The Central Nervous System. In this portion of the subject our knowledge is advancing 'by leaps and bounds,' and it is difficult to keep pace with it. If, among the many works which I have consulted, I were to single out one as that to which I am particularly indebted, it would be the admirable book of Dr. Barker. The additions in other parts of the volume have been for the most part balanced by the omission of some passages and the abridgment of others, and its bulk is only a little increased.

G. N. STEWART.

Cleveland, *August* 13, 1900.

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CHIRURGICAL

A MANUAL OF PHYSIOLOGY.

INTRODUCTION.

'Life is a power superadded to matter; organization arises from, and depends on, life, and is the condition of vital action; but life never can arise out of, or depend on, organization.'—JOHN HUNTER.

LIVING matter, whether it is studied in plants or in animals, has certain peculiarities of chemical composition and structure, but especially certain peculiarities of action or function which mark it off from the unorganized material of the dead world around it.

Chemical Composition of Living Matter.—Although we cannot analyze the living substance as such, we can to a certain, but limited, extent reconstruct it, so to speak, from its ruins. When subjected to analytical processes, which necessarily kill it, living matter invariably yields bodies of the class of *proteids*, which have approximately the following composition: Carbon, 51·5 to 54·5 per cent.; oxygen, 20·9 to 23·5 per cent.; nitrogen, 15·2 to 17 per cent.; hydrogen, 6·9 to 7·3 per cent., with small quantities of sulphur and generally of phosphorus. *Nucleo-proteids*, which are compounds of proteid with nucleins, a series of bodies very rich in phosphorus, are also constantly met with. Certain *carbo-hydrates*, composed of carbon, hydrogen, and oxygen (the last two in the proportions necessary to form water), of which glycogen ($C_6H_{10}O_5$) may be taken as a type, appear to be always present. *Fats*, which consist of carbon, hydrogen, and oxygen, and of which tristearin, a compound of stearic acid with glycerine, of the formula C_3H_5, $3(C_{18}H_{35}O_2)$, may be given as an example, are often, but perhaps not always, found. Finally, water and certain inorganic salts, such as

the chlorides and phosphates of sodium, potassium, and calcium, are constantly present.

Structure of Living Matter.—The Cell.—Protoplasm or living substance, when examined in its most primitive, undifferentiated condition in such cells as the Amœba or the white blood-corpuscles, appears a homogeneous, structureless mass, except for certain granules embedded in it, and consisting either of products formed by its activity or of food materials. But in many cells the protoplasm presents the appearance of a honeycomb or network, with granules usually situated at the nodes, and holding in its vesicles or meshes a fluid, perhaps containing pabulum, from which the waste of the living framework is made good, or material upon which it works, and which it is its business to transform. Some observers, however, maintain that the network is an artificial appearance produced by the precipitation of the colloid constituents of the protoplasm by the fixing reagent or even by the coagulative processes associated with the act of dying. However this may be, in building up our typical cell we start with a piece of protoplasm. Somewhere in the midst of this we find a body which, if not absolutely different in kind from the protoplasm of the cell, is yet marked off from it by very definite morphological and chemical characters. This is the nucleus, generally of round or oval shape, and often bounded by an envelope. Within the envelope lies a second network of fine threads, which do not themselves stain with nuclear dyes such as hæmatoxylin. But in or on these 'achromatic' filaments lie small, highly refractive particles, staining readily and deeply with dyes, and therefore described as consisting of *chromatin*. This chromatin is either made up of nucleins (substances composed of a sulphur-free organic acid, nucleic acid, combined in various proportions with proteids), or yields nucleins by its decomposition; and it seems to owe its affinity for certain staining substances to the presence of nucleic acid. When the nucleus is about to divide in the manner known as indirect division or karyokinesis, the chromatin granules arrange themselves into one or more coiled filaments or skeins. The meshes of the nuclear reticulum contain a semi-fluid material, which does not readily stain. Besides the nucleus, another much smaller structure, the centrosome, surrounded by the attraction sphere, is differentiated from the protoplasm of the cell.

When we carry back the analysis of an organized body as far as we can, we find that every organ of it is made up of cells, which upon the whole conform to the type we have been describing, although there are many differences in details. Some organisms there are, low down in the scale, whose whole activity is confined within the narrow limits of a single cell. The Amœba sets up in life as a cell split off from its parent. It divides in its turn, and each half is a complete Amœba. When we come a little higher than the

Amœba, we find organisms which consist of several cells, and 'specialization of function' begins to appear. Thus the Hydra, the 'common fresh-water Polyp' of our ponds and marshes, has an outer set of cells, the ectoderm, and an inner set, the endoderm. Through the superficial portions of the former it learns what is going on in the world; by the contraction of their deeply-placed processes it shapes its life to its environment. As we mount in the animal scale, specialization of structure and of function are found continually advancing, and the various kinds of cells are grouped together into colonies or organs.

The Functions of Living Matter.—The peculiar *functions* of living matter as exhibited in the animal body will form the subject of the main portion of this book; and we need only say here (1) that in all living organisms *certain chemical changes go on*, the sum total of which constitutes the *metabolism* of the body. These may be divided into (*a*) *integrative* or *anabolic* changes, by which complex substances (including the living matter itself) are built up from simpler materials; and (*b*) *disintegrative* or *katabolic* changes, in which complex substances (including the living substance) are broken down into comparatively simple products. In plants, upon the whole, it is integration which predominates; from substances so simple as the carbon dioxide of the air and the nitrates of the soil the plant builds up its carbo-hydrates and its proteids. In animals the main drift of the metabolic current is from the complex to the simple; no animal can construct its own protoplasm from the inorganic materials that lie around it; it must have ready-made proteid in its food. But in all plants there is some disintegration; in all animals there is some synthesis. (2) The living substance is *excitable*—that is, it responds to certain external impressions, or *stimuli*, by actions peculiar to each kind of cell. (3) The living substance *reproduces* itself. All the manifold activities included under these three heads have but one source, the transformation of the energy of the food. It is not, however, upon the whole, peculiarities in food, but in molecular structure, that underlie the peculiarities of function of different living cells. A locomotive is fed with coal; a

steam-pump is fed with coal. The one carries the mail, and the other keeps a mine from being flooded. Wherein lies the difference of action? Clearly in the build, the structure of the mechanism, which determines the manner in which energy shall be transformed within it, not in any difference in the source of the energy. So one animal cell, when it is stimulated, shortens or contracts; another, fed perhaps with the same food, selects certain constituents from the blood or lymph and passes them through its substance, changing them, it may be, on the way; and a third sets up impulses which, when transmitted to the other two, initiate the contraction or secretion. In the living body the cell is the machine; the transformation of the energy of the food is the process which 'runs' it. The structure and arrangement of cells and the steps by which energy is transformed within them sum up the whole of biology.

PRACTICAL EXERCISES.

Reactions of Proteids.

1. **General Reactions of Proteids.**—Egg-albumin may be taken as a type. Prepare a solution of it. In breaking the egg, take care that none of the yolk gets mixed with the white. Snip the white up with scissors in a large capsule, then add ten or fifteen times its volume of distilled water. The solution becomes turbid from the precipitation of traces of globulin, since globulins are insoluble in distilled water. Stir thoroughly, strain through several layers of muslin, and then filter through paper

(1) Add to a little of the solution in a test-tube a few drops of strong nitric acid. A precipitate is thrown down, which becomes yellow on boiling. Cool, and add strong ammonia; the colour changes to orange (*xantho-proteic reaction*).

(2) Acidify another portion strongly with acetic acid, and add a few drops of a solution of potassium ferrocyanide. A white precipitate is obtained. Peptones do not give this reaction.

(3) To a third portion add a drop or two of *very dilute* cupric sulphate and excess of sodium or potassium hydrate; a violet colour appears. Peptones and proteoses (albumoses) give a pink (*biuret reaction*).* See p. 378.

(4) To another portion add Millon's reagent ;† a precipitate comes

* The reaction is also given, although more faintly, with the hydrates of lithium, strontium, and barium.

† Millon's reagent consists of a mixture of the nitrates of mercury with nitric acid in excess, and some nitrous acid. To make it, dissolve mercury

down, which is turned reddish on boiling. If only traces of proteid are present, no precipitate is caused, but the liquid takes on a red tinge.

(5) Heat a portion to 30° C. on a water-bath. Saturate with crystals of ammonium sulphate; the albumin is precipitated. Filter, and test the filtrate for proteids by (3). None, or only slight traces, will be found. The sodium hydrate must be added in more than sufficient quantity to decompose all the ammonium sulphate. It will be best to add a piece of the solid hydrate. Peptones are not precipitated by ammonium sulphate, but all other proteids are.

2. **Special Reactions of Groups of Proteids**—(1) **Coagulable Proteids**: (*a*) **Native Albumins.**—(α) Heat a little of the solution of *egg-albumin* in a test-tube; it coagulates. With another sample determine the temperature of coagulation, first slightly acidulating with dilute acetic acid—a drop or two of a 2 per cent. solution.

To determine the Temperature of Coagulation.—Support a beaker by a ring which just grips it at the rim. Nearly fill the beaker with water, and slide the ring on the stand till the lower part of the beaker is immersed in a small water-bath (a tin can will do quite well). In this beaker place a test-tube, and in the test-tube a thermometer, both supported by rings or clamps attached to the same stand. Put into the test-tube at least enough of the albumin solution to completely cover the bulb of the thermometer, and heat the bath, stirring the water in the beaker occasionally with a feather, or a splinter of wood, or a glass rod, the end of which is guarded with a piece of indiarubber tubing. Note the temperature at which the solution becomes turbid, and then the temperature at which a distinct coagulum or precipitate is formed.

(β) A similar experiment may be performed with *serum-albumin.* obtained as on p. 60.

(*b*) **Globulins.**—Use *serum-globulin* (p. 60), or *myosin* (p. 602), *Fibrinogen* is also a globulin, but cannot easily be obtained in quantity. Verify the following properties of globulins:

(α) They coagulate on heating.

(β) They are insoluble in distilled water (p. 60).

(γ) They are precipitated by saturation with magnesium sulphate or sodium chloride (p. 60).

They give the general proteid tests (1) to (5).

(2) **Derived Albumins or Albuminates**—(*a*) *Acid-albumin.*—To a solution of egg-albumin add a little ·2 per cent. hydrochloric acid, and heat to about body temperature—say 40° C.—for a few minutes. Acid-albumin is formed. It can be produced from all albumins and globulins by the action of dilute acid. Make the following tests:

(α) Add to a portion of the solution in a test-tube a few drops of a solution of litmus; the colour becomes red. Now add drop by drop sodium carbonate or dilute sodium hydrate solution till the tint just begins to change to blue. A precipitate of acid-albumin is

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in its own weight of strong nitric acid, and add to the solution thus obtained twice its volume of water. Let it stand for a short time, and then decant the clear liquid, which is the reagent.

thrown down. Add a little more of the alkali, and the precipitate is redissolved. It can be again brought down by neutralizing with acid.

(β) Heat a portion of the solution to boiling; no precipitate is formed.

(γ) Add strong nitric acid; a precipitate appears, which dissolves on heating, and the liquid becomes yellow.

(*b*) *Alkali-albumin.*—To a solution of egg-albumin add a little sodium hydrate, and heat gently for a few minutes. Alkali-albumin is produced. It can also be derived by similar treatment from any albumin or globulin.

(α) Neutralize, after colouring with litmus solution, by the addition of dilute hydrochloric or acetic acid. Alkali-albumin is precipitated when neutralization has been reached. It is redissolved in excess of the acid.

(β) To another portion of the solution of alkali-albumin add a few drops of sodium phosphate solution, then litmus, and then dilute acid till the alkali-albumin is precipitated. More of the dilute acid should now be required to precipitate the alkali-albumin, since the sodium phosphate must first be changed into acid sodium phosphate.

(γ) On heating the solution of alkali-albumin there is no coagulation.

(3) **Proteoses (Albumoses).**—For preparation and reactions, see p. 377. They differ from group (1) in not being coagulated by heat, and from group (2) in not being precipitated by neutralization. They are soluble (with the exception of hetero- and dys-albumose), in distilled water, and are not precipitated by saturation of their solutions with magnesium sulphate or sodium chloride. Saturation with ammonium sulphate precipitates them. With a solution of commercial 'peptone,' which consists chiefly of albumoses, and contains only a little true peptone, perform the following tests:

(α) Boil the solution; there is no coagulation.

(β) Biuret reaction, (3) p. 20.

(γ) Add to a little of the solution a drop of strong nitric acid by means of a glass rod or small pipette; a precipitate is formed, which dissolves on heating, and reappears on cooling.

(4) **Peptones.**—For preparation and tests, see p. 378. They differ from groups (1) and (2) in the same way as albumoses, and they differ from albumoses in not being precipitated by ammonium sulphate. Saturate the solution of commercial 'peptone' with ammonium sulphate; the albumoses are precipitated. Filter; the peptones are contained in the filtrate. On it perform the biuret test, as described in (5), p. 21; and note that the pink colour is the same as that given by albumoses.

(5) **Coagulated Proteids.**—These are divided into two classes:

(*a*) Proteids coagulated by heat, such as boiled white of egg.

(*b*) Proteids whose coagulation is determined by the action of ferments. Of these, fibrin is a type. Both classes give such of the general proteid tests, (1), (3), (4), p. 20, as with suitable modifications can be instituted on solid substances. Thus, in performing (3), a flake of fibrin or a small piece of the boiled egg-white should

be soaked for a few minutes in a dilute solution of cupric sulphate. Then the excess of the cupric sulphate should be poured off, and sodium hydrate added, when the coagulated proteid will become violet. Heat-coagulated proteids are insoluble in water, weak acids and alkalies, and saline solutions, but fibrin is slightly soluble in the latter.

Carbo-hydrates.

1. **Glucose or Dextrose.**—Make a solution of dextrose in water, and apply to it **Trommer's test for reducing sugar.** Put some of the dextrose solution in a test-tube, then a few drops of cupric sulphate, and then excess of sodium or potassium hydrate. The blue precipitate of cupric hydrate which is first thrown down is immediately dissolved in the presence of dextrose and many other organic substances. Now boil the blue liquid, and a yellow or red precipitate (cuprous hydrate or oxide) is formed.

2. **Cane-sugar.**—Perform Trommer's test with a sample of a solution. A blue liquid is obtained, which is not changed on boiling. Now put the rest of the solution in a flask. Add $\frac{1}{20}$th of its bulk of strong hydrochloric acid, and boil for a quarter of an hour. Again perform Trommer's test. It shows that much reducing sugar is now present. The cane-sugar has been 'inverted,' *i.e.*, changed into a mixture of dextrose and levulose.

3. **Starch.**—(1) Cut a slice from a well-washed potato; take a scraping from it with a knife, and examine with the microscope. Note the starch granules with their concentric markings, using a small diaphragm. Run a drop of dilute iodine solution under the cover-slip, and observe that the granules become bluish. Examine also with a polarization microscope. (2) Rub up a little starch in a mortar with cold water, then add boiling water and stir thoroughly. Decant into a capsule or beaker, and boil for a few minutes. After the liquid has cooled, perform the following experiments:

(*a*) Add a few drops of iodine solution to a little of the thin starch mucilage in a test-tube. A blue colour is produced, which disappears on heating, returns on cooling, is bleached by the addition of a little sodium hydrate, and restored by dilute acid.

(*b*) Test the starch solution for reducing sugar by Trommer's test. If none is found, boil some of the mucilage with a little dilute sulphuric acid in a flask for twenty minutes, and again perform Trommer's test. Abundance of reducing sugar will now be present.

4. **Dextrin.**—Dissolve some dextrin in boiling water. Cool. Add iodine solution to a portion; a reddish-brown (port-wine) colour results, which disappears on heating and returns on cooling. The colour is also bleached by alkali, restored by acid. If too little iodine has been added there may be no restoration of the colour by the acid. The addition of a little more iodine to the acid solution will then cause the port-wine colour to return, and this may be again bleached by alkali, and will now be restored by acid.

5. **Glycogen.**—See p. 511.

Fats.

(α) Take a little lard or olive-oil, and observe that fat is soluble in ether or warm alcohol, but not in water. Put a drop of the ethereal solution of fat on a piece of paper, and note that it leaves a greasy stain.

(β) Boil a little lard with potassium hydrate in a capsule. The fat is broken up into glycerine and fatty acid, and the latter unites with the alkali to form a soap. Add a small quantity of a 20 per cent. solution of sulphuric acid, and heat. The fatty acids are set free and collect on the surface.

(γ) *Emulsification.*—Put in one watch-glass a few drops of neutral (fresh) olive-oil, and in another a few drops of a rancid oil containing fatty acids. Add a dilute solution (0·25 per cent.) of sodium carbonate to each. An emulsion will be formed in the second watch-glass, but not in the first. Examine it under the microscope, and note the globules of oil of various sizes.

Or the watch-glasses may first be filled with the sodium carbonate solution, and a drop of fresh oil then placed on the surface of the solution in one and of rancid oil in the other, by means of a small pipette. A creamy white ring will soon spread out from the rancid oil, and cover the sodium carbonate solution.

SCHEME FOR TESTING A SOLUTION FOR THE MORE COMMON PROTEIDS AND CARBO-HYDRATES.

1. Note the reaction, and whether the liquid is coloured or colourless, clear or opalescent. A reddish colour suggests **blood**; opalescence suggests **glycogen** or **starch**. Try one or more of the general proteid tests (*e.g.*, the xantho-proteic or biuret). If the result is positive, proceed as in 2; if negative, pass to 3.

2. **Test for Proteids.**—(1) If the reaction is acid or alkaline, neutralize with very dilute sodium carbonate or sulphuric acid. A precipitate = **acid- or alkali-albumin**, according as the original reaction is acid or alkaline. If the original reaction is neutral, no acid- or alkali-albumin can be present in solution. Filter off the precipitate, if any.

(2) Boil some of the filtrate from (1) (or of the original solution if it is neutral), acidulating slightly with dilute acetic acid. A precipitate = **albumin** or **globulin**. Filter, and keep the filtrate.

(3) If a precipitate has been obtained in (2), (*a*) saturate some of the original solution with magnesium sulphate, or half saturate it with ammonium sulphate (*i.e.*, add to it an equal volume of saturated ammonium sulphate solution). If there is no precipitate, **globulin** is absent, and therefore the precipitate obtained in (2) must be **albumin**. A precipitate = **globulin**. But albumin may also be present in the solution. To see whether this is so, filter off the globulin and boil the filtrate after acidulation with acetic acid. A precipitate = **albumin.**

(*b*) Keep a small portion of the filtrate. Saturate the rest of the filtrate from (2) with ammonium sulphate. A precipitate = **proteose.** Filter from (2) for (*d*).

(*c*) To the filtrate from (*b*) add excess of solid sodium hydrate in small pieces at a time. Much ammonia is given off. Allow the test-tube to stand fifteen minutes, shaking it at intervals. Then add dilute cupric sulphate, and if much of the sodium sulphate formed remains undissolved, add water to dissolve it. A well-marked rose colour = **peptone.**

(*d*) If proteoses have been indicated by (*b*), confirm by adding to the filtrate from (2) strong nitric acid. A precipitate which disappears on heating and reappears on cooling = **proteose.** But one of the members of the proteose group, deutero-albumose, is not precipitated till sodium chloride is added as well as nitric acid. This reaction will not detect small quantities of proteose.

(4) If no precipitate has been obtained in (2), the solution contains neither albumin nor globulin. To test whether proteose or peptone is present apply (3) (*b*), (*c*), and (*d*).

3. **Test for Carbo-hydrates.**—Use the original solution, freed from coagulable proteids, if such have been found, by acidulation and boiling.

(1) Add iodine. If the solution is alkaline neutralize it before adding the iodine. *A blue colour* = **starch.** Confirm by boiling with dilute sulphuric acid and testing for reducing sugar. *A reddish-brown colour* = **glycogen or dextrin.**

Glycogen gives an opalescent, dextrin a clear, solution. Glycogen is precipitated by basic lead acetate, dextrin is not. Both are changed into reducing sugar by boiling with dilute acid.

(2) Add to some of the original solution cupric sulphate and excess of sodium hydrate, and boil. Yellow or red precipitate = **reducing sugar.**

(3) If (1) and (2) are negative, boil some of the liquid with one-twentieth of its volume of strong hydrochloric acid for fifteen minutes, and test as in (2). A red or yellow precipitate shows that cane-sugar was originally present, and has been inverted.

CHAPTER I.

THE CIRCULATING LIQUIDS OF THE BODY.

In the living cells of the animal body chemical changes are constantly going on; energy, on the whole, is running down; complex substances are being broken up into simpler combinations. So long as life lasts, food must be brought to the tissues, and waste products carried away from them. In lowly forms like the amœba, these functions are performed by interchange at the surface of the animal without any special mechanism; but in all complex organisms they are the business of special liquids, which circulate in finely branching channels, and are brought into close relation at various parts of their course with absorbing organs, with eliminating organs, and with the tissue elements in general.

In the higher animals three circulating liquids have been distinguished: blood, lymph, and chyle. But it is to be remarked that chyle is only lymph derived from the walls of the alimentary canal, and therefore, during digestion, containing certain freshly-absorbed constituents of the food; while both ordinary lymph and chyle ultimately find their way into the blood, and are in their turn recruited from it. The blood contains at one time or another everything which is about to become part of the tissues, and everything which has ceased to belong to them. It is at once the scavenger and the food-provider of the cell. But no bloodvessel enters any cell; and if we could unravel the complex mass of tissue elements which essentially constitute what we call an organ, we should see a sheet of cells, with capillaries in very close relation to them, but everywhere

separated from them by a thin layer of lymph. And to describe in a word the circulation of the food substances, we may say *that the blood feeds the lymph, and the lymph feeds the cell.*

Morphology of the Blood.

The blood consists essentially of a liquid part, the plasma, in which are suspended cellular elements, the corpuscles. When the circulation in a frog's web or lung or in the tail of a tadpole is examined under the microscope, the blood-vessels are seen to be crowded with oval bodies—of a yellowish tinge in a thin layer, but in thick layers crimson—which move with varying velocity, now in single file, now jostling each other two or three abreast, as they are borne along in the axis of an apparently scanty stream of transparent liquid. Nearer the walls of the vessels, sometimes clinging to them for a little and then being washed away again, may be seen, especially as the blood-flow slackens, a few comparatively small, round, colourless cells. The oval bodies are the red or coloured corpuscles; the colourless elements are the white blood-corpuscles or leucocytes; the liquid in which they float is the plasma ('Practical Exercises,' p. 168).

The Red Blood-corpuscles differ in shape and size and in other respects in different animal groups. In amphibians, such as the frog and the newt, they are flattened ellipsoids containing a nucleus, and the same is true of nearly all the other vertebrates, except mammals. In mammals they are discs, hollowed out on both the flat surfaces, or biconcave, and possess no nucleus. But the red corpuscles of the llama and the camel, although non-nucleated, are ellipsoidal in shape like those of the lower vertebrates. As to size, the average diameter in man is between 7 and 8 μ.* In the frog the long diameter is about 22 μ, while in Proteus it is as much as 60 μ, and in Amphiuma, the corpuscles of which can be seen with the naked eye, nearly 80 μ (Plate I., 1).

As regards the structure of the red corpuscles the most probable view is that they are solid bodies, with a spongy and elastic structureless framework, denser at the surface of

* A micro-millimetre, represented by symbol μ, is $\frac{1}{1000}$ millimetre.

the corpuscle than in its centre, but continuous throughout its whole mass (Rollett). The denser peripheral layer constitutes a physiological envelope which permits the passage of certain substances into or out of the corpuscles, and hinders the passage of others.

Envelope and spongework are sometimes spoken of as the stroma of the corpuscle, in contradistinction to its most important constituent, a highly complex pigment, the hæmoglobin, which, not in solution as such, but either in solution as a compound with some other unknown substance, or bound in some solid or semi-solid combination to the stroma, fills up the whole space within the envelope and all the interstices of the spongework. To the physical properties of the stroma it is usual to attribute the great elasticity of the corpuscles—that is, the power of recovering

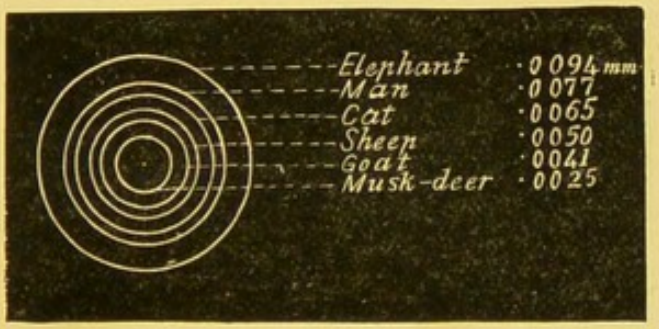


FIG. 1.—DIAGRAM SHOWING RELATIVE SIZE OF RED CORPUSCLES OF VARIOUS ANIMALS.

their original shape after distortion—for their elasticity is no wise impaired by the removal of the hæmoglobin.

When blood with disc-shaped corpuscles is shed, there is a great tendency for the corpuscles to run together into groups resembling *rouleaux*, or piles of coin. No satisfactory explanation of this curious fact has yet been given.

Crenation of the corpuscles, a condition in which they become studded with fine projections, is caused by the addition of moderately strong salt solution, by the passage of shocks of electricity at high potential, as from a Leyden jar, by simple exposure to the air, and in poisoning with Calabar bean. Concentrated saline solutions, which abstract water from the corpuscles and cause them to shrink, make the colour of blood a brighter red, because more light is now reflected from the crumpled surfaces. On the other

hand, the addition of water renders the corpuscles spherical; more of the light passes through them, less is reflected, and the colour becomes dark crimson (Plate I.).

The White Blood-corpuscles, or Leucocytes.—The red corpuscles are peculiar to blood. The white corpuscles may be looked upon as peripatetic portions of the mesoblast (see Chap. XIV.), and some of them ought not in strictness to be called blood-corpuscles. They are more truly **body**-corpuscles. Similar cells are found in many situations, and wander everywhere in the spaces of the connective tissue. They pass into the bloodvessels with the lymph, and may pass out of them again in virtue of their amœboid power. They consist of undifferentiated living substance or 'proto-

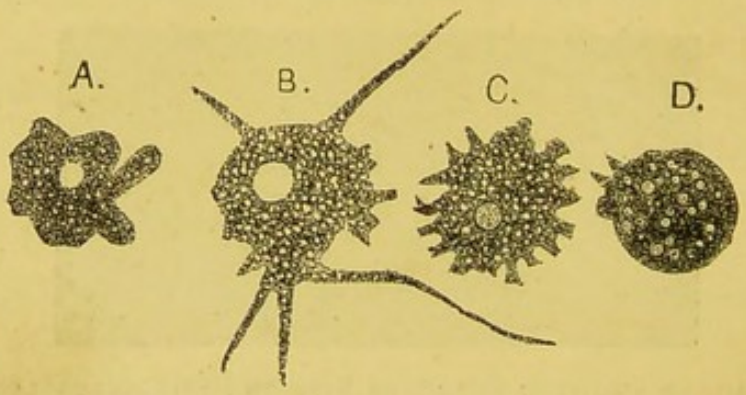


FIG. 2.—AMŒBOID MOVEMENT.
A, B, C, D, successive changes in the form of an amœba.

plasm,' and under the microscope appear as granular, colourless, transparent bodies, spherical in form when at rest, and containing a nucleus, often tri- or multi-lobed. Many of the leucocytes of frog's blood at the ordinary temperature, and of mammalian blood when artificially heated on the warm stage, may be seen to undergo slow changes of form. Processes called pseudopodia are pushed out at one portion of the surface, retracted at another, and thus the corpuscle gradually moves or 'flows' from place to place, and envelops or eats up substances, such as grains of carmine, which come in its way. This kind of motion was first observed in the amœba, and is therefore called amœboid. The leucocytes of human blood are not all of the same size,

and differ also in other respects. They may be classified (1) according to the presence or absence of granules in their protoplasm, and the fineness or coarseness of the granules; (2) according to the chemical nature of the dyes with which the granules stain. The most important recent work on this subject is that of Kanthack and Hardy. They find that Ehrlich's 'neutrophile' cells are in reality oxyphile —that is, their granules do not stain with neutral dyes, such as fuchsin or methyl green, but do stain with acid dyes like eosin (Plate I., 2). They classify the wandering cells of the blood into five varieties, as follows:

Oxyphile (granules staining with eosin).	(1) Coarsely granular (eosinophile cell of Ehrlich) -	10-11 μ in diam.
	(2) Finely granular (neutrophile and amphophile cells of Ehrlich) - - -	8-9 μ "
Basophile (granules staining with methylene blue).	(3) Finely granular (tri-lobed nucleus) - - - -	7 μ "
	(4) Hyaline cells, free from granules (one nucleus, generally spherical) - -	8·5-10 μ "
	(5) Lymphocytes, possessing a single large nucleus with comparatively little protoplasm around it - -	6 μ "

In human blood the finely granular oxyphile cells make up 60 to 80 per cent. of the whole number of leucocytes, the lymphocytes (and hyaline cells) 20 to 30 per cent., and the coarsely granular oxyphile cells less than 5 per cent.; but these proportions are far from being constant.

Blood-plates.—When blood is examined immediately after being shed, small colourless bodies (0·5 to 5 μ in diameter) of various shapes—sometimes flat and of nearly circular outline, sometimes irregular—may be seen. These are the blood-plates or platelets. They can be best studied when the blood is run directly into some fixing solution.* Their significance is unknown; but they are not produced by the breaking up of other elements of the shed blood, for they have been observed within the freshly excised and therefore still living capillaries—in the mesentery of the guinea-pig and rat (Osler).

* Such as Hayem's solution (sodium chloride, 1 grm.; sodium sulphate, 5 grm.; mercuric chloride, 0·5 grm.; water, 200 grm.).

Enumeration of the Blood-corpuscles.—This is done by taking a measured quantity of blood, diluting it to a known extent with a liquid which does not destroy the corpuscles, and counting the number in a given volume of the diluted blood (p. 61).

The average number of red corpuscles in a cubic millimetre of blood is about 5,000,000 in a healthy man, and about 4,500,000 in a healthy woman, but a variation of 1,000,000 up or down can hardly be considered abnormal. In persons suffering from profound anæmia the number may sink to 1,000,000 per cubic millimetre, or even less, while in new-born children and in the inhabitants of high plateaus or mountains it may rise to 8,000,000, or even more. In the latter instance a residence of a fortnight in

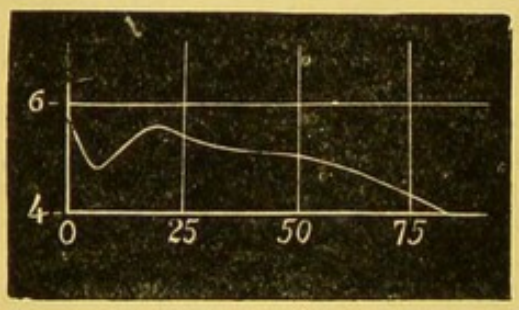


FIG. 3.—CURVE SHOWING THE NUMBER OF RED CORPUSCLES AT DIFFERENT AGES (AFTER SÖRENSEN'S ESTIMATIONS).

The figures along the horizontal axis are years of age, those along the vertical axis millions of corpuscles per cub. mm. of blood.

the rarefied air is sufficient to bring about the increase, and a subsequent residence of a fortnight in the lowlands to annul it.*

The number of white blood-corpuscles is on the average about 10,000 per cubic millimetre of blood, or one leucocyte for every 500 red blood-corpuscles. In leukæmia the number of white corpuscles is enormously increased—it may be in extreme cases to 500,000 per cubic millimetre—while at the same time the number of the red corpuscles is diminished; and the ratio of white to red may approach 1 : 4. An increase has also been observed in certain infective diseases as part of the inflammatory reaction. There are also physiological variations, even within short periods of time; for example, the number of lymphocytes is in-

* In 113 apparently healthy students (male) the average number of red corpuscles was 5,190,000 per cubic millimetre. In 104 of these, the number ranged from 4,000,000 to 6,400,000; in 71 (or 63 per cent. of the whole), from 4,400,000 to 5,500,000; in 3, from 3,500,000 to 3,900,000; in 5, from 6,500,000 to 7,000,000. In one observation the number reached 7,300,000.

creased when digestion is going on. The number of blood-plates is about 300,000 to the cubic millimetre of blood.

Life-history of the Corpuscles.—The corpuscles of the blood, like the body itself, fulfil the allotted round of life, and then die. They arise, perform their functions for a time, and disappear. But although the place and mode of their origin, the seat of their destruction or decay, and the average length of their life, have been the subject of active research and still more active discussion for many years, much yet remains unsettled.

In the embryo the red corpuscles, even of those forms (mammals) which have non-nucleated corpuscles in adult life, are at first possessed of nuclei. In the human fœtus, at the fourth week all the red corpuscles are nucleated.

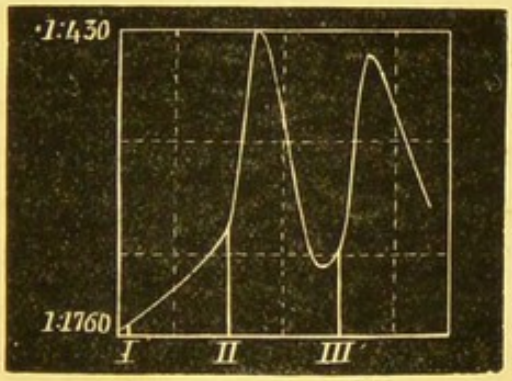


FIG. 4.—CURVE SHOWING PROPORTION OF WHITE CORPUSCLES TO RED AT DIFFERENT TIMES OF THE DAY (AFTER THE RESULTS OF HIRT).

At I the morning meal was taken; at II the mid-day meal; at III the evening meal. During active digestion the number of lymphocytes in the blood is greatly increased, both absolutely and relatively to the number of the other leucocytes.

Later on the nucleated corpuscles gradually diminish in number, and at birth they have almost or altogether disappeared, some of them, at least, having been converted by a shrivelling of the nucleus into the ordinary non-nucleated form. In the newly-born rat, which comes into the world in a comparatively immature state, many of the red corpuscles may be seen to be still nucleated. The first corpuscles formed in embryonic life are developed outside of the embryo altogether (in the guinea-pig). Even before the heart has as yet begun to beat, certain cells of the mesoblast (see Chap. XIV.) in a zone ('vascular area') around the growing embryo begin to sprout into long, anastomosing processes, which afterwards become hollowed out to form

capillary bloodvessels. At the same time clumps of nuclei, formed by division of the original nuclei of the cells, gather at the nodes of the network. Around each nucleus clings a little lump of protoplasm, which soon develops hæmoglobin in its substance; and the new-made corpuscles float away within the new-made vessels. In later embryonic life the nucleated corpuscles seem in part to be developed in the liver, spleen, red bone-marrow, and the blood itself by division of previously existing nucleated corpuscles, in part to be formed endogenously within special cells in the liver, spleen, and perhaps the lymphatic glands.

In the mammal in extra-uterine life the chief seat of formation of the red blood-corpuscles seems to be the red marrow of the bones of the skull and trunk, and of the ends of the long bones of the limbs. For a short time, however, after birth the formation of non-nucleated corpuscles may still go on in other situations, as in certain cells in the omentum of the rabbit (Ranvier), and in the subcutaneous connective-tissue corpuscles (Schäfer); while at any time the spleen (Bizzozero and Salvioli) in dogs and guinea-pigs, and probably other organs, may in emergency—for instance, when the number of blood-corpuscles has been seriously diminished by hæmorrhage—take on a blood-forming function. In the red marrow special nucleated, feebly amœboid cells, originally colourless or nearly so, multiply by karyokinesis or indirect division, and are transformed by various stages into the ordinary non-nucleated red corpuscles, which are washed away in the blood-stream. These blood-forming cells have received the name of erythroblasts or hæmatoblasts.

A constant destruction of red blood-corpuscles must go on, for the bile-pigment and the pigments of the urine are derived from blood-pigment. The bile-pigment is formed in the liver. It contains no iron; but the liver-cells are rich in iron, and on treatment with hydrochloric acid and potassium ferrocyanide, a section of liver is coloured by Prussian blue. Iron must, therefore, be removed by the liver from the blood-pigment or from one of its derivatives; and there is other evidence that the liver is one of the places

in which red corpuscles are actually destroyed.* Destruction of the corpuscles also seems to take place in the spleen and bone-marrow. Although the statement that free blood-pigment exists in the plasma of the splenic vein is incorrect, red corpuscles have been seen in various stages of decomposition within large amœboid cells in the splenic pulp; and deposits containing iron have been found there and in the red bone-marrow in certain pathological conditions. It is not unlikely that the coloured corpuscles may break up also in other localities, and even to some extent in the blood itself.

The lymphocytes are undoubtedly, the coarsely granular oxyphile cells probably, and the hyaline cells possibly, derived from the lymph. The lymphocytes are probably identical with the small lymph-corpuscles, and have little, if any, power of amœboid movement. They are formed largely in the lymphatic glands, for the lymph coming to the glands is much poorer in corpuscles than that which leaves them. The lymphatic glands, however, are not the only seat of formation of leucocytes, for lymph contains some corpuscles before it has passed through any gland; and although a certain number of these may have found their way by diapedesis from the blood, others are formed in the diffuse adenoid tissue, or in special collections of it, such as the tonsils, the Peyer's patches and solitary follicles of the intestine, and the splenic corpuscles. To a very small extent white blood-corpuscles may multiply by karyokinesis in the blood.

The fate of the leucocytes is even less known than that of the red corpuscles, for they contain no characteristic substance, like the blood-pigment, by which their destruction may be traced. That they are constantly breaking down is certain, for they are constantly being produced. But we do not know whether, under normal conditions, this process takes place exclusively in the blood-plasma or in particular organs or tissues.

* Although it cannot be doubted that in all animals whose blood contains hæmoglobin the iron found in the liver bears an important relation to the building up or breaking down of the blood-pigment, the injection of hæmoglobin or hæmin, indeed, increasing markedly the amount of iron in the liver, as well as in the spleen, bone-marrow and other tissues, this does not seem to be the only function of the hepatic iron, for the liver of the crayfish and the lobster, which have colourless blood, is rich in iron.

Physical and Chemical Properties of the Blood.

Fresh blood varies in colour, from scarlet in the arteries to purple-red in the veins. It is a somewhat viscid liquid, with a saline taste and a peculiar odour. Its **reaction** is alkaline to litmus-paper, chiefly owing to the presence of di-sodium phosphate (Na_2HPO_4) and sodium carbonate. The alkalinity is not constant; it is increased during digestion, when the acid of the gastric juice is being formed; it is lowest in the morning, and highest in the afternoon. It is diminished by muscular exertion, owing to the formation of lactic acid; and since acid substances seem to be produced in all active tissues, the alkalinity of venous is less than that of arterial blood. In herbivorous animals the alkalinity of the blood is easily lessened by the administration of acids, but in carnivora and in man it is much more difficult to bring about such a change, the acid being neutralized by ammonia, which is split off from the proteids. In many diseases, however, and particularly in those accompanied by fever, this protective mechanism breaks down, the alkalinity of the blood becomes seriously reduced, or even, as has sometimes been observed in diabetic coma, gives place to an acid reaction. Chloroform appears to cause a diminution in the alkalinity of the blood, and acute alcoholic intoxication has a similar effect, owing to the production of volatile fatty acids. It is possible that the use of ammonia after a drinking bout for the bracing effect attributed to it by experienced topers may be explained by its power of neutralizing these acid products. The average alkalinity of human blood, as estimated by titration with a standard acid after the corpuscles have been broken up, is that of a ·4 per cent. solution of sodium hydrate (Loewy).

The average **specific gravity** of blood is about 1066 at birth. It falls during infancy to about 1050 in the third year, then rises till puberty is reached to about 1058 in males (at the seventeenth year), and 1055 in females (at the fourteenth year). It remains at this level during middle life in males, but falls somewhat in females. In chlorotic

anæmia of young women it may be as low as 1030 or 1035. It rises in starvation. Sleep and regular exercise increase it (Lloyd Jones).* The specific gravity of the serum or plasma varies from 1026 to 1032.

The Electrical Conductivity of Blood.—The liquid portion of the blood conducts the current entirely by means of the electrolytes dissolved in it, the most important of these being the inorganic salts; and the conductivity of the serum varies, in different specimens of blood, within a comparatively narrow range. The conductivity of entire (defibrinated) blood, on the contrary, varies within wide limits; and the most influential factor which governs this variation is the number of the corpuscles suspended in it. When the blood is relatively rich in corpuscles and poor in serum, its conductivity is low; when it is poor in corpuscles and rich in serum, its conductivity is high. The explanation is that the envelope of the corpuscle refuses passage to the dissociated molecules (the ions), which, in virtue of their electrical charges, render a liquid like blood a conductor (p. 362), or permits them only to pass very slowly, so that the intact red corpuscles have an electrical conductivity so many times less than that of serum, that they may, in comparison, be looked upon as non-conductors.

The Relative Volume of Corpuscles and Plasma in Unclotted Blood, or, what can be converted into this by a small correction, the relative volume of corpuscles and serum in defibrinated blood, can be easily determined, with approximate accuracy, by comparing the electrical conductivity of entire blood with that of its serum.† Another simple method is to centrifugalize a small quantity of blood, after mixing it with a known amount of a $2\frac{1}{2}$ per cent. solution of potassium bichromate, in a glass tube of narrow bore (hæmatocrite) until the corpuscles have been collected into a solid 'thread' at the outer extremity of the tube. Their volume and that of the clear liquid which has been separated from them are then read off on an adjacent scale. By these and other methods too elaborate for description here, it has been shown that the plasma or serum usually makes up rather less than two-thirds, and the corpuscles rather more than one-third, of the blood. But this proportion is, of course, liable to the same variations as the number of corpuscles in a cubic millimetre of blood. It depends, further, the number of corpuscles being

* In 165 students (male) the average specific gravity of the blood, as determined by Hammerschlag's method (p. 57) was 1054·4. In 149 of these the variation was from 1050 to 1065; in 94 (or 57 per cent. of the whole), from 1054 to 1060; in 4, from 1046 to 1049; in 9, from 1066 to 1070. In 3 the specific gravity was only 1040 to 1042.

† The formula $p = \frac{\lambda(b)}{\lambda(s)}(174 - \lambda(b))$, where p is the number of c.c. of serum in 100 c.c. of blood; $\lambda(b)$, $\lambda(s)$, the conductivity respectively of the blood and serum (both measured at or reduced to 5° C., and expressed in reciprocal ohms multiplied by 10^8), may be used in the calculation.

given, on the average volume of each corpuscle. For instance, when the molecular concentration, and therefore the osmotic pressure (p. 360), of the plasma is reduced, as by the addition of water or the abstraction of salts, water passes into the corpuscles and they swell; when the molecular concentration of the plasma is increased, by the abstraction of water or the addition of salts, water passes out of the corpuscles, and they shrink.

Laking of Blood.—Even in thin layers blood is opaque, owing to reflection of the light by the red corpuscles. It becomes transparent or 'laky' when by any means the pigment is brought out of the corpuscles and goes into true solution. Repeated freezing and thawing of the blood, the addition of water, the passage of electrical currents, constant and induced,* putrefaction, heating the blood to 60° C., and many chemical agents (as bile-salts, ether, saponin), cause this change. The blood-serum of certain animals breaks up the coloured corpuscles of others, and sets free their pigment—for example, the serum of the dog destroys the corpuscles of the rabbit.

Since changes begin in the blood as soon as it is shed, having for their outcome clotting or coagulation, we have to gather from the composition of the stable factors of clotted blood, or of blood which has been artificially prevented from clotting, some notion of the composition of the unaltered fluid as it circulates within the vessels. The first step, therefore, in the study of the chemistry of blood is the study of coagulation.

Coagulation of the Blood.—When blood is shed, its viscidity soon begins to increase, and after an interval, varying with the kind of blood, the temperature of the air, and other conditions, but in man seldom exceeding ten, or falling below three, minutes, it sets into a firm jelly. This jelly gradually shrinks and squeezes out a straw-coloured liquid, the serum. Under the microscope the serum is seen to contain few or no red corpuscles; these are nearly all in the clot, entangled in the meshes of a kind of network of fine fibrils composed of fibrin. In uncoagulated blood no such fibrils are present; they have accordingly been formed by a change in some constituent or constituents of the normal blood. Now, it has been shown that there exists in the plasma—the liquid portion of unclotted blood—a substance from which fibrin can be derived, while no such substance is present in the corpuscles. In various ways coagulation can be prevented or delayed, and the plasma separated from

* Hermann has shown that the laking action of induced currents is due simply to the heating of the blood.

the corpuscles. For example, the blood of the horse clots very slowly, and a low temperature lessens the rapidity of coagulation of every kind of blood. If horse's blood is run into a vessel surrounded by ice and allowed to stand, the corpuscles, being of greater specific gravity than the plasma, gradually sink to the bottom, and the clear straw-yellow plasma can be pipetted off. Or, again, the addition of neutral salts to blood may be used to delay coagulation, the blood being run direct from the animal into, say, a third of its volume of saturated magnesium sulphate solution. The plasma may then be conveniently separated from the corpuscles by means of a centrifugal machine. Again, two ligatures may be placed on a large bloodvessel, so that a portion of it can be excised full of blood and suspended vertically; coagulation is long delayed, and the corpuscles sink to the lower end. In these and many other ways plasma free from corpuscles can be got; and it is found that when the conditions which restrain coagulation are removed—when, for instance, the temperature of the horse's plasma is allowed to rise, or the magnesium sulphate plasma is diluted with several times its bulk of water—clotting takes place, with formation of fibrin in all respects similar to that of ordinary blood-clot. The corpuscles themselves cannot form a clot. From this we conclude that the essential process in coagulation of the blood is the formation of fibrin from some constituent of the plasma, and that the presence of corpuscles in ordinary blood-clot is accidental. In accordance with this conclusion, we find that lymph entirely free from red corpuscles clots spontaneously, with formation of fibrin; and when fibrin is removed from newly-shed blood by whipping it with a bundle of twigs or a piece of wood, it will no longer coagulate, although all the corpuscles are still there.

What, now, is the substance in the plasma which is changed into fibrin when blood coagulates? If plasma, obtained in any of the ways described above, be saturated with sodium chloride, a precipitate is thrown down. The filtrate separated from this precipitate does not coagulate on dilution with water; but the precipitate itself—the so-

called **plasmine** of Denis—on being dissolved in a little water, does form a clot. Fibrin is therefore derived from something in this precipitate. Now, 'plasmine' contains two proteid bodies—**fibrinogen**, which coagulates by heat at about 56° C., and **serum-globulin**, which coagulates at about 75° C., and it was at one time believed that both of these entered into the formation of fibrin (Schmidt). Hammersten, however, has shown that fibrinogen alone is a precursor of fibrin; pure serum-globulin neither helps nor hinders its formation. This observer isolated fibrinogen from blood-plasma by adding sodium chloride till about 13 per cent. was present. With this amount the fibrinogen is precipitated, while serum-globulin is not precipitated till 20 per cent. of salt is reached. After precipitation of the fibrinogen the plasma no longer coagulates; and a solution of pure fibrinogen can be made to clot and to form fibrin, while a solution of serum-globulin cannot. Blood-serum, too, which contains abundance of serum-globulin, but no fibrinogen, will not coagulate.

So far, then, we have reached the conclusion that *fibrin is formed by a change in a substance, fibrinogen*, which can be obtained by certain methods from blood-plasma. It may be added that there is evidence that fibrinogen exists as such in the circulating blood; for if unclotted blood be suddenly heated to about 56°, the temperature of heat-coagulation of fibrinogen, the blood loses its power of clotting. Since fibrinogen is readily soluble in dilute saline solutions and fibrin only soluble with great difficulty, we may say that in coagulation of the blood a substance soluble in the plasma passes into an insoluble form. But this is not a mere physical change, for it seems to be initiated by a splitting up of the fibrinogen into two proteid bodies—thrombosin and fibrinoglobulin—only the former of which is transformed into fibrin, while the latter remains in solution.

How is this change determined when blood is shed? We have said that a solution of pure fibrinogen can be made to coagulate, but it does not coagulate of itself. The addition of another substance in extremely minute quantity is necessary. This other substance is **fibrin ferment**, which can be

obtained by precipitating blood-serum, or defibrinated blood, with fifteen to twenty times its bulk of alcohol, letting the whole stand for a month or more, and then extracting the precipitate with water (Schmidt). All the ordinary proteids of the blood having been rendered insoluble by the alcohol, the fibrin-ferment passes into solution in the water, and the addition of a trace of the extract to a solution of fibrinogen causes coagulation. The active substance itself does not seem to be used up in the process, nor to enter bodily into the fibrin formed; a small quantity of it can cause an indefinitely large amount of fibrinogen to clot; its power is abolished by boiling. For these reasons it is considered to be a ferment.

This action of the fibrin-ferment on fibrinogen helps to

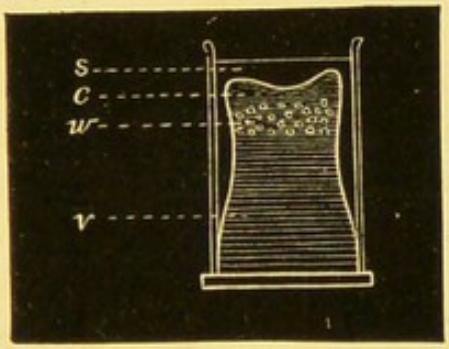


FIG. 5.—DIAGRAM OF CLOT WITH BUFFY COAT.

v, Lower portion of clot with red corpuscles; *w*, white corpuscles in upper layer of clot; *c*, cupped upper surface of clot; *s*, serum.

explain many experiments in coagulation. Thus, transudations like hydrocele fluid do not clot spontaneously, although they contain fibrinogen, which can be precipitated from them by a stream of carbon dioxide or by sodium chloride. But the addition of a little fibrin-ferment causes hydrocele fluid to coagulate. So does the addition of serum, not because of the serum-globulin which it contains, as was once believed, but because of the fibrin-ferment in it. The addition of blood-clot, either before or after the corpuscles have been washed away, or of serum-globulin obtained from serum, also causes coagulation of hydrocele fluid, and for a similar reason, the fibrin-ferment having a tendency to cling to everything derived from a liquid containing it. On the other hand, serum, which does not of itself clot, although

fibrin-ferment is present in it, because the fibrinogen has all been changed into fibrin during coagulation of the blood, can be made to coagulate by the addition of hydrocele fluid, which contains fibrinogen. We have thus arrived a step farther in our attempt to explain the coagulation of the blood: *it is essentially due to the formation of fibrin from the fibrinogen of the plasma under the influence of fibrin-ferment.*

What is the nature of the fibrin-ferment, and what is its source? There seems good reason for believing that it has very close relations with a substance or substances belonging to the group of nucleo-proteids, for nucleo-proteid can be obtained from solutions of fibrin-ferment, and, by appropriate treatment and in the presence of proper conditions, solutions of nucleo-proteid can either be made to yield fibrin-ferment or to develop that influence on coagulation which is the characteristic test by which we recognise it. Nucleo-proteids are contained in the nuclei and protoplasm of cells, and have been prepared from the thymus, testis, kidney, lymphatic glands, and other organs, by precipitating their watery extracts with dilute acetic acid (Wooldridge), or by extracting with sodium chloride and then precipitating with excess of water (Halliburton). The precipitated nucleo-proteid can be dissolved in dilute sodium carbonate solution. When it is injected slowly or in small amount into the veins of an animal, it abolishes for a time the power of coagulation of the blood; and when this 'negative phase,' as it is called, has been once established, even a very large and rapid injection produces no further effect. If, however, a considerable quantity of the solution has been injected at the first, the result is very different: extensive intravascular clotting instantly ensues; the animal dies in a few minutes; and the right side of the heart, the venæ cavæ, the portal vein, and perhaps the pulmonary arteries, may be found choked with thrombi. Curiously enough, no such effects are produced in albino rabbits or in Norway hares in their albino condition (Pickering). A solution of fibrin-ferment prepared by Schmidt's method behaves, when injected into the blood-stream, like a weak solution of nucleo-proteid, readily producing the negative phase, but causing

with difficulty intravascular coagulation. On the other hand, while fibrin-ferment favours, in a high degree, the clotting of blood-plasma after it has been shed, nucleo-proteid is a much less efficient coagulant outside than inside the vessels. There are other facts, to which we shall immediately refer, which show that fibrin-ferment is not precisely identical with nucleo-proteid, although it is derived from it.

Our discussion of the nature and relationships of the fibrin-ferment throws light upon its source. It exists only in small amount in the circulating blood; for when blood is received into alcohol direct from an artery, but little ferment is found in it. In shed and clotting blood the only possible sources of nucleo-proteid, so far as we know, are the corpuscles and the blood-plates. The red corpuscles we may at once dismiss, for although they contain a small amount of nucleo-proteid, not only do they remain intact under ordinary circumstances during coagulation, but there is the strongest evidence, as has already been pointed out, that they do not make any essential contribution to the process. We have left over the leucocytes and the platelets. The latter are said, and the former are known, to yield nucleo-proteids when they are broken up in the laboratory; and it is highly probable that from both, but especially from the white corpuscles, nucleo-proteid is liberated in the first moments after blood is shed, and that this nucleo-proteid is then changed into actual fibrin-ferment. This surmise is strengthened by the fact that in freshly-shed blood destruction of leucocytes and blood-plates takes place; and Hardy has shown that the blood of the crayfish, which coagulates with extreme rapidity, contains certain colourless corpuscles which, immediately it is shed, break up with explosive suddenness, and that substances which hinder the breaking up of these corpuscles restrain coagulation. Further, the white layer or 'buffy coat' which tops the tardily-formed clot of horse's blood (Fig. 5), and consists of the lighter, and therefore more slowly sinking, white corpuscles, causes clotting in otherwise incoagulable liquids like hydrocele fluid, much more

readily than the red portion of the clot, and yields far more fibrin-ferment on treatment with alcohol.

But when we have traced the fibrin-ferment to the nucleo-proteid of the leucocytes, and the fibrinogen to the plasma, and have seen that the interaction of the two causes, first a splitting up of the fibrinogen, and then the formation of fibrin from its thrombosin constituent, we have not yet got to the bottom of coagulation. We have still to ask what it is that happens to the inert nucleo-proteid in the first moments after the blood has been shed and converts it into active fibrin-ferment. The researches of late years have shown that a third factor is involved: *calcium is present in some form or other wherever coagulation occurs.* The following facts illustrate the *rôle* of the calcium: A solution of fibrinogen free from calcium will not coagulate on the addition of calcium-free nucleo-proteid, but will coagulate if a soluble calcium salt be also added. The addition of a soluble oxalate to blood (·2 or ·3 per cent. potassium oxalate) prevents coagulation by precipitating the calcium as insoluble calcium oxalate. From plasma prepared in this way a nucleo-proteid may be separated which contains little or no calcium and does not cause coagulation, but which on treatment with a calcium salt acquires the properties of fibrin-ferment. The same is true of the nucleo-proteid which can be extracted from so many organs by Wooldridge's method. And the most probable explanation of the intravascular coagulation caused by the injection of nucleo-proteid is that in the presence of the calcium salts of the plasma it produces fibrin-ferment, although it has not as yet been conclusively shown that the amount of fibrin-ferment obtainable from the blood is increased after injection of nucleo-proteid. In the curious hereditary disease known as hæmophilia, a deficiency of calcium seems occasionally to be responsible for the diminished coagulability of the blood; and the internal administration of a solution of calcium chloride has sometimes been thought to lessen the tendency to hæmorrhage, or its local application to cut short an actual attack. Injection of commercial peptone into the veins of a dog, though not of a rabbit, deprives the blood

for a time of its power of coagulation, apparently in part by reason of the affinity of peptone for calcium salts, for its action can be prevented by injection of calcium chloride (Pekelhäring), and imitated by injection of potassium oxalate, while the peptone plasma outside of the body can sometimes, though not invariably, be caused to clot by the addition of a soluble salt of calcium. (But see p. 45.) Soaps hinder coagulation in the same way. The precise action of the calcium has not yet been made clear. Pekelhäring supposes that active fibrin-ferment is a compound of calcium with nucleo-proteid, and that in coagulation calcium is handed over to the fibrinogen by the fibrin-ferment. Lilienfeld imagines that the nucleo-proteid first acts on the fibrinogen, causing it to split up into thrombosin and fibrinoglobulin, and that the thrombosin then unites with calcium to form fibrin. *To sum up, we may say that there is a general agreement that the presence of calcium is essential to the formation of fibrin, and a preponderance of opinion that the fibrin is formed by the union of calcium with fibrinogen (or thrombosin) under the influence of fibrin-ferment (or nucleo-proteid).*

To a certain extent the action of nucleo-proteid in coagulation can be imitated by other substances of animal origin, such as the albumoses of snake venom (Martin), and even by certain artificial products of the laboratory, the synthesized colloids of Grimaux, which, when injected into the blood, produce the same phenomena of intravascular coagulation down to the finest detail, and including the negative phase. It is not known whether these substances act on the leucocytes or other cells, and thus cause an increased production or an increased liberation of nucleo-proteid, or whether they actually take its place.

So far we have been considering the problem of coagulation as if all the data for its solution could be obtained by a study of the blood itself. In other words, our main business up to this point has been the explanation of coagulation in the shed blood; it has been only incidentally, and with the object of casting light on the question of extravascular clotting, that we have touched on the coagulation of the blood within the living vessels. It is not possible here to adequately discuss, nor even to define, the differences between the two problems. All we can do is to warn the student, and to emphasize our warning by one or two illustrations, that valuable as is the knowledge derived from experiments on extravascular coagulation, it would be totally misleading if applied without modification to the circulating blood. For instance, we have recognised in the leucocytes an important source of the nucleo-proteid which plays so

great a part in the clotting of shed blood; but we know that leucocytes are constantly breaking down in the lymph and the blood, and we have to inquire how it is that coagulation does not occur, except in disease, within the vessels. Calcium is not wanting to the circulating plasma, fibrinogen is not wanting, and it has already been mentioned (p. 41) that a small amount of fibrin-ferment can be obtained from the perfectly fresh and, as we might almost say, still living blood. Why, then, does it not coagulate? Some have said that the quantity of fibrin-ferment is too small; but if any is present, some coagulation ought to occur if the conditions were exactly the same as in a test-tube. Others have said that coagulation is 'restrained' by the contact of the living walls of the bloodvessels; but although it is certain that the contact of foreign matter, and all dead matter is foreign to living cells, does hasten the destruction of leucocytes, and therefore the liberation of fibrin-ferment, it is evident that it is just this 'restraining' influence of the vessels which has to be explained. Schmidt has attempted a chemical explanation. He starts with the assumption that some ready-made fibrin-ferment, or its precursor, exists not only in the circulating blood, but in the circulating plasma, for he finds that the blood-plasma of the horse, entirely freed from formed elements by filtration through several folds of filter-paper at a temperature of 0° to 0·5° C., remains fluid at the ordinary temperature of the air for hours, but eventually coagulates. On this and other evidence he bases the view that substances formed by the breaking down of white blood-corpuscles in shed blood are not the only cause of coagulation, although they undoubtedly greatly accelerate it. According to Schmidt, a precursor, or mother-substance of fibrin-ferment, is produced in the body from all, or most, protoplasmic cells, from white blood-corpuscles among the rest, but not exclusively, nor even pre-eminently, from them. This substance passes continually into the blood, and fibrin-ferment is continually formed from it, but is always being neutralized by other chemical processes. So that living blood within the living vessels may be said to be acted upon by two sets of influences, one tending to coagulation, the other opposing it. Under normal conditions, the processes that make for coagulation never obtain the upper hand; but anything which interrupts the circulation, and consequently the free interchange between blood and tissues, interferes with the entrance of the substances that render the fibrin-ferment inactive. In the clotting of extravascular plasma, free from corpuscles, Schmidt sees the continuation, under modified conditions, of a normal process always going on within the bloodvessels. In the lungs it would seem that the forces which favour coagulation are feeble, or the forces that resist it strong, for blood, after passing many times through the pulmonary circulation without being allowed to enter the systemic vessels, loses its power of clotting (Ludwig and Pawlow).

The liver is another organ whose relations to the coagulation of the blood are peculiar. We have already mentioned that the injection of commercial peptone, which consists chiefly of proteoses, into the blood of dogs causes it to lose its coagulability. The effect gradually

passes away, till after some hours the original power of coagulation is restored (p. 189). The liver is known to be intimately concerned in the production of this remarkable result, for if the circulation through it be interrupted, the injection of proteose is ineffective. Further, if a solution of proteose is artificially circulated through an excised liver, a substance is formed which is capable of suspending the coagulation of blood outside of the body, a property which proteoses themselves do not possess. It is not believed that the proteose is actually changed into this anticoagulant substance, but rather that the liver cells produce it as a 'reaction' to the presence of the foreign substance, being perhaps stimulated in some way by the circulating proteose. Under certain conditions, some of which are known and others not, the injection even of one or other of the purified proteoses causes not retardation, but hastening, of coagulation; and if this has been the result of a first injection, a second is equally unsuccessful. It is possible that by an effort of the organism to restore the normal coagulability of the blood, on which its very existence depends, a second substance with fibrinoplastic powers is produced, and that the result of an injection of proteose is determined by the relative amount of coagulant and anticoagulant secreted in a given time. On the other hand, pure hemipeptone always retards, and pure antipeptone (p. 308) always favours coagulation (Thompson).

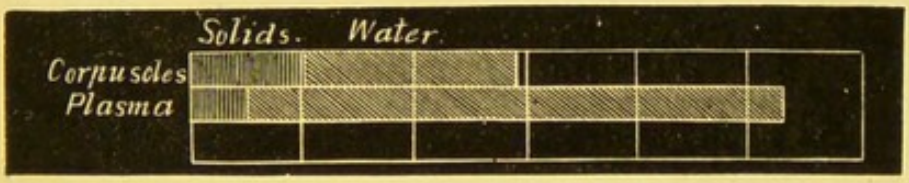


FIG. 6.—DIAGRAM SHOWING RELATIVE QUANTITY OF SOLIDS AND WATER IN RED CORPUSCLES AND PLASMA.

The Chemical Composition of Blood.

The serum of coagulated blood represents the plasma *minus* fibrinogen (or its thrombosin element); the clot represents the corpuscles *plus* fibrin. Thus:

Plasma − Fibrin(ogen) = Serum.
Corpuscles + Fibrin = Clot.
Plasma + Corpuscles = Serum + Clot = Blood.

Bulky as the clot is, the quantity of fibrin is trifling (·2 to ·4 per cent. in human blood). The plasma contains about 10 per cent. of solids, the red corpuscles about 40 per cent., the entire blood about 20 per cent.

Serum contains 8 to 9 per cent. of proteids, about ·8 per cent. of inorganic salts, and small quantities of neutral fats, urea, kreatin, grape-sugar, lactic acid, and other substances. The proteids are *serum-albumin* and *serum-globulin*. In the rabbit the former, in the horse the latter, is the more abundant; in man they exist in not far from equal amount.

The quantitative composition of serum, especially as regards the inorganic salts, is remarkably constant in animals of the same species, and even in animals of different species belonging to the same, or to not very widely-separated, natural groups. In cold-blooded animals the serum-albumin is scantier than in mammals, the globulin relatively more plentiful.

Serum-albumin belongs to the class of native albumins. It has been obtained in a crystalline form from the serum of horse's blood. It is soluble in distilled water, and is not precipitated by saturating its solutions with certain neutral salts. Heated in neutral or slightly acid solution, it coagulates first at 73°, then at 77°, then at 84° C. But this is not sufficient proof that it consists of a mixture of three proteids, as has been held.

Serum-globulin belongs to the globulin group of proteids. It is insoluble in distilled water, and is precipitated in saturated solutions of neutral salts. When heated, it coagulates at about 75° C. (p. 60).

Of the inorganic salts of serum, the most important are sodium chloride and sodium carbonate. Small amounts of potassium,

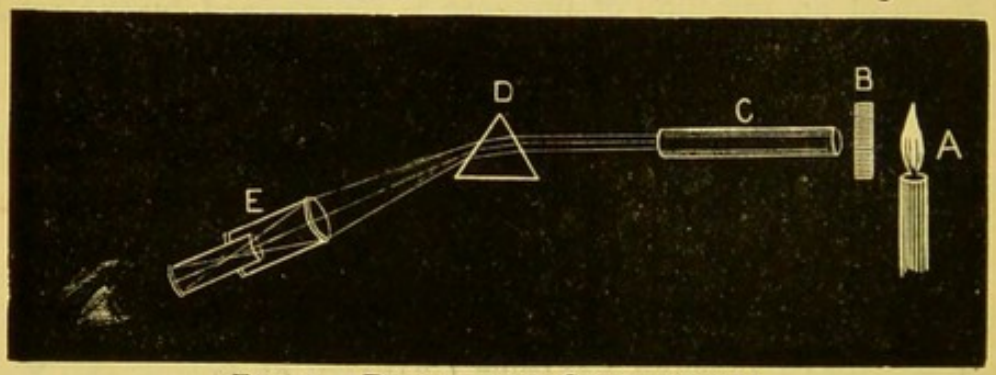


FIG. 7.—DIAGRAM OF SPECTROSCOPE.

A, source of light; B, layer of blood; C, collimator for rendering rays parallel; D, prism; E, telescope.

calcium, and magnesium, united with phosphoric acid or chlorine, and a trace of a fluoride, are also present.

The Red Corpuscles consist of rather less than 60 per cent. of water and rather more than 40 per cent. of solids. Of the solids the pigment hæmoglobin makes up about 90 per cent.; the proteids and nucleo-proteid of the stroma about 8 per cent.; lecithin and cholesterin less than 1 per cent.; inorganic salts (which vary greatly in their relative proportions in different animals, but in man consist chiefly of phosphates and chloride of potassium, with a much smaller amount of sodium chloride) 1·5 per cent.

Hæmoglobin.—Of all the solid constituents of the blood hæmoglobin is present in greatest amount, constituting, as it does, no less than 13 per cent., by weight, of that liquid. It is an exceedingly complex body, containing carbon, hydrogen, nitrogen, and oxygen in much the same proportions in which they exist in proteids (p. 17). Iron is also present to the extent of almost exactly one-third

of 1 per cent., and there is also a little sulphur, the amount of which stands in a very simple relation to the quantity of iron (1 atom of iron to 3 of sulphur in dog's hæmoglobin, and 1 atom of iron to 2 of sulphur in the hæmoglobin of the horse, ox, and pig). Hæmoglobin appears to be made up of a proteid element which contains all the sulphur, and a pigment which contains all the iron, the proteid constituting by far the larger portion of the gigantic molecule, whose weight has been estimated at more than 16,000 times that of a molecule of hydrogen. Since its percentage composition is still undetermined with absolute precision, it is impossible to give an empirical formula that is more than approximately correct. For dog's hæmoglobin Jaquet gives $C_{758}H_{1203}N_{195}S_3FeO_{218}$, which would make the molecular weight 16,669.

The most remarkable property of hæmoglobin is its power of combining loosely with oxygen when exposed to an atmosphere containing it, and of again giving it up in the presence of oxidizable substances or in an atmosphere in which the partial pressure of oxygen (pp. 231, 236), has been reduced below a certain limit. It is this property that enables hæmoglobin to perform the part of an oxygen-carrier to the tissues, a function of the first importance, which will be more minutely considered when we come to deal with respiration.

The bright-red colour of blood drawn from an artery or of venous blood after free exposure to air is due to the fact that the hæmoglobin is in the oxidized state—in the state of oxyhæmoglobin, as it is called. If the oxygen is removed by means of reducing agents, such as ammonium sulphide, or by exposure to the vacuum of an air-pump, the colour darkens, the blood-pigment being now in the form of reduced hæmoglobin. In ordinary venous blood a large proportion of the pigment is in this condition, but there is always oxyhæmoglobin present as well. In asphyxia (p. 217), however, the whole of the oxyhæmoglobin may disappear.

Crystallization of Hæmoglobin.—In the circulating blood the hæmoglobin is related in such a way to the stroma of the corpuscles that, although the latter are suspended in a liquid readily capable of dissolving the pigment, it yet remains under ordinary circumstances strictly within them. In a few invertebrates, however, it is normally in solution in the circulating liquid. As a rare occurrence hæmoglobin may form crystals inside the corpuscles. When it is in any way brought into solution outside the body, it shows in many animals,

but not in the same degree in all, a tendency to crystallization; and the ease with which crystallization can be induced is in inverse proportion to the solubility of the hæmoglobin. Thus, it is far more difficult to obtain crystals of oxyhæmoglobin from human blood than from the blood of the rat, guinea-pig, or dog, whose blood-pigment is less soluble than that of man, and for a like reason the oxyhæmoglobin of the bird, the rabbit, or the frog crystallizes still less readily than that of human blood.

As to the form of the crystals, in the vast majority of animals they

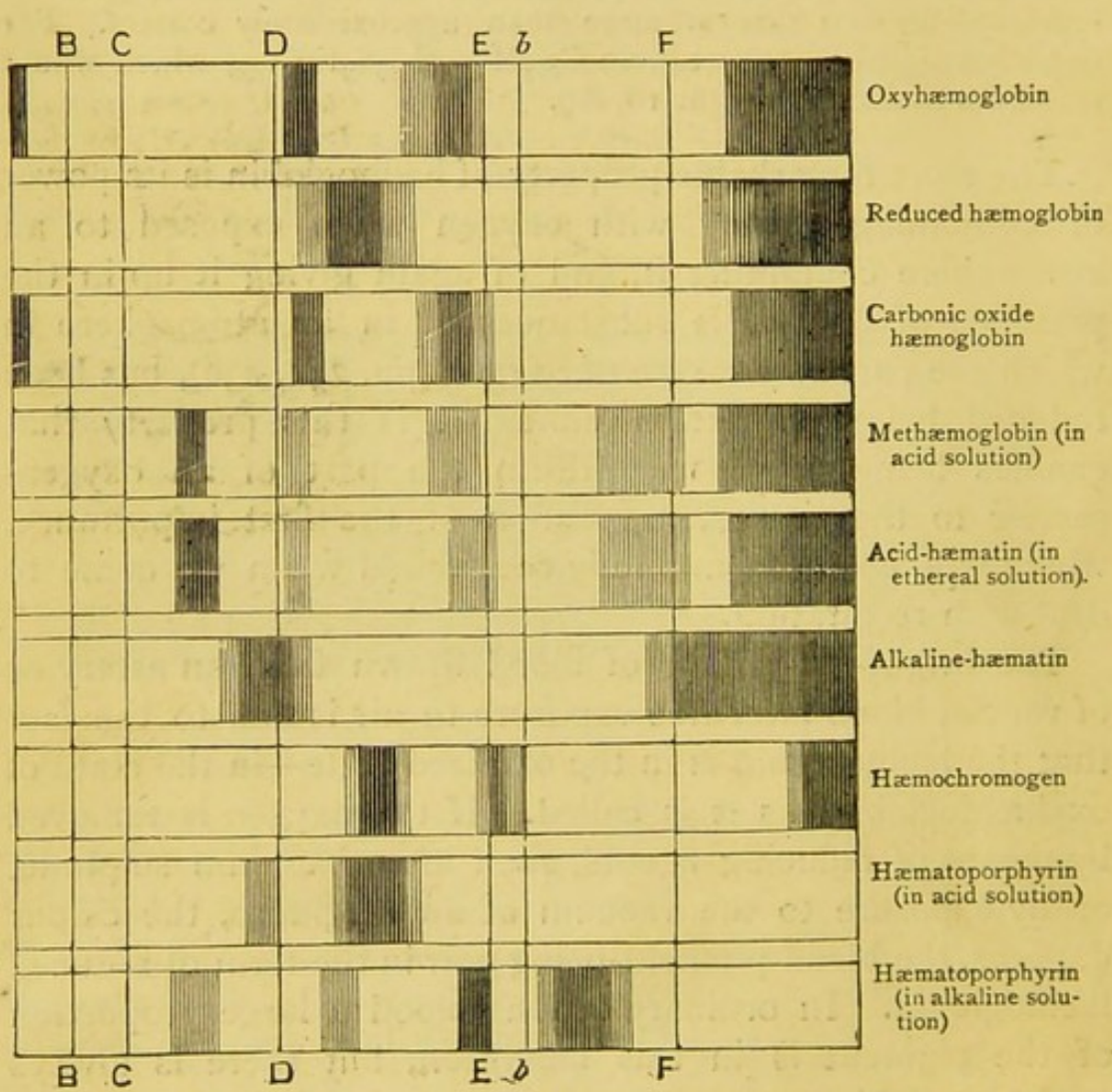


FIG. 8.—TABLE OF SPECTRA OF HÆMOGLOBIN AND ITS DERIVATIVES.
B, oxygen line; D, sodium line; C and F, hydrogen lines; *b*, magnesium line.

are rhombic prisms or needles, but in the guinea-pig they are tetrahedra belonging to the rhombic system, and in the squirrel six-sided plates of the hexagonal system.

Reduced hæmoglobin can also be caused to crystallize, though with more difficulty than oxyhæmoglobin, since it is more soluble. Crystals of reduced hæmoglobin were first prepared from human blood by Hüfner, who allowed it to putrefy in sealed tubes for several weeks.

When a solution of oxyhæmoglobin of moderate strength is examined with the spectroscope, two well-marked absorption bands are seen, one a little to the right of Fraunhofer's line D, and the other a little to the left of E. A third band exists in the extreme violet between G and H. It cannot be detected with an ordinary spectroscope, but has been studied by the aid of a fluorescent eye-piece (Soret), by projecting the spectrum on a fluorescent screen, and by photographing the spectrum (Gamgee). The addition of a reducing agent, such as ammonium sulphide, causes the bands in the visible spectrum to disappear, and they are replaced by a less sharply-defined band, of which the centre is about equidistant from D and E. This is the characteristic band of reduced hæmoglobin. The spectrum of ordinary venous blood shows the bands of oxyhæmoglobin.

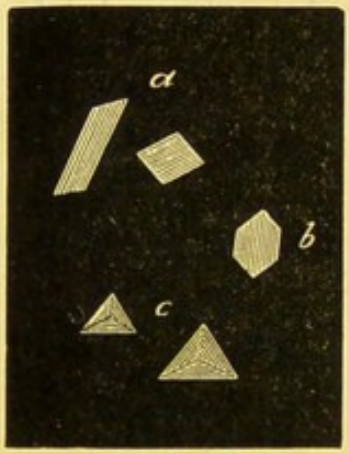


FIG. 9.—CRYSTALS OF OXY-HÆMOGLOBIN.
a, human; *b*, squirrel; *c*, guinea-pig.

Carbonic oxide hæmoglobin is a representative of a class of hæmoglobin compounds analogous to oxyhæmoglobin, in which the loosely-combined oxygen has been replaced by other gases (carbon monoxide, nitric oxide) in firmer union. Its spectrum shows two bands very like those of oxyhæmoglobin, but a little nearer the violet end. Carbonic oxide hæmoglobin is formed in poisoning with coal gas. Owing to the great stability of the compound, the hæmoglobin can no longer be oxidized in the lungs, and death may take place from asphyxia. It is, however, gradually broken up, and this is an indication that artificial respiration may sometimes be of use in such cases.

Methæmoglobin is a derivative of oxyhæmoglobin which can be formed from it in various ways, *e.g.*, by the addition of ferricyanide of potassium or nitrite of amyl (Gamgee), or by electrolysis (in the neighbourhood of the anode). It very often appears in an oxyhæmoglobin solution which is exposed to the air. It has been found in the urine in cases of hæmoglobinuria, in the fluid of ovarian cysts, and in hæmatoceles. The strongest band in its spectrum is in the red, between C and D, but nearer C, nearly in the same position as the band of acid-hæmatin. Reducing agents, such as ammonium sulphide, change methæmoglobin first into oxyhæmoglobin and then into reduced hæmoglobin. It has by some been regarded as a more highly oxidized hæmoglobin than oxyhæmoglobin. Rebutting evidence has, however, been offered to the effect that the same

quantity of oxygen is required to saturate both pigments, and this evidence appears to be sound. The difference seems to lie rather in the manner in which the oxygen is united to the hæmoglobin in the methæmoglobin molecule than in the quantity of oxygen which it contains. For methæmoglobin, unlike oxyhæmoglobin, parts with no oxygen to the vacuum, while, on the other hand, in the presence of reducing agents it yields up its oxygen even more readily than oxyhæmoglobin does (Haldane).

By the action of acids or alkalies oxyhæmoglobin is split into hæmatin and proteid bodies, of which the exact nature is little known. When the hæmoglobin is acted on by acids in the absence of oxygen, hæmochromogen is first formed, which then gradually loses its iron and is changed into hæmatoporphyrin. If oxygen be present, hæmatin is the final product. By the action of alkalies reduced

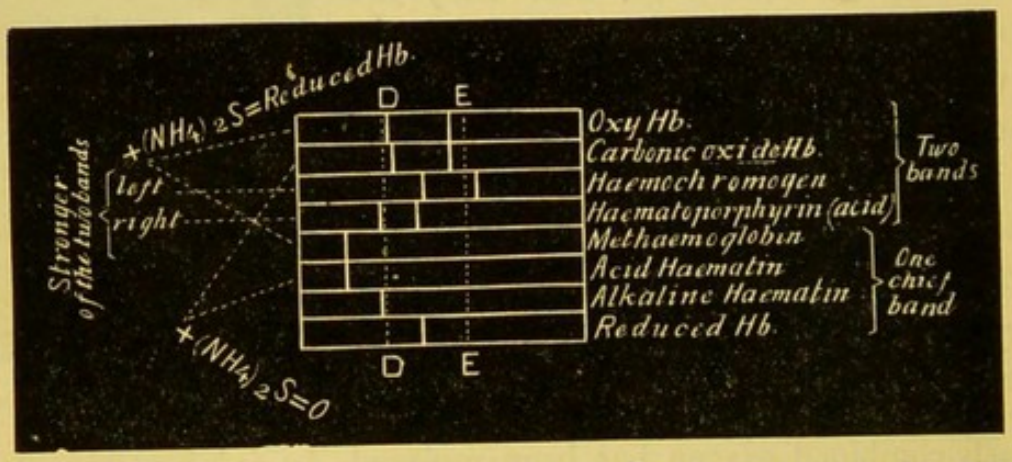


FIG. 10.—DIAGRAM TO SHOW THE CHIEF CHARACTERISTICS BY WHICH HÆMOGLOBIN AND SOME OF ITS DERIVATIVES MAY BE RECOGNISED SPECTROSCOPICALLY. THE POSITION OF THE MIDDLE OF EACH BAND IS INDICATED ROUGHLY BY A VERTICAL LINE.

hæmoglobin yields *hæmochromogen*, which is stable in alkaline solution, and gives a beautiful spectrum with two bands, bearing some resemblance to those of oxyhæmoglobin, but placed nearer the violet end. The band next the red end of the spectrum is much sharper than the other.

Hæmatin, the most frequent result of the splitting up of hæmoglobin, is generally obtained as an amorphous substance with a bluish-black colour and a metallic lustre, insoluble in water, but soluble in dilute alkalies and acids, or in alcohol containing them. In addition to the iron of the hæmoglobin, hæmatin contains the four chief elements of proteid bodies, carbon, hydrogen, nitrogen and oxygen.

Hæmatoporphyrin, or iron-free hæmatin, may be obtained from blood or hæmoglobin by the action of strong sulphuric acid. Its spectrum in acid solution shows two bands, one just to the left of D, the other about midway between D and E. Like oxyhæmoglobin, reduced hæmoglobin, carbonic oxide hæmoglobin, methæmoglobin and other derivatives of hæmoglobin, it also has a band in the ultra-violet.

Hæmin is a compound of hæmatin and hydrochloric acid, which

crystallizes in the form of small rhombic plates, of a brownish or brownish-black colour. They are insoluble in water, but readily soluble in dilute alkalies (see Practical Exercises, p. 66).

Chemistry of the White Blood Corpuscles.—The composition of pus-cells and the leucocytes of lymphatic glands has alone been investigated. The chief constituents of the latter are a globulin coagulating by heat at 48° to 50° C.; a nucleo-proteid coagulating in 5 per cent. magnesium sulphate solution at 75° C., and causing coagulation of the blood on injection into the veins of rabbits; an albumin coagulating at 73° C.; and a ferment with powers like the pepsin of the gastric juice. In pus-cells glycogen has been found.

The Quantity of Blood.—The quantity of blood in an animal is best determined by the method of Welcker. The animal is bled from the carotid into a weighed flask. When blood

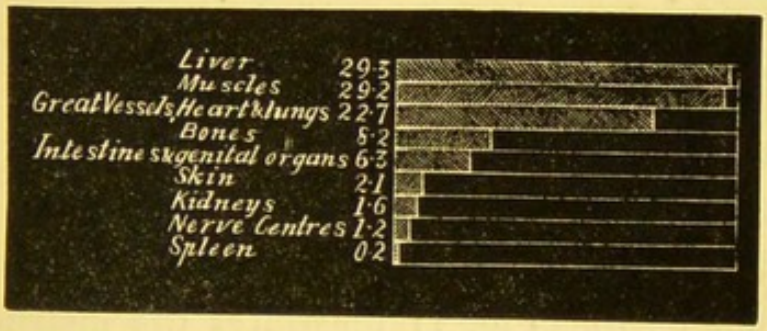


FIG. 11.—DIAGRAM TO ILLUSTRATE THE DISTRIBUTION OF THE BLOOD IN THE VARIOUS ORGANS OF A RABBIT (AFTER RANKE'S MEASUREMENTS).
The numbers are percentages of the total blood.

has ceased to flow, the vessels are washed out with water or normal saline solution, and the last traces of blood are removed by chopping up the body, after the intestinal contents have been cleared away, and extracting it with water. The extract and washings are mixed and weighed; a given quantity of the mixture is placed in a hæmatinometer (a glass trough with parallel sides, *e.g.*), and a weighed quantity of the unmixed blood diluted in a similar vessel till the tint is the same in both. From the amount of dilution required, the quantity of blood in the watery solution can be calculated. This is added to the amount of unmixed blood directly determined.

Many other methods have been devised on the principle of injecting a known quantity of some substance into the circulating blood, and then, after an interval has been allowed for mixture, determining the change produced in a

sample. Thus, the specific gravity of a drop of blood having been measured, a certain quantity of normal saline (a ·5 to ·7 per cent. solution of sodium chloride) may be injected into a vein, and the specific gravity again determined. Or the electrical resistance of a small sample of blood may be measured before and after injection of a given quantity of a substance, such as sodium chloride, which reduces it. Or the total solids may be determined in a specimen before and after injection of a known weight of distilled water. Or an animal may be caused to inspire carbonic oxide for a given time; from the quantity taken in, and the quantity fixed by a known weight of blood withdrawn from the animal, the weight of the whole blood may be calculated.

The quantity of blood in the body was greatly over-estimated by the ancient physicians. Avicenna put it at 25 lb., and many loose statements are on record of as much as 20 lb. being lost by a patient without causing death. The proportion of blood to body-weight has been found by accurate experiments to be in man and the dog 1 : 13, new-born child 1 : 19, cat 1 : 14, horse 1 : 15, frog 1 : 17, rabbit 1 : 19. Fig. 11 illustrates the distribution of the blood in the various organs of a rabbit. The liver and skeletal muscles each contain rather more than one-fourth; the heart, lungs, and great vessels rather less than one-fourth; and the rest of the body about one-fifth, of the total blood. The kidney and spleen of the rabbit each contain one-eighth of their own weight of blood, the liver between one-third and one-fourth of its weight, the muscles only one-twentieth of their weight.

Lymph and Chyle.

Lymph has been defined as blood without its red corpuscles (Johannes Müller); it is, in fact, a dilute blood-plasma, containing leucocytes, some of which (lymphocytes) are common to lymph and blood, others (coarsely granular basophile cells) are absent from the blood. The reason of this similarity appears when it is recognised that the plasma of lymph is derived from the plasma of blood by a process of physiological filtration (or secretion) through the walls of

the capillaries into the lymph-spaces that everywhere occupy the interstices of areolar tissue. But in addition to the constituents of the plasma, lymph appears to contain certain toxic substances produced in the metabolism of the tissues and destroyed in the lymphatic glands. Lymph, as obtained from one of the large lymphatic vessels of the limbs, or from the thoracic duct of a fasting animal, is a colourless or sometimes yellowish or slightly reddish liquid of alkaline reaction. Its specific gravity is much less than that of the blood (1015 to 1030). It coagulates spontaneously, but the clot is always less firm and less bulky than that of blood. The plasma contains fibrinogen, from which the fibrin of the clot is derived. Serum-albumin and serum-globulin are present in much the same relative proportion as in blood, although in smaller absolute amount. Neutral fats, urea, and sugar are also found in small quantities. The inorganic salts are the same as those of the blood-serum, and exist in about the same amount, sodium preponderating among the bases, as it does in serum. The following table shows the results of analyses of lymph from man and the horse (Munk):

		Man.		*Horse.*	
Water		95·0 p.c.		95·8 p.c.	
Solids	Fibrin	0·1	5·0	0·1	4·2
	Other proteids	4·1		2·9	
	Fat	trace		trace	
	Extractives*	0·3		0·1	
	Salts	0·5		1·1	

Chyle is merely the name given to the lymph coming from the alimentary canal. The fat of the food is absorbed by the lymphatics, and during digestion the chyle is crowded with fine fatty globules, which give it a milky appearance. There may also be in chyle a few red blood-corpuscles, carried into the thoracic duct by a back-flow from the veins into which it opens. Chyle clots like ordinary lymph. The following is the composition of a sample analyzed by Paton, and obtained from a fistula of the thoracic duct in a man:

* The term 'extractives' is somewhat loosely applied to organic substances which exist in so small an amount, or have such indefinite chemical characters that they cannot be separately estimated.

Water	953·4
Solids	46·6
Inorganic	6·5
Organic	40·1
Proteids	13·7
Fats	24·06
Cholesterin	0·6
Lecithin	0·36

The quantity of chyle flowing from the fistula was estimated at as much as 3 to 4 kilos per twenty-four hours, or nearly as much as the whole of the blood. The flow has been calculated in various animals at one-eighteenth to one-seventh of the body-weight in the twenty-four hours. The quantity of lymph in the body is unknown, but it must be very great—perhaps two or three times that of the blood.

The gases of the blood and lymph will be treated of in Chapter III.

The Functions of Blood and Lymph.

We have already said that these liquids provide the tissues with the materials they require, and carry away from them materials which have served their turn and are done with. These materials are gaseous, liquid, and solid. Oxygen is brought to the tissues in the red corpuscles; carbon dioxide is carried away from them chiefly in the plasma of the blood and lymph. The water and solids which the cells of the body take in and give out are also, at one time or another, constituents of the plasma. The heat produced in the tissues, too, is, to a large extent, conducted into the blood and distributed by it throughout the body. It is not known whether the leucocytes play any part in the normal nutrition of other cells, although it is probable that they exercise an influence on the plasma in which they live; but they have important functions of another kind, to which it is necessary to refer briefly here.

Phagocytosis.—Certain of the amœboid cells of blood and lymph, and the cells of the splenic pulp, are able to include or 'eat up' foreign bodies with which they come in contact, in the same way as the amœba takes in its food. Such cells are

called phagocytes; and it is to be remarked that this term neither comprises all leucocytes nor excludes all other cells, for some fixed cells, such as those of the endothelial lining of bloodvessels, are phagocytes in virtue of their power of sending out protoplasmic processes, while the small, immobile, uninuclear leucocyte, or lymphocyte, is not a phagocyte.

Although it is not at present possible to assign a physiological value to all the phenomena of phagocytosis, either as regards the phagocytes themselves or as regards the organism of which they form a part, there seems little doubt that under certain circumstances the process is connected with the removal of structures which in the course of development have become obsolete, or with the neutralization or elimination of harmful substances introduced from without, or formed by the activity of bacteria within the tissues. During the metamorphosis of some larvæ, groups of cilia and muscle-fibres may be absorbed and eaten up by the leucocytes. In the metamorphosis of maggots, for example, the muscular fibres of the abdominal wall, which are used in creeping, and are therefore not required in the adult, degenerate, and are devoured by swarms of leucocytes which migrate into them.

But the behaviour of phagocytes towards pathogenic micro-organisms is of even greater interest and importance. Metschnikoff laid the foundation of our knowledge of this subject by his researches on Daphnia, a small crustacean with transparent tissues, which can be observed under the microscope. When this creature is fed with a fungus, Monospora, the spores of the latter find their way into the body-cavity. Here they are at once attacked by the leucocytes, ingested, and destroyed. But after a time so many spores get through that the leucocytes are unable to deal with them all; some of them develop into the first or 'conidium' stage of the fungus; the conidia poison the leucocytes, instead of being destroyed by them, and the animal generally dies. Occasionally, however, the leucocytes are able to destroy all the spores, and the life of the Daphnia is preserved. This battle, ending sometimes in victory, sometimes in defeat, is believed by Metschnikoff to

be typical of the struggle which the phagocytes of higher animals and of man seem to engage in when the germs of disease are introduced into the organism. He supposes that the immunity to certain diseases possessed naturally by some animals, and which may be conferred on others by vaccination with various protective substances,* is, to a large extent, due to the early and complete success of the phagocytes in the fight with the bacteria; and that in rapidly-fatal diseases—such as chicken-cholera in birds and rabbits, and anthrax in mice—the absence of any effective phagocytosis is the factor which determines the result. Others have laid stress on the action of protective substances supposed to exist in the living plasma itself, although only as yet demonstrated in the serum. It is possible that such substances are manufactured by the leucocytes, and either given off by them to the plasma by a process of 'excretion,' or liberated by their complete solution. And it may be that it is only when the bacteria have been crippled by contact with these defensive 'alexins' that the leucocytes are able to ingest them and complete their destruction. It has been actually observed that the oxyphile cells of frog's lymph retard the growth of certain bacteria by coating them with a kind of slime derived from the oxyphile granules.

Diapedesis.—The fact that leucocytes can pass out of the bloodvessels into the tissues (Waller, Cohnheim) has a very important bearing on the subject of phagocytosis. The phenomenon is called diapedesis, and is best seen when a transparent part, such as the mesentery of the frog, is

* The most recent investigations go to show that Metschnikoff's phagocytic theory of immunity requires modification in the case of the higher animals and man, although the brilliant biological observations on which it was originally built retain all their value. He supposed that in the immunizing process the leucocytes underwent certain changes, acquired, so to speak, a sort of 'education' that enabled them to cope with bacteria against which they were previously powerless. It seems more probable that in the presence of the substances that confer immunity, not only the leucocytes, but other cells, are stimulated to produce bodies which cut short the life, or at least inhibit the growth, of the bacteria. It may be, however that the leucocytes take the lead in this reaction. And the voracious and at first sight almost undiscriminating appetite displayed by cells which appear to englobe with equal avidity a granule of carmine or a particle of proteid, a globule of fat or a fragment of carbon, renders it difficult to believe that they do not also act, to some extent, directly as phagocytes in the presence of pathogenic organisms.

irritated. The first effect of irritation is an increase in the flow of blood through the affected region. If the irritation continues, or if it was originally severe, the current soon begins to slacken, the corpuscles stagnate in the vessels, and inflammatory stasis is produced. The leucocytes adhere in large numbers to the walls of the capillaries, and particularly of the small veins, and then begin to pass slowly through them by amœboid movements, the passage taking place at the junctions between, or it may be through the substance of, the endothelial cells. Plasma is also poured out into the tissues, the whole forming an inflammatory exudation. Even red blood-corpuscles may pass out of the vessels in small numbers. The exudation may be gradually reabsorbed, or destruction of tissue may ensue, and a collection of pus be formed. The cells of pus are largely, if not entirely, emigrated leucocytes.

PRACTICAL EXERCISES ON CHAPTER I.

N.B.—*In the following exercises all experiments on animals which would cause pain are to be done under complete anæsthesia.*

1. **Reaction of Blood.**—With a clean suture-needle prick one of the fingers behind the nail. Bandaging the finger with a handkerchief from above downwards, so as to render its tip congested, will often facilitate the getting of a good-sized drop. Put a drop of blood on a piece of glazed neutral litmus paper; wash off in 10 to 30 seconds with distilled water. A blue stain will be left, showing that fresh blood is alkaline.

2. **Specific Gravity of Blood**—(1) *Hammerschlag's Method.*—Put a mixture of chloroform and benzol of specific gravity 1·060 into a small glass cylinder. Obtain a drop of blood as in 1. Put it in the mixture by means of a small pipette. If it sinks, add chloroform, if it rises, add benzol, till it just remains suspended when the liquid has been well stirred. Then with a small hydrometer measure the specific gravity of the mixture, which is now equal to that of the blood. Filter the liquid to free it from blood, and put it back into the stock-bottle. This is a convenient method, but some prefer—

(2) *Roy's Method.*—Take 25 small bottles containing mixtures of glycerine and water of specific gravity 1·027, 1·029 . . . 1·070. Begin with bottle 1·059. Pour a little of the liquid into a small vessel. Then prick the finger with a sharp, clean suture-needle, and suck up a small drop of blood into the horizontal limb of a capillary tube with a rectangular elbow. Immerse the horizontal part of the tube in the glycerine mixture, and gently blow the drop of blood into

it. If it neither rises nor sinks, the specific gravity of the blood is 1·059. If it sinks, the experiment must be repeated with a mixture of higher specific gravity, say 1·061; if it rises, with a mixture of lower specific gravity, say 1·057, and so on. If the drop of blood rises in mixture 1·061 and sinks in mixture 1·059, the specific gravity is between those two figures, and may be taken as 1·060.

3. **Coagulation of Blood.**—(1) Take two tumblers or beakers, label them α and β, and measure into each 100 c.c. of water. Mark the level of the water by strips of gummed paper, and pour it out. (If a sufficient number of graduated cylinders is available, they may of course be used, and this measurement avoided.) Into α put 25 c.c. of a saturated solution of magnesium sulphate, and into β 25 c.c. of a 1 per cent. solution of potassium oxalate in normal saline solution (·7 per cent. solution of sodium chloride). If the dog provided is a large one, these quantities may be all doubled.

(2) Insert a cannula into the central end of the carotid artery of a dog anæsthetized with morphia* and ether, or A.C.E. mixture.†

To put a Cannula into an Artery.—Select a glass cannula of suitable size, feel for the artery, make an incision in its course through the skin, then isolate about an inch of it with forceps or a blunt needle, carefully clearing away the fascia, or connective tissue. Next pass a small pair of forceps under the artery, and draw two ligatures through below it. If the cannula is to be inserted into the central end of the artery, tie the ligature which is farthest from the heart, and cut one end short. Then between the heart and the other ligature compress the artery with a small clamp (often spoken of as 'bulldog' forceps). Now lift the artery by the distal ligature, make a transverse slit in it with a pair of fine scissors, insert the cannula, and tie the ligature over its neck. Cut the ends of the ligatures short. If the cannula is to be put into the distal end of the artery, both ligatures must be between the clamp and the heart, and the bulldog must be put on before the first ligature (the one nearest the heart) is tied, so that the piece of bloodvessel between it and the ligature may be full of blood, as this facilitates the opening of the artery.

(3) Run into α and β enough blood to fill them to the mark.

(4) Take a small thin copper or brass vessel, and place it in a freezing mixture of ice and salt. Run into it some of the blood from the artery. It soon freezes to a hard mass. Now take the vessel out of the freezing mixture and allow the blood to thaw. It will be seen that it remains liquid for a short time and then clots.

(5) Run some of the blood into a porcelain capsule, stirring it vigorously with a glass rod. The fibrin collects on the rod; the blood is defibrinated and will no longer clot.

(6) Now let the dog bleed to death, and collect the whole of the blood in a jar. Observe that the flow of blood is temporarily

* One to two centigrammes of morphia hydrochlorate per kilogramme of body-weight should be injected subcutaneously about half an hour before the operation. Ten c.c. of a 2 per cent. solution is sufficient for a dog of good size. Note that diarrhœa and salivation are caused by such a dose. For directions for fastening the dog on the holder, see footnote on p. 176.

† A mixture of equal parts of alcohol, ether, and chloroform. Half of the chloroform in the mixture may be advantageously replaced by gasoline.

increased by pressure on the abdominal walls, which squeezes it towards the heart, by passive pumping movements of the hind-legs, and also during the convulsions of asphyxia, which soon appear. Notice that the blood begins to clot in a few minutes, and that very soon the vessel can be tilted without spilling the blood. Set it aside in a cool place, and observe next day that some clear yellow serum has separated from the clot.

(7) Observe that the blood in α and β has not coagulated. Label four test-tubes A, B, C, D, and put into each about 5 c.c. of the oxalated blood. Add to A and B 5 or 6 drops of a 2 per cent. solution of calcium chloride, to C 12 drops, and to D as much as there is of the blood. Leave A at the ordinary temperature, put the other test-tubes in a water-bath at 40° C., and note when clotting occurs.

(8) By means of a centrifuge (Fig. 12) separate the plasma from the corpuscles in α and β. (With Jung's hand centrifuge fairly clear oxalated plasma may generally be obtained in about twenty minutes. Magnesium sulphate ['salted'] plasma usually takes a little longer to separate.)

With the decalcified plasma from β repeat the observations in (7).

With the plasma from α perform the following experiments: (*a*) Put a small quantity of the plasma into eight test-tubes, labelling them E, F, G, H, I, K, L, and M. Dilute E and F with ten times, and G and H with five times, as much distilled water as was taken of plasma; dilute the plasma in I and K with ten times, and in L and M with five times, its volume of a solution of fibrin-ferment containing some calcium chloride. Put E, G, I, and L in the bath at 40° C., and leave the rest of the test-tubes at room temperature. Observe in which of the test-tubes, if any, coagulation occurs, and the time of its occurrence, and report the result.

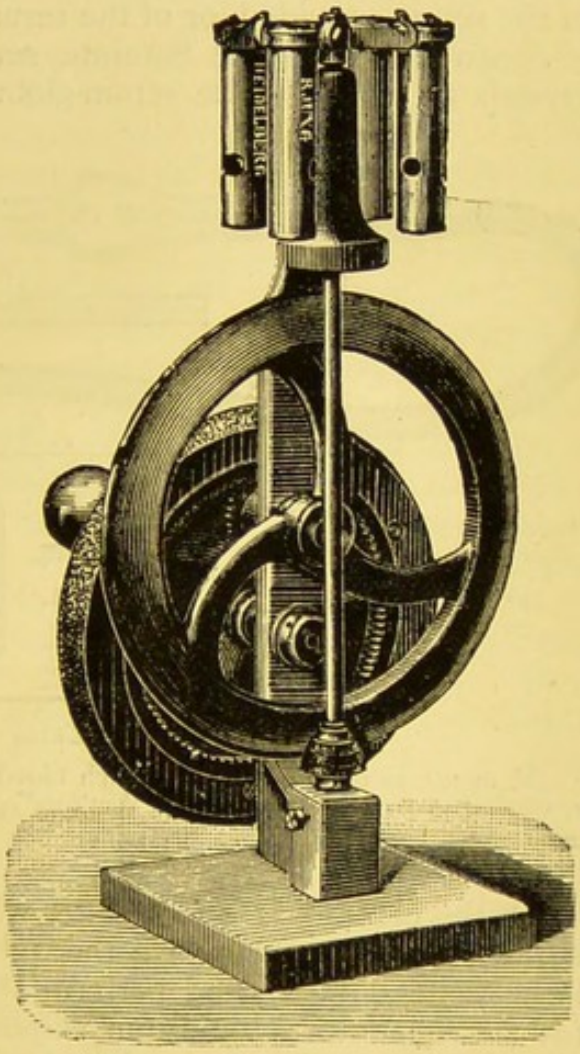


FIG. 12.—CENTRIFUGE (JUNG).

The four cylinders shown at the top of the figure are so swung that they become horizontal as soon as speed is got up.

If no centrifuge is available, the decalcified and salted blood must be left standing in a cool place for twenty-four hours or more till the

corpuscles settle. The plasma can then be siphoned or pipetted off. Instead of dog's blood, the blood of an ox or pig may be obtained at the slaughter-house.

4. **Preparation of Fibrin-Ferment.**—Precipitate blood-serum with ten times its volume of alcohol. Let it stand for several weeks, then extract the precipitate with water. The water dissolves out the fibrin-ferment, but not the other coagulated proteids.

5. **Serum.**—Test the reaction, and determine, both by the hydrometer and the pycnometer, or specific gravity bottle, the specific gravity of the serum provided, or of the serum obtained in experiment 3.

Serum Proteids.—(1) Saturate serum with magnesium sulphate crystals at 30° C. The serum-globulin is precipitated. Filter off.

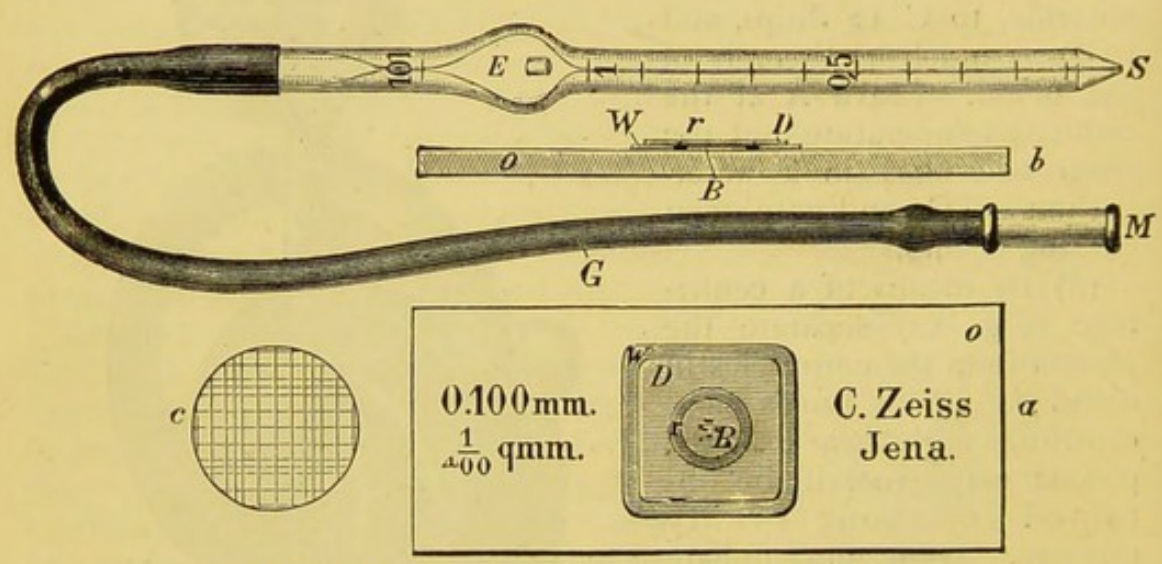


FIG. 13.—THOMA-ZEISS HÆMOCYTOMETER.

M, mouth-piece of tube *G*, by which blood is sucked into *S*; *E*, bead for mixing; *a*, view of slide from above; *b*, in section; *c*, squares in middle of *B*, as seen under microscope.

Wash the precipitate on the filter with a saturated solution of magnesium sulphate. Dissolve the precipitate by the addition of a little distilled water, and perform the following tests for globulins: (*a*) Saturate with magnesium sulphate. A precipitate is obtained. (*b*) Drop into a large quantity of water, and a flocculent precipitate falls down. (*c*) Heat. Coagulation occurs. Determine the temperature of coagulation (p. 21).

(2) To a portion of the filtrate from (1) add sodium sulphate to saturation. The serum-albumin is precipitated. (Neither magnesium sulphate nor sodium sulphate precipitates serum-albumin alone, but the double salt sodio-magnesium sulphate precipitates it, and this is formed when sodium sulphate is added to magnesium sulphate.)

(3) Dilute another portion of the filtrate from (1) with its own bulk of water. Slightly acidulate with dilute acetic acid, and determine the temperature of heat coagulation.

(4) Precipitate the serum-globulin from another portion of serum by adding to it an equal volume of saturated solution of ammonium

sulphate. Filter. Precipitate the serum-albumin from the filtrate by saturating with ammonium sulphate crystals.

(5) Dilute serum with ten to twenty times its volume of distilled water, and pass through it a stream of carbon dioxide. The serum-globulin is partially precipitated. This is the starting-point of a method said to be the best for obtaining pure serum-globulin.

(6) Acidulate some serum with dilute acetic acid and boil. Filter off the coagulum, and to the filtrate add silver nitrate. A non-proteid precipitate insoluble in nitric acid but soluble in ammonia indicates the presence of chlorides.

6. **Enumeration of the Blood-corpuscles.**—Use the Thoma-Zeiss apparatus (Fig. 13). Prick the finger to obtain a drop of blood. Suck the blood up into the capillary tube S to the mark 1.* Wipe off any blood which may adhere to the end of the tube. Then fill it with Hayem's solution (p. 29) or 3 per cent. sodium chloride to the mark 101. This represents a dilution of 100 times. Mix the blood and solution thoroughly, then blow out a drop or two of the liquid to remove all the solution which remains in the capillary tube. Now fill the shallow cell B with the blood mixture. Slide the cover-glass on, taking care that it does not float on the liquid, but that the cell is exactly filled. Put the slide under the microscope (say Leitz's oc. III., obj. 5), and count the number of red corpuscles in not less than ten to twenty squares. The greater the number of squares counted, the nearer will be the approximation to the truth. Now take the average number in a square. The depth of the cell is $\frac{1}{10}$ mm., the area of each square $\frac{1}{400}$ sq. mm. The volume of the column of liquid standing upon a square is $\frac{1}{4000}$ cub. mm. One cub. mm. of the diluted blood would therefore contain 4,000 times as many corpuscles as one square. But the blood has been diluted 100 times, therefore 1 cub. mm. of the undiluted blood would contain 400,000 times the number of corpuscles in one square. Suppose the average for a square is found to be 13. This would correspond to 5,200,000 corpuscles in 1 cub. mm. of blood.

7. **Opacity of Blood.**—Smear a little fresh blood on a glass slide, and lay the slide on some printed matter. It will not be possible to read it, because the light is reflected from the corpuscles in all directions, and little of it passes through.

8. **Laking of Blood.**—(1) Put a little fresh blood in three test-tubes, A B and C. Dilute A with an equal volume, B with two volumes, and C with three volumes, of distilled water, and repeat experiment 7. The print can now be read probably through a layer of A, but certainly through B and C, since the hæmoglobin is dissolved out of the corpuscles by the water and goes into solution, the blood becoming transparent or laked. That the difference is not due merely to dilution can be shown by putting an equal quantity of blood in two test-tubes, and gradually diluting one with distilled water and the other with a 0·9 per cent. solution of sodium chloride, which does not dissolve out the hæmoglobin. Print can be read

* If the tube has not been properly filled, blow the blood out immediately. On no account permit it to clot in the capillary tube.

through the first with a smaller degree of dilution than through the second. Examine the laked blood with the microscope for the 'ghosts,' or shadows of the red corpuscles. The addition of a drop or two of methylene blue will render them somewhat more distinct.

(2) Put some blood in a test-tube, or flask; cork up, and let stand till it begins to putrefy. It becomes laked.

9. **Globulicidal Action of Serum.**—(1) To a small quantity of rabbit's blood add an equal volume of dog's serum. Mix and let stand for fifteen or twenty minutes. The colour of the blood is now darker than before, and it can be seen to be laked. Examine microscopically.

(2) Place a small drop of rabbit's blood and a somewhat larger drop of the dog's serum on a slide, near, but not quite in contact with, each other. Now put on a cover-slip, so that the drops just come together, and examine at once with the microscope with a moderately high power. Where the two drops mingle, the red corpuscles will be seen to fade out, leaving only their 'ghosts.' A few of the corpuscles which come into contact with the, as yet, undiluted serum may be entirely dissolved.

(3) Heat some of the dog's serum to 60° C. for ten minutes, and repeat (1) and (2). No effect will now be produced on the rabbit's corpuscles.

(4) Repeat (1) and (2) with dog's blood and rabbit's serum. The blood will not be laked.

10. **Blood-pigment**—(1) **Preparation of Hæmoglobin Crystals.**—(*a*) Heat some dog's blood to 60° or 65° C. in a water-bath for about ten minutes, taking care that the latter temperature is not exceeded. Cool, and examine the oxyhæmoglobin crystals with the microscope. They form long rhombic prisms and needles.

(*b*) Add a little crude saponin to dog's blood in a test-tube. Shake up well, and allow it to stand till the colour becomes dark. Then shake vigorously, and a mass of hæmoglobin crystals will be formed.

(*c*) Put a small drop of guinea-pig's blood on a slide. Mix with a drop of Canada balsam and cover. Tetrahedral crystals of oxyhæmoglobin will soon form. The slide may be kept.

(2) **Spectroscopic Examination of Hæmoglobin and its Derivatives.**—(*a*) With a small, direct-vision spectroscope look first at a bright part of the sky. Focus by pulling out or pushing in the eyepiece until the numerous fine dark lines (Fraunhofer's lines), running vertically across the spectrum, are seen. Narrow the slit by moving the milled edge till the lines are as sharp as they can be made. Note especially the line D in the orange, the lines E and *b* in the green and F in the blue. Always hold the spectroscope so that the red is at the left of the field. Now dip an iron or platinum wire with a loop on the end of it into water, and then into some common salt or sodium carbonate, and fasten or hold it in the flame of a fishtail burner. On examining the flame with the spectroscope, a bright yellow line will be seen occupying the position of the dark line D in the solar spectrum. This is a convenient line of reference in the spectrum, and in studying the spectra of hæmoglobin and its derivatives, the position

of the absorption bands with regard to the D line should always be noted. The dark lines in the solar spectrum are due to the absorption of light of a definite range of wave-lengths by metals in a state of vapour in the sun's atmosphere, and of course no dark lines are seen in the spectrum of a gas-flame. Half fill a test-tube with defibrinated blood. Fasten it vertically in a clamp in front of the flame and examine it with the spectroscope, holding the latter in one hand with the slit close to the test-tube, and focussing the eyepiece with the other. Or arrange the spectroscope, test-tube and gas-flame on a stand as in Fig. 14. Nothing can be seen till the blood is diluted. Pour a little of the blood into another test-tube, and go on diluting till, on focussing, two *bands of oxyhæmoglobin* are seen in the position indicated in Fig. 8. Draw the spectrum ; then dilute

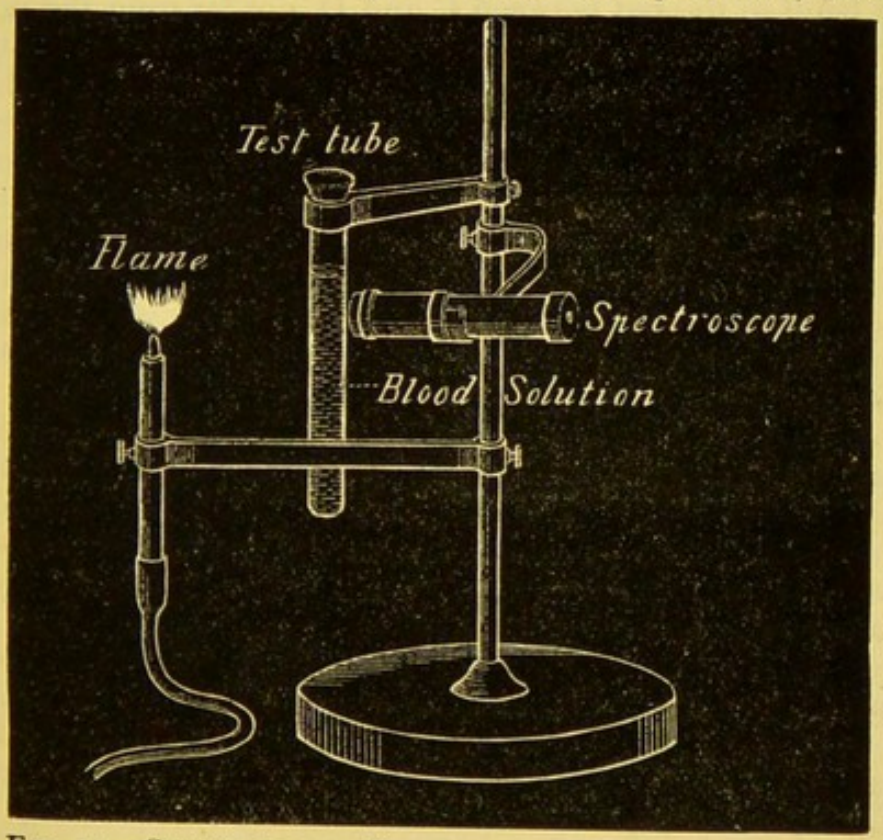


FIG. 14.—SPECTROSCOPIC EXAMINATION OF BLOOD-PIGMENT.

still more, and observe which of the bands first disappears. Now put 5 c.c. of the blood into another test-tube, and dilute it with four times its volume of water. Take 5 c.c. of this dilution, and again add four times as much water, and so on till the solution is only faintly coloured. Note with what degree of dilution the bands disappear. Then examine each of the solutions with the spectroscope and draw its spectrum.

(*b*) Make a solution of blood which shows the oxyhæmoglobin bands sharply. Add some ammonium sulphide solution to reduce the oxyhæmoglobin. Heat gently to about body-temperature. A single, ill-defined band now appears, occupying a position midway between the oxyhæmoglobin bands, and the latter disappear. This is the band of *reduced hæmoglobin* (Fig. 8).

(*c*) *Carbonic Oxide Hæmoglobin.*—Pass coal-gas through blood for

a considerable time. Examine some of the blood (after dilution) with the spectroscope. Two bands, almost in the position of the oxyhæmoglobin bands, are seen; but no change is caused by the addition of ammonium sulphide, since carbonic oxide hæmoglobin is a more stable compound than oxyhæmoglobin.

(*d*) *Methæmoglobin.*—Put some blood into a test-tube, add a few drops of a solution of ferricyanide of potassium, and heat gently. On diluting, a well-marked band will be seen in the red. On addition of ammonium sulphide this band disappears; the oxyhæmoglobin bands are seen for a moment, and then give place to the band of reduced hæmoglobin (Fig. 8).

(*e*) *Acid Hæmatin.*—To a little diluted blood add strong acetic acid and heat gently. The colour becomes brownish. The spectrum shows a band in the red between C and D, not far from the position of the band of methæmoglobin. The addition of a drop or two of ammonium sulphide causes no change in the spectrum, and this is a means of distinguishing acid-hæmatin from methæmoglobin. If more ammonium sulphide be added, hæmatin will be precipitated when the acid solution has been rendered neutral, and a further addition of ammonium sulphide or sodium hydrate will cause the hæmatin to be again dissolved, a solution of alkaline hæmatin being formed. This in its turn may be reduced by an excess of ammonium sulphide, and the spectrum of hæmochromogen may be obtained (Fig. 8).

(*f*) *Alkaline Hæmatin.*—To diluted blood add strong acetic acid and warm gently for a few minutes. Then, when the spectroscopic examination of a sample shows that acid-hæmatin has been formed, neutralize with sodium hydrate. A brownish precipitate of hæmatin is thrown down, which dissolves in an excess of sodium hydrate, giving a solution of alkaline hæmatin.

Or add sodium hydrate to blood directly, and warm for a couple of minutes after the colour has changed decidedly to brownish-black. The spectrum of alkaline hæmatin is a broad but ill-defined band just overlapping the D line, and situated chiefly to the red side of it (Fig. 8).

(*g*) *Hæmochromogen.*—To a solution of alkaline hæmatin add a drop or two of ammonium sulphide. The band near D disappears, and two bands make their appearance in the green (Fig. 8).

(*h*) *Hæmatoporphyrin.*—Put some strong sulphuric acid in a test-tube. Add a few drops of blood, agitate the test-tube till the blood dissolves, and examine the purple liquid, diluting it, if necessary, with sulphuric acid. Its spectrum shows two well-marked bands, one just to the left of D, and the other midway between D and E (Fig. 8).

(3) **Guaiacum Test for Blood.**—A test for blood—much used in hospitals, and, indeed, a delicate one, but not always trustworthy unless certain precautions be taken—is the guaiacum test. A drop of freshly-prepared tincture of guaiacum is added to the liquid to be tested, and then ozonic ether (peroxide of hydrogen). If blood be present, the guaiacum strikes a blue colour. The decomposition of the peroxide by the blood seems to be due to the stroma of the cor-

puscles rather than to the pigment, and other 'oxygen-carriers'—*e.g.*, fresh vegetable protoplasm, milk, seminal fluid, and pus—will cause the same colour. The test is chiefly of value as a negative test. When the blue colour is *not* obtained, we have good evidence that blood is absent.

(4) **Quantitative Estimation of Hæmoglobin**—(*a*) By *Fleischl's Hæmometer* (Fig. 15).—Fill with distilled water that compartment *a'* of the small cylinder (above the stage) which is over the tinted wedge. Put a little distilled water into the other compartment *a*. Now prick the finger and fill one of the small capillary tubes with blood. See that none of the blood is smeared on the outside of the tube. Then wash all the blood into the water in compartment *a*, and fill it to the brim with distilled water. By means of the milled head *T* move the

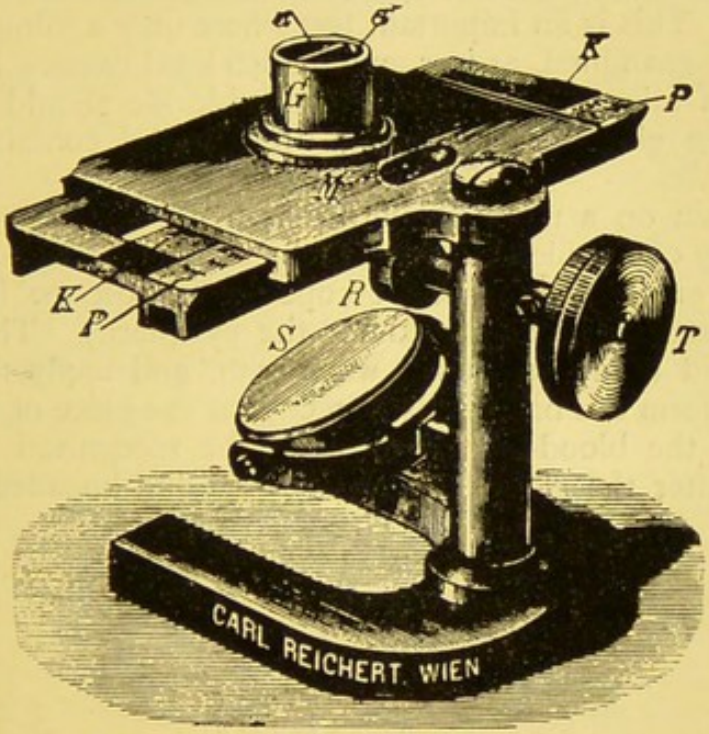


FIG. 15.—FLEISCHL'S HÆMOMETER.

tinted wedge *K* till the depth of colour is the same in the two compartments. The percentage of the normal quantity of hæmoglobin is given by the graduated scale *P*. For example, if the reading is 90, the blood contains 90 per cent. of the normal amount; if 100, it contains the normal quantity. The observations should be made in a dark room, the white surface *S*, arranged below the compartments *a* and *a'*, being illuminated by a lamp. Or the instrument may be placed in a small box, lighted by a candle. It is best that each result should be the mean of two readings, one just too large and the other just too small.

(*b*) *Hoppe-Seyler's Method.*—Two parallel-sided glass troughs are used. In one is put a standard solution of oxy-hæmoglobin of known strength, in the other a measured quantity of the blood to be tested. The latter is diluted with water until its tint appears the same as that

of the standard solution, when the troughs are placed side by side on white paper. From the quantity of water added it is easy to calculate the proportion of hæmoglobin in the undiluted blood. Greater accuracy is said to be obtained if the hæmoglobin in the standard solution and that of the blood are converted into carbonic oxide hæmoglobin by passing a stream of coal-gas through them.

(5) **Microscopic Test for Blood-pigment.**—Put a drop of blood on a slide. Allow the blood to dry or heat it gently over a flame, so as to evaporate the water. Add a drop of glacial acetic acid; put on a cover-glass, and again heat slowly till the liquid just begins to boil. Take the slide away from the flame for a few seconds, then heat it again for a moment; and repeat this process two or three times. Now let the slide cool, and examine with the microscope (high power). The small black, or brownish-black, crystals of hæmin will be seen (Plate I., 3). This is an important test where only a minute trace of blood is to be examined, as in some medico-legal cases. If a blood-stain is old, a minute crystal of sodium chloride should be added along with the glacial acetic acid. Fresh blood contains enough sodium chloride.

A blood-stain on a piece of cloth may first of all be soaked in a small quantity of distilled water, and the liquid examined with the spectroscope or the micro-spectroscope (a microscope in which a small spectroscope is substituted for the eye-piece). Then evaporate the liquid to dryness on a water-bath, and apply the hæmin test. Or perform the hæmin test directly on the piece of cloth. In a fresh stain the blood-corpuscles might be recognised under the microscope, after the cloth had been soaked and kneaded in a little glycerine.

CHAPTER II.

THE CIRCULATION OF THE BLOOD AND LYMPH.

THE blood can only fulfil its functions by continual movement. This movement implies a constant transformation of energy; and in the animal body the transformation of energy into mechanical work is almost entirely allotted to a special form of tissue, muscle. In most animals there exist one or more rhythmically contractile muscular organs, or hearts, upon which the chief share of the work of keeping up the circulation falls.

Comparative.—In Echinus a contractile tube connects the two vascular rings that surround the beginning and end of the alimentary canal, and plays the part of a heart. In the lower crustacea and in insects the heart is simply the contractile and generally sacculated dorsal bloodvessel; in the higher crustacea, such as the lobster, it is a well-defined muscular sac situated dorsally. A closed vascular system is the exception among invertebrates. In most of them the blood passes from the arteries into irregular spaces or lacunæ in the tissues, and thence finds its way back to the heart. Amphioxus, the lowest vertebrate, has a primitive lacunar vascular system; a contractile dorsal bloodvessel serves as arterial or systemic heart, a contractile ventral vessel as venous or respiratory heart. From the latter, vessels go to the gills. Fishes possess only a respiratory heart, consisting of a venous sinus, auricle, and ventricle. This drives the blood to the gills, from which it is gathered into the aorta; it has thence to find its way without further propulsion through the systemic vessels. Amphibians have two auricles and a single ventricle; reptiles, two auricles and two incompletely-separated ventricles. In birds and mammals the respiratory and systemic hearts are completely separated. The former, consisting of the right auricle and ventricle, propels the blood through the lungs; the latter, consisting of the left auricle and ventricle, receives it from the pulmonary veins, and sends it through the systemic vessels.

General View of the Circulation in Man.—The whole circuit

of the blood is divided into two portions, very distinct from each other, both anatomically and functionally—the respiratory or lesser circulation, and the systemic or greater circulation. Starting from the left ventricle, the blood passes along the systemic vessels—arteries, capillaries, veins—and, on returning to the heart, is poured into the right auricle, and thence into the right ventricle. From the latter it is driven through the pulmonary artery to the lungs, passes

FIG. 16.—DIAGRAM OF THE GENERAL COURSE OF THE CIRCULATION. RA, LA, right and left auricles; RV, LV, right and left ventricles.

through the capillaries of these organs, and returns through the pulmonary veins to the left auricle and ventricle. The portal system, which gathers up the blood from the intestines, forms a kind of loop on the systemic circulation. The lymph-current is also in a sense a slow and stagnant side-stream of the blood circulation; for substances are constantly passing from the bloodvessels into the lymph-spaces, and returning, although after a comparatively long interval, into the blood by the great lymphatic trunks.

Physiological Anatomy of the Vascular System.—The heart is to be looked upon as a portion of a bloodvessel which has

been modified to act as a pump for driving the blood in a definite direction. Morphologically it is a bloodvessel; and the physiological property of rhythmical contraction which belongs to the muscle of the heart in so eminent a degree is, as has been mentioned (p. 67), an endowment of bloodvessels in many animals that possess no localized heart. Even in some mammals contractile bloodvessels occur; the veins of the bat's wing, for example, beat with a regular rhythm, and perform the function of accessory hearts.

The whole vascular system is lined with a single layer of endothelial cells. In the capillaries nothing else is present; the endothelial layer forms the whole thickness of the wall. In young animals, at any rate, the endothelial cells of the capillaries are capable of contracting when stimulated; and changes in the calibre of these vessels can be brought about in this way. The walls of the arteries and veins are chiefly made up of two kinds of tissue, which render them distensible and elastic: non-striped muscular fibres and yellow elastic fibres. The muscular fibres are mainly arranged as a circular middle coat, which, especially in the smaller arteries, is relatively thick. One conspicuous layer of elastic fibres marks the boundary between the middle and inner coats. In the larger arteries elastic laminæ are also scattered freely among the muscular fibres of the middle coat. The outer coat is composed chiefly of ordinary connective tissue. The veins differ from the arteries in having thinner walls, with the layers less distinctly marked, and containing a smaller proportion of non-striped muscle and elastic tissue; although in some veins, those of the pregnant uterus, for instance, and the cardiac ends of the large thoracic veins, there is a great development of muscular tissue. Further, and this is of prime physiological importance, valves are present in many veins. These are semilunar folds of the internal coat projecting into the lumen in such a direction as to favour the flow of blood towards the heart, but to check its return. In some veins, as the venæ cavæ, the pulmonary veins, the veins of most internal organs, and of bone, there are no valves; in the portal system they are rudimentary in man and the great majority of mammals.

The valves are especially well marked in the lower limbs, where the venous circulation is uphill. When a valve ceases to perform its function of supporting the column of blood between it and the valve next above, the foundation of varicose veins is laid; the valve immediately below the incompetent one, having to bear up too great a weight of blood, tends to yield in its turn, and so the condition spreads. The smallest veins, or venules, are very like the smallest arteries, or arterioles, but somewhat wider and less muscular. The transition from the capillaries to the arterioles and venules is not abrupt, but may be considered as marked by the appearance of the non-striped muscular fibres, at first scattered singly, but gradually becoming closer and more numerous as we pass away from the capillaries, until at length they form a complete layer.

In the heart the muscular element is greatly developed and differentiated. Both histologically and physiologically the fibres seem to stand between the striated skeletal muscle and the smooth muscle. In the mammal the cardiac muscular fibres are made up of short oblong cells, devoid of a sarcolemma, often branched, and arranged in anastomosing rows. Each cell has a single nucleus in the middle of it. The fibres are transversely striated, but the striæ are not so distinct as in skeletal muscle. Many fibres pass from one auricle to the other, and from one ventricle to the other. The auricles and ventricles are also, in some mammals at least, connected in early life by muscular tissue; and even in the adult traces of this connection may persist (Plate I., 4).

In the frog's heart the muscular fibres are spindle-shaped, like those of smooth muscle, but transversely striated, like those of skeletal muscle. From the sinus to the apex of the ventricle there is a continuous sheet of muscular tissue.

The problems of the circulation are partly physical, partly vital. Some of the phenomena observed in the blood-stream of a living animal can be reproduced on an artificial model; and they may justly be called the physical phenomena of the circulation. Others are essentially bound up with the properties of living tissues; and these may be classified as the vital or physiological phenomena of the circulation. The

distinction, although by no means sharp and absolute, is a convenient one—at least, for purposes of description; and as such we shall use it. But it must not be forgotten that the physiological factors play into the sphere of the physical, and the physical factors modify the physiological. Considered in its physical relations, the circulation of the blood is the flow of a liquid along a system of elastic tubes, the bloodvessels, under the influence of an intermittent pressure produced by the action of a central pump, the heart. But the branch of dynamics which treats of the movement of liquids, or hydrodynamics, is one of the most difficult parts of physics, and, in spite of the labours of many eminent men, is as yet so little advanced that even in the physical portion of our subject we are forced to rely chiefly on empirical methods. It would, therefore, not be profitable to enter here into mathematical theory, but it may be well to recall to the mind of the reader one or two of the simplest data connected with the flow of liquids through tubes:

Torricelli's Theorem.—Suppose a vessel filled with water, the level of which is kept constant; the velocity with which the water will escape from a hole in the side of the vessel at a vertical depth h below the surface will be $v = \sqrt{2gh}$, where g is the acceleration produced by gravity.* In other words, the velocity is that which the water would have acquired in falling in vacuo through the distance h. This formula was deduced experimentally by Torricelli, and holds only when the resistance to the outflow is so small as to be negligable. The reason of this restriction will be easily seen, if we consider that when a mass m of water has flowed out of the opening, and an equal mass m has flowed in at the top to maintain the old level, everything is the same as before, except that energy of position equal to that possessed by a mass m at a height h has disappeared. If this has all been changed into kinetic energy E, in the form of visible motion of the escaping water, then $E = \frac{1}{2}mv^2 = mgh$, *i.e.*, $v = \sqrt{2gh}$. If, however, there has been any sensible resistance to the outflow, any sensible friction, some of the potential energy (energy of position), will have been spent in overcoming this, and will have ultimately been transformed into the kinetic energy of molecular motion, or heat.

Flow of a Liquid through Tubes.—Next let a horizontal tube of uniform cross-section be fitted on to the orifice. The velocity of outflow will be diminished, for resistances now come into play. When the liquid flowing through a tube wets it, the layer next the wall of the tube is prevented by adhesion from moving on. The particles next

* *I.e.*, the amount added per second to the velocity of a falling body (g=32 feet).

this stationary layer rub on it, so to speak, and are retarded, although not stopped altogether. The next layer rubs on the comparatively slowly moving particles outside it, and is also delayed, although not so much as that in contact with the immovable layer on the walls of the tube. In this way it comes about that every particle of the liquid is hindered by its friction against others—those in the axis of the tube least, those near the periphery most—and part of the energy of position of the water in the reservoir is used up in overcoming this resistance, only the remainder being transformed into the visible kinetic energy of the liquid escaping from the open end of the tube.

If vertical tubes be inserted at different points of the horizontal tube, it will be found that the water stands at continually decreasing heights as we pass away from the reservoir towards the open end of the tube. The height of the liquid in any of the vertical tubes indicates the lateral pressure at the point at which it is inserted; in other words, the excess of potential energy, or energy of position, which at that point the liquid possesses as compared with the water at the free end, where the pressure is zero. If the centre of the cross-section of

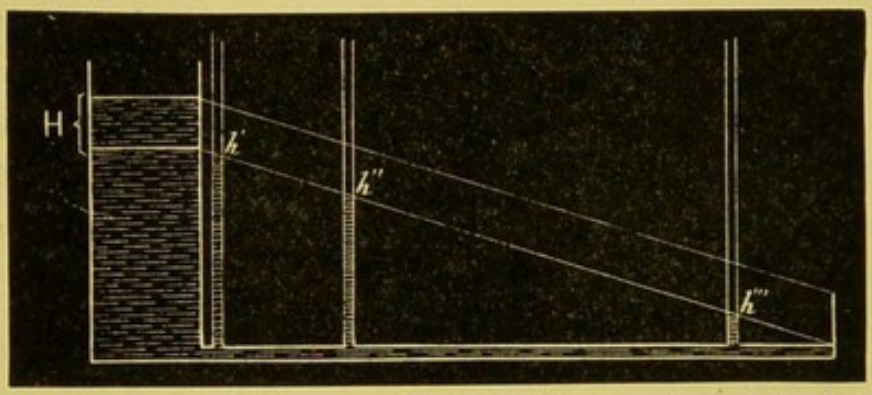


FIG. 17.—DIAGRAM TO ILLUSTRATE FLOW OF WATER ALONG A HORIZONTAL TUBE CONNECTED WITH A RESERVOIR.

the free end of the tube be joined to the centres of all the menisci, it will be found that the line is a straight line. The lateral pressure at any point of the tube is therefore proportional to its distance from the free end. Since the same quantity of water must pass through each cross-section of the horizontal tube in a given time as flows out at the open end, the kinetic energy of the liquid at every cross-section must be constant and equal to $\frac{1}{2}mv^2$, where v is the mean velocity (the quantity which escapes in unit of time divided by the cross-section) of the water at the free end.

Just inside the orifice the total energy of a mass m of water is mgh; just beyond it at the first vertical tube, $mgh' + \frac{1}{2}mv^2$, where h' is the lateral pressure. On the assumption that between the inside of the orifice and the first tube, no energy has been transformed into heat (an assumption the more nearly correct the smaller the distance between it and the inside of the orifice is made), we have $mgh = mgh' + \frac{1}{2}mv^2$. *i.e.*, $\frac{1}{2}mv^2 = mg(h - h')$. In other words, the portion of the energy of position of the water in the reservoir which is transformed into the kinetic energy of the water flowing along the horizontal tube is measured by the difference between the height of the level of the

reservoir and the lateral pressure at the beginning of the horizontal tube—that is, the height at which the straight line joining the menisci of the vertical tubes intersects the column of water in the reservoir. Let H represent the height corresponding to that part of the energy of position which is transformed into the kinetic energy of the flowing water. H is easily calculated when the mean velocity of efflux is known. For $v = \sqrt{2gH}$ by Torricelli's theorem (since none of the energy corresponding to H is supposed to be used up in overcoming friction), or $H = \frac{v^2}{2g}$. At the second tube the lateral pressure is only h''. The sum of the visible kinetic and potential energy here is therefore $\frac{1}{2}mv^2 + mgh''$. A quantity of energy $mg\,(h' - h'')$ must have been transformed into heat owing to the resistance caused by fluid friction in the portion of the horizontal tube between the first two vertical tubes. In general the energy of position represented by the lateral pressure at any point is equal to the energy used up in overcoming the resistance of the portion of the path beyond this point.

Velocity of Outflow.—It has been found by experiment that v, the mean velocity of outflow, when the tube is not of very small calibre, varies directly as the diameter, and therefore the volume of outflow as the cube of the diameter. In fine capillary tubes the mean velocity is proportional to the square, and the volume of outflow to the fourth power of the diameter (Poiseuille). If, for example, the linear velocity of the blood in a capillary of 10 μ in diameter is $\frac{1}{2}$ mm. per sec., it will be four times as great (or 2 mm. per sec.) in a capillary of 20 μ diameter, and one-fourth as great (or $\frac{1}{8}$ mm. per sec.) in a capillary of 5 μ diameter, the pressure being supposed equal in all. The volume of outflow per second is obtained by multiplying the cross-section by the linear velocity. The cross-section of a circular capillary, 10 μ in diameter, is $\pi\,(5 \times \frac{1}{1000})^2 =$, say, $\frac{1}{12500}$ sq. mm. The outflow will be $\frac{1}{12500} \times \frac{1}{2} = \frac{1}{25000}$ cub. mm. per sec. The outflow from the capillary of 20 μ diameter would be sixteen times as much, from the 5 μ capillary only one-sixteenth as much. Some idea of the extremely minute scale on which the blood-flow through a single capillary takes place, may be obtained if we consider that for the capillary of 10 μ diameter a flow of $\frac{1}{25000}$ cub. mm. per sec. would scarcely amount to 1 cub. mm. in six hours, or to 1 cc. in 250 days.

When the initial energy is obtained in any other way than by means of a 'head' of water in a reservoir—say, by the descent of a piston which keeps up a constant pressure in a cylinder filled with liquid—the results are exactly the same. Even when the horizontal tube is distensible and elastic, there is no difference when once the tube has taken up its position of equilibrium for any given pressure, and that pressure does not vary.

Flow with Intermittent Pressure.—When this acts on a rigid tube, everything is the same as before. When the pressure alters, the flow at once comes to correspond with the new pressure. Water thrown by a force-pump into a system of rigid tubes escapes

at every stroke of the pump in exactly the quantity in which it enters, for water is practically incompressible, and the total quantity present at one time in the system cannot be sensibly altered. In the intervals between the strokes the flow ceases; in other words, it is intermittent. It is very different with a system of distensible and elastic tubes. During each stroke the tubes expand, and make room for a portion of the extra liquid thrown into them, so that a smaller quantity flows out than passes in. In the intervals between the strokes the distended tubes, in virtue of their elasticity, tend to regain their original calibre. Pressure is thus exerted upon the liquid, and it continues to be forced out, so that when the strokes of the pump succeed each other with sufficient rapidity, the outflow becomes continuous. This is the state of affairs in the vascular system. The intermittent action of the heart is toned down in the elastic vessels to a continuous steady flow.

The Beat of the Heart.—In the frog's heart the contraction can be seen to begin about the mouths of the great veins which open into the sinus venosus. Thence it spreads in succession over the sinus and auricles, hesitates for a moment at the auriculo-ventricular junction, and then with a certain suddenness invades the ventricle. In all probability the contraction wave is propagated without the intervention of nerves, from fibre to fibre of the muscular tissue, which, although presenting certain variations in its character in the different divisions of the heart and at their junctions, forms a more or less continuous sheet over the whole of the organ. This conclusion rests in part upon the observation that the delay of the wave at the auriculo-ventricular groove is much greater than it ought to be if the excitation were transmitted by nerves, since the velocity of the nerve-impulse is exceedingly great (p. 582); and the further observation that, when the ventricle is caused to contract by artificial stimulation of the auricle, this delay is appreciably greater when the stimulus is applied as far from the ventricle as possible than when it is applied as near to it as possible. In the mammalian heart the starting-point of the contraction is likewise the mouths of the veins opening into the auricles, which are richly provided with muscular fibres akin to those of the heart. But the wave advances so rapidly that it is difficult, if not impossible, to trace in its course a regular progress from base to apex, although the ventricular beat undoubtedly follows that of the auricle, and

the capillary electrometer indicates that, in a heart beating normally, the negative change associated with contraction begins at the base and then reaches the apex (p. 622).

It is not definitely known how in the mammal the beat of the ventricle is co-ordinated with that of the auricle. The alleged absence of muscular connection has led to a very general belief that the link is a nervous one; and certainly there is no dearth of nerves running between the auricles and the ventricles that might serve as such a bridge. But recent work makes it probable that the contraction wave spreads as in the frog's heart, along muscular fibres which, in the form of slender strands, interpenetrate the ring of fibrous tissue between the auricles and ventricles (Kent). For it has been shown that the ventricles (in the dog and cat) continue to beat in unison, even after any nerves connecting them have been almost certainly severed by extensive zig-zag incisions, so long as they are united by a narrow bridge of muscular tissue (Porter). The impulses, by means of which the co-ordination of the ventricles is achieved, are accordingly transmitted along the muscular fibres from one ventricle to the other. And if an excitation can travel in this way from ventricle to ventricle, it is natural to suppose that it can also do so from auricle to ventricle.

The most conspicuous events in the beat of the heart, in their normal sequence, are: (1) the auricular contraction or systole; (2) the ventricular contraction or systole; (3) the pause or diastole. The auricles, into which, and beyond which into the ventricles, blood has been flowing during the pause from the great thoracic veins, contract sharply. The contraction begins in the muscular rings that surround the orifices of the veins, so that these, destitute of valves as they are, are sealed up for an instant, and regurgitation of blood into them is prevented. The filling of the ventricles is thus completed; their contraction begins either simultaneously with the relaxation of the auricles or a little before it. The mitral and tricuspid valves, whose strong but delicate curtains have during the diastole been hanging down into the ventricles and swinging freely in the entering current of blood, are floated up as the intraventricular pressure begins to rise, so that, in the first moment of the sudden and powerful ventricular systole, the free edges of their segments come together, and the auriculo-ventricular orifices are completely closed (Fig. 68, p. 181). In the measure in which the pressure in the contracting ventricle increases, the contact of the valvular segments becomes

closer and more extensive; and their tendency to belly into the auricle is opposed by the pull of the chordæ tendineæ, whose slender cords, inserted into the valves from border to base, are kept taut, in spite of the shortening of the ventricle by the contraction of the papillary muscles. During the systole, the ventricles change their shape in such a way that their combined cross-section—which in the relaxed state is a rough ellipse with the major axis from right to left—becomes approximately circular, and they then form a right circular cone. As soon as the pressure of the blood within the contracting ventricles exceeds that in the aorta and pulmonary artery respectively, the semilunar valves, which at the beginning of the ventricular systole are closed, yield to the pressure, and blood is driven from the ventricles into these arteries.

The ventricles are more or less completely emptied during the contraction, which seems still to be maintained for a short time after the blood has ceased to pass out. The contraction is followed by sudden relaxation. The intraventricular pressure falls. The lunules of the semilunar valves slap together under the weight of the blood as it attempts to regurgitate, the corpora Arantii seal up the central chink, and the aorta and pulmonary artery are thus cut off from the heart. Then follows an interval during which the whole heart is at rest, namely, the interval between the end of the relaxation of the ventricles and the beginning of the systole of the auricles. This constitutes the pause. The whole series of events is called a cardiac cycle or revolution (see Practical Exercises, p. 176).

It will be easily understood that the time occupied by any one of the events of the cardiac cycle is not constant, for the rate of the heart is variable. If we take about 70 beats a minute as the average normal rate in a man, the ventricular systole will occupy about ·3 second; the ventricular diastole, including the relaxation, about ·5 second. The systole of the auricle is one-third as long as that of the ventricle.

This rhythmical beat of the heart is the ground phenomenon of the circulation. It reveals itself by certain tokens—sounds, surface-movements or pulsations, alterations of the pressure and velocity of the blood, changes of volume in parts—all periodic phenomena, continually recurring

with the same period as the heart-beat, and all fundamentally connected together. And if we hold fast the idea that when we take a pulse-tracing, or a blood-pressure curve, or a plethysmographic record, we are really investigating the same fact from different sides, we shall be able, by following the cardiac rhythm and its consequences as far as we can trace them, to hang upon a single thread many of the most important of the physical phenomena of the circulation.

The Sounds of the Heart.—When the ear is applied to the chest, or to a stethoscope placed over the cardiac region, two sounds are heard with every beat of the heart; they follow each other closely, and are succeeded by a period of silence. The dull booming 'first sound' is heard loudest in a region which we shall afterwards have to speak of as that of the 'cardiac impulse' (p. 79); the short, sharp, 'second sound' over the junction of the second right costal cartilage with the sternum.

There has been much discussion as to the cause of the first sound. That a sound corresponding with it in time is heard in an excised bloodless heart when it contracts, is certain; and therefore the first sound cannot be exclusively due, as some have asserted, to vibrations of the auriculo-ventricular valves when they are suddenly rendered tense by the contraction of the ventricles, for, of course, in a bloodless heart the valves are not stretched. Part of the sound must accordingly be associated with the muscular contraction, as such.

As we shall see (p. 557), the sound caused by a contracting muscle is probably, in part at least, a resonance tone of the ear; and the vibrations in the muscle which call forth this resonance tone are not necessarily produced by a series of regularly repeated contractions and relaxations. This lessens the difficulty of understanding how a simple non-tetanic contraction like that of the heart should give rise to a 'muscular' sound of definite pitch.

Further, the fact that the first sound is heard during the whole, or nearly the whole, of the ventricular systole is against the idea that it is exclusively due to the vibrations of membranes like the valves, which would speedily be damped by the blood and rendered inaudible. But there is undoubtedly a valvular as well as a muscular factor involved; and, indeed, there is reason to believe that the valvular note is the essen-

tial part of the sound, which perhaps acquires its peculiar booming character from the resonance tones of the ear, and possibly of the chest-wall, set up by the muscular contraction. Some observers have been able to distinguish in the first sound the valvular and the muscular elements, the former being higher in pitch than the latter, but a minor third below the second sound. Further, when the mitral valve is prevented from closing by experimental division of the chordæ tendineæ, or by pathological lesions, the first sound of the heart is altered or replaced by a 'murmur.' This evidence is not only important as regards the physiological question, but of great practical interest from its bearing on the diagnosis of cardiac disease. It may be added that the point of the chest-wall at which the first sound is most easily recognised is also the point at which a changed sound or murmur connected with disease of the mitral valve is most distinctly heard. The sound is, therefore, best conducted from the mitral valve along the heart to the point at which it comes in contact with the wall of the chest. Changes in the first sound connected with disease of the tricuspid valve are heard best, in the comparatively rare cases where they can be distinctly recognised, in the third to the fifth interspace, a little to the right of the sternum.

Sir Richard Quain has recently revived the theory that the first sound is due, not to the vibrations of the auriculo-ventricular valves, nor to the muscle-sound of the contracting ventricles, but to the impact of the ventricular blood on the semilunar valves at the moment of systole, and the resistance which it encounters as it passes through the orifices of the aorta and pulmonary artery. But although some of the facts which he cites seem to favour such a view, there are many difficulties in the way of its acceptance.

The second sound is caused by the vibrations of the semilunar valves when suddenly closed, 'the recoiling blood forcing them back, as one unfurls an umbrella, and with an audible check as they tighten' (Watson). The sharpness of its note is lost, and nothing but a rushing noise or bruit can be heard, when the valves are hooked back and prevented from closing. It is altered, or replaced by a murmur when the valves are diseased. As there is a mitral and a tricuspid factor in the first sound, so there is an aortic and a pulmonary factor in the second. The place where the

second sound is best heard (over the junction of the second right costal cartilage and sternum) is that at which any change produced by disease of the aortic valves is most easily recognised. The sound is conducted up from the valves along the aorta, which comes nearest to the surface at this point. Changes connected with disease of the pulmonary valves are most readily detected over the second left intercostal space near the edge of the sternum, for here the pulmonary artery most nearly approaches the chest-wall.

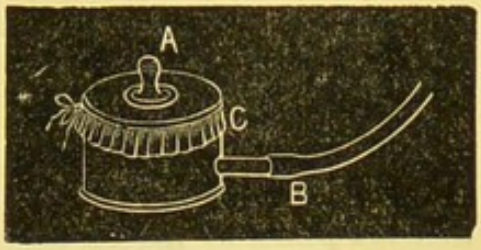


FIG. 18.—DIAGRAM OF MAREY'S CARDIOGRAPH.

A, knob attached to flexible membrane tied over end of metal box—the knob is placed over the apex-beat; C is the folded edge of the membrane; B is the tube communicating with a recording tambour.

The first sound is 'systolic'—that is, it occurs during the ventricular systole; the second is 'diastolic,' beginning at the commencement of the diastole.

The Cardiac Impulse.—A surface-movement is seen, or an impulse felt, at every cardiac contraction in various situations where the heart or arteries approach the surface. The pulsation, or **impulse**, of the heart, often styled the **apex-beat**, is usually most distinct to sight and touch in a small area lying in the fifth left intercostal space, between the mammary and the parasternal lines* and generally, in an adult, about an inch and a half to the sternal side of the former. It is due to the systolic hardening of the ventricles, which are here in contact with the chest-wall, the contact being at the same time rendered closer by their change of shape, and by a slight movement of rotation of the heart from left to right during the contraction (Practical Exercises, p. 182). Even in health the position of the impulse varies somewhat with the position of the body and the respiratory movements. In children it is usually situated in the fourth intercostal space. In disease its displacement is an important diagnostic sign, and may be very marked, especially in cases of effusion of fluid into the pleural cavity.

Various instruments, called **cardiographs**, have been devised

* The mammary line is an imaginary vertical line supposed to be drawn on the chest through the middle point of the clavicle. It usually, but not necessarily, passes through the nipple. The parasternal line is the vertical line lying midway between the mammary line and the corresponding border of the sternum

for magnifying and recording the movements produced by the cardiac impulse. Marey's cardiograph consists essentially of a small chamber, or tambour, filled with air, and closed at one end by a flexible membrane carrying a button, which can be adjusted to the wall of the chest. This *receiving* tambour is connected by a tube with a *recording* tambour, the flexible plate of which acts upon a lever writing on a travelling surface—a uniformly-rotating drum, for example — covered with smoked paper. Any movement communicated to the button forces in the end of the tambour to which it is attached, and thus raises the pressure of the air in it and in the recording tambour; the flexible plate of the latter moves in response, and the lever transfers the movement to the paper. The tracing, or cardiogram, obtained in this way shows a small elevation corresponding to the auricular systole, succeeded by a large abrupt rise corresponding to the beginning of the first sound, and caused by the ventricular systole. This ventricular elevation is the essential portion of the curve; it is alone felt by the palpating hand, and the auricular elevation is often absent from the cardiogram in man. The rise is maintained, with small secondary oscillations, for about ·3 of a second in a tracing from a normal man, then gives way to a sudden descent, that marks the relaxation of the ventricles, the beginning of the second sound, and the closure of the semilunar valves. An interval of about ·5 second elapses before the curve begins again to rise at the next auricular contraction.

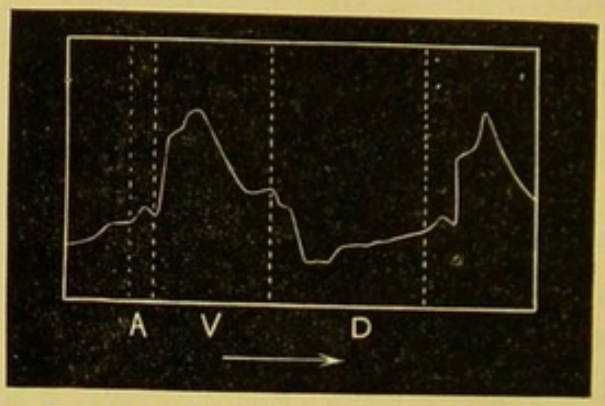


FIG. 19.—CARDIOGRAM TAKEN WITH MAREY'S CARDIOGRAPH.

A, auricular systole; V, ventricular systole; D, diastole. The arrow shows the direction in which the tracing is to be read.

Such was the interpretation which Chauveau and Marey put upon their tracings. Although neither their results nor their deductions from them have escaped the criticism of succeeding investigators, it is doubtful whether any adequate reason has been brought forward for discarding them, and Chauveau has recently furnished fresh proofs of their accuracy. The difficulties that beset the subject are great, for

the cardiogram is a record of a complex series of events. The very rapid variation of pressure within the ventricles, the change of shape of the heart, the slight change of position of its apex, if such occurs, must all leave their mark upon the curve, which is besides distorted by the resistance of the elastic chest-wall, the inertia of the recording lever, and the compression of the air in the connecting tubes. It is only by comparing in animals the cardiographic record with the changes of blood-pressure in the heart and arteries that our present degree of knowledge of the human cardiogram has been attained.

Endocardiac Pressure.—The function of the heart is to maintain an excess of pressure in the aorta and pulmonary artery sufficient to overcome the friction of the whole vascular channel, and to keep up the flow of blood. So long as the semilunar valves are closed, most of the work

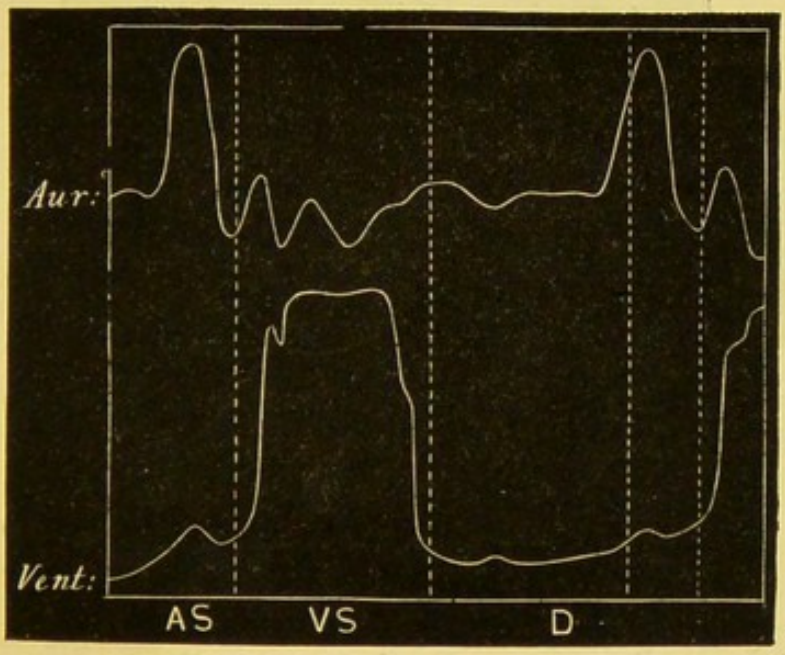


FIG. 20.—CURVES OF ENDOCARDIAC PRESSURE TAKEN WITH CARDIAC SOUNDS.

Aur., auricular curve; *Vent.*, ventricular curve; AS, period of auricular systole; VS, of ventricular systole; D, diastole.

of the contracting ventricles is expended in raising the pressure of the blood within them. At the moment when blood begins to pass into the arteries, nearly all the energy of this blood is potential; it is the energy of a liquid under pressure. During a cardiac cycle the pressure in the cavities of the heart, or the endocardiac pressure, varies from moment to moment, and its variations afford important data for the study of the mechanics of the circulation.

For the study of the endocardiac pressure, the ordinary mercurial manometer (p. 99) is unsuitable, since, owing to the relatively great amount of work required to produce a given displacement of the

mercury, it does not readily follow rapid changes of pressure, and the mercurial column, once displaced, continues for a time to execute vibrations of its own, which are compounded with the true oscillations of blood-pressure. But by introducing in the connection between the manometer and the heart a valve so arranged as to oppose the passage of blood towards the heart, while it favours its passage towards the manometer, the maximum pressure attained in the cardiac cavities during the cycle may be measured with considerable accuracy. When the valve is reversed the apparatus becomes a minimum manometer. In this way it has been found that in large dogs the pressure in the left ventricle may rise as high as 230 to 240 mm. of mercury, and sink as low as −30 to −40 mm.; while in the right ventricle it may be as much as 70 mm., and

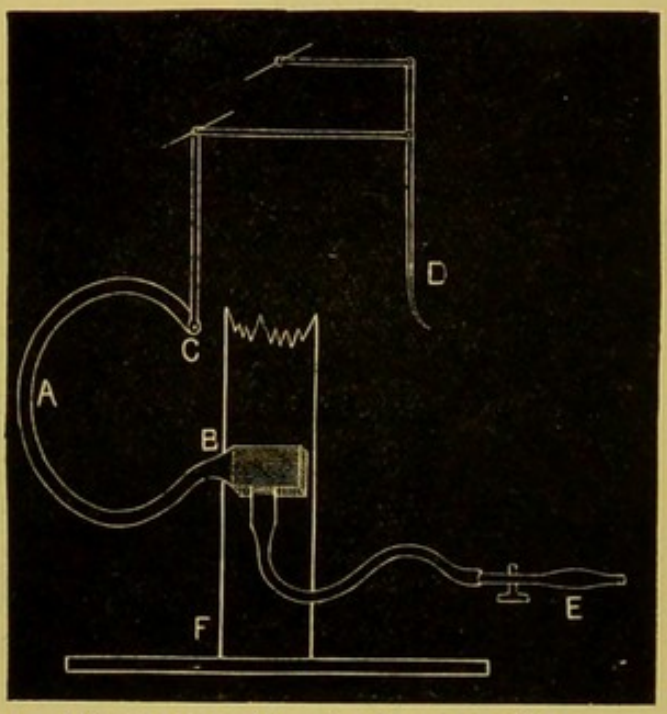


FIG. 21.—DIAGRAM OF FICK'S C-SPRING MANOMETER.

A, hollow spring filled with alcohol. Its open end B is covered with a membrane and is fixed to the upright F; the other end C is free to move, and is connected with a system of levers, which move the writing point D; E is the cannula, which is connected with the bloodvessel. When the pressure in the spring is increased it tends to straighten itself.

as little as −25 mm. In the right auricle a maximum pressure of 20 mm. of mercury has been recorded.

Our knowledge of the maximum and minimum pressure attained in the cavities of the heart, even if it were far more precise than it actually is, would only carry us a little way in the study of the endocardiac pressure-curve, for it would merely tell us how far above the base-line of atmospheric pressure the curve ascends, and how far below the base-line it sinks. To exhaust the problem, we require to have tracings of the exact form of the curve for each of the cavities of the heart, and to know the time-relations of the curves so as to be able to compare them with each other, and with the pressure-

curves of the great arteries and great veins. To obtain satisfactory tracings of the swiftly-changing endocardiac pressure is a task of the highest technical difficulty, and it is only in very recent years that it has been accomplished with any approach to accuracy by the use of elastic manometers, in which the blood-pressure is counterbalanced, not by the weight of a column of liquid, as in the mercurial manometer, but by the tension of an elastic disc or of a spring. One of the earliest of these was the now perhaps somewhat obsolete C-spring manometer of Fick (an adaptation of Bourdon's pressure-gauge), of which a diagram is given in Fig. 21. Probably the most perfect elastic manometers of the modern type are the improved instrument of Fick (Fig. 22), with the various modifications it has undergone in the hands of v. Frey and others, and especially the manometers of Hürthle.

Hürthle's spring manometer consists of a small drum covered with an indiarubber membrane, loosely arranged so as not to vibrate with a period of its own. The drum is connected with the heart or with a vessel, and the blood-pressure is transmitted to a steel spring

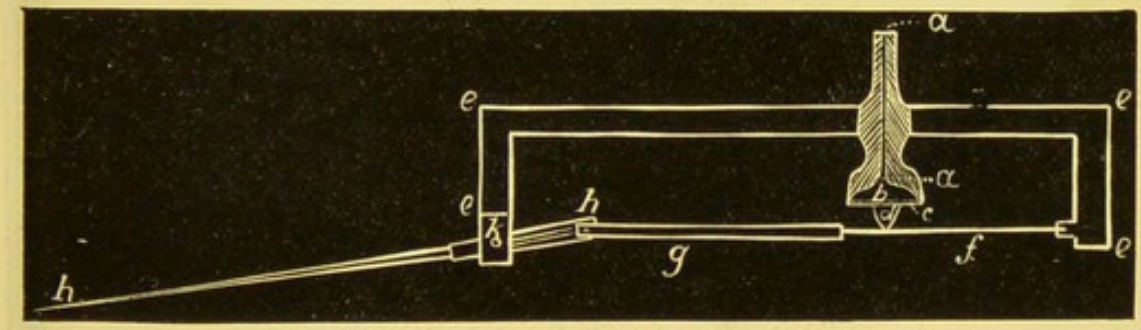


FIG. 22.—FICK'S ELASTIC MANOMETER.

a a is a metal piece tunnelled by a narrow canal of about 1 mm. in diameter, which enlarges below to a shallow saucer-shaped space *b*. The wide opening of *b* is covered by a thin piece of indiarubber *c*, to the centre of which an ivory button *d* is attached. The button presses on a strong steel spring *f*, which is attached at one end to the brass frame *e e*, and at the other, by means of an intermediate piece *g*, to the lever *h*; *b* is filled with a few drops of water, but the canal *a* contains only air. When *a* is connected with the interior of the heart or of an artery, the changes of pressure are transmitted to the spring, and recorded by the writing-point of the lever.

by means of a light metal disc fastened on the membrane. The spring acts on a writing lever. The instrument is so constructed that for a given change of pressure the quantity of liquid displaced is as small as possible, and it is on this that its capacity to follow sudden variations of pressure chiefly depends. The manometer is connected with the cavity of the heart by an appropriately-curved cannula of metal or glass, which, after being filled with some liquid that prevents coagulation (Practical Exercises, p. 185), is pushed through the jugular vein into the right auricle or ventricle, or through the carotid artery and aorta into the left ventricle. Some observers fill only the cannula with liquid, and leave the capsule of the elastic manometer and as much of the connections as possible full of air. Others fill the whole system with liquid. And around the question of the relative merits of 'transmission' by liquid and by air has raged

a controversy which does not even yet show signs of coming to an end, for there is reason to suppose that the character of the curves obtained is to some extent modified by the manner in which the pressure is transmitted.

Thus, the pressure-curve of the ventricle, according to Hürthle and those who, like him, have employed manometers with liquid transmission (Fig. 23), remains after the first abrupt rise, which undoubtedly corresponds to the ventricular systole, almost parallel to the abscissa line for a considerable time, and then descends somewhat less suddenly than it rose. This systolic 'plateau,' although usually broken by minor heights and hollows, perhaps due to inertia oscillations of the liquid or the recording apparatus, would indicate that the ventricular pressure, after reaching its maximum,

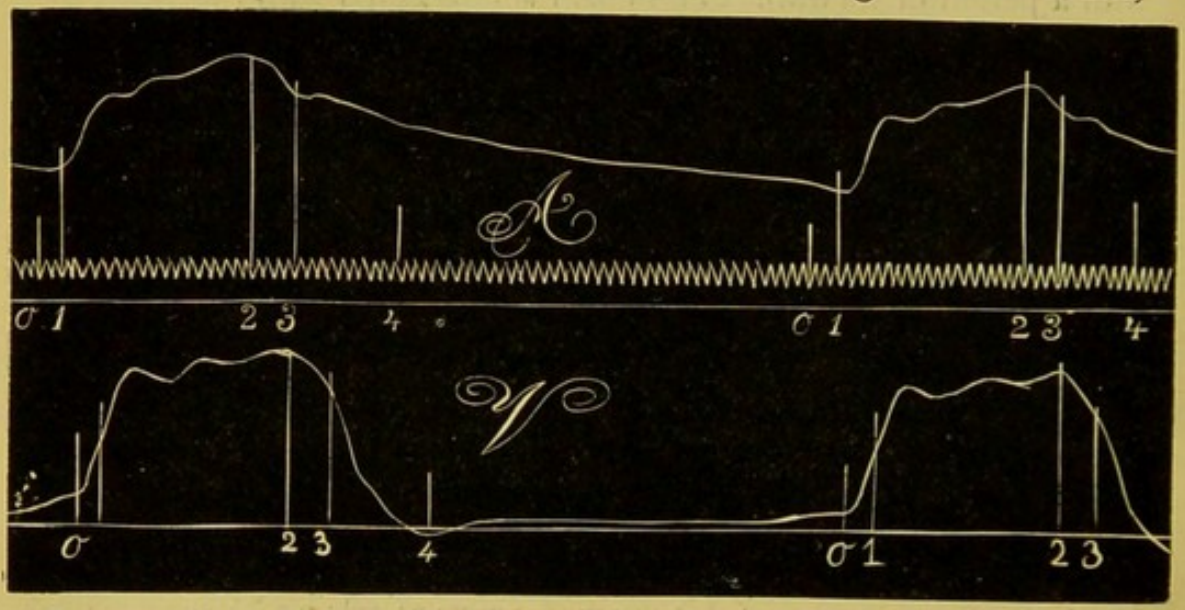


FIG. 23.—SIMULTANEOUS RECORD OF PRESSURE IN LEFT VENTRICLE (V) AND AORTA (A). (HÜRTHLE.)

The tracings were taken with elastic manometers; *o* indicates a point just before the closure of the mitral valve; 1, the opening of the semilunar valve; 2, beginning of the relaxation of the ventricle; 3, the closure of the semilunar valve; 4, the opening of the mitral valve. The ventricular curve shows a 'plateau.'

maintained itself there throughout the greater part of the systole. The tracings yielded by the best manometers with air transmission (Fig. 24) show the same suddenness in the first part of the upstroke and the last part of the descent—that is, the same abruptness in the beginning of the contraction and the end of the relaxation. But they differ totally in the intermediate portion of the curve, which, climbing ever more gradually as it nears its apex, remains

but a moment at the maximum, then immediately descending forms a 'peak,' and not a plateau.

While perhaps it is hardly possible at present to decide finally between the plateau and the peak, yet the bulk of the evidence goes to show that the former is not, as the advocates of the peak have claimed, an artificial phenomenon, but does in reality correspond to that continuation of the systole of the ventricle, that dogged grip, if we may so phrase it, which it seems to maintain upon the blood after the greater

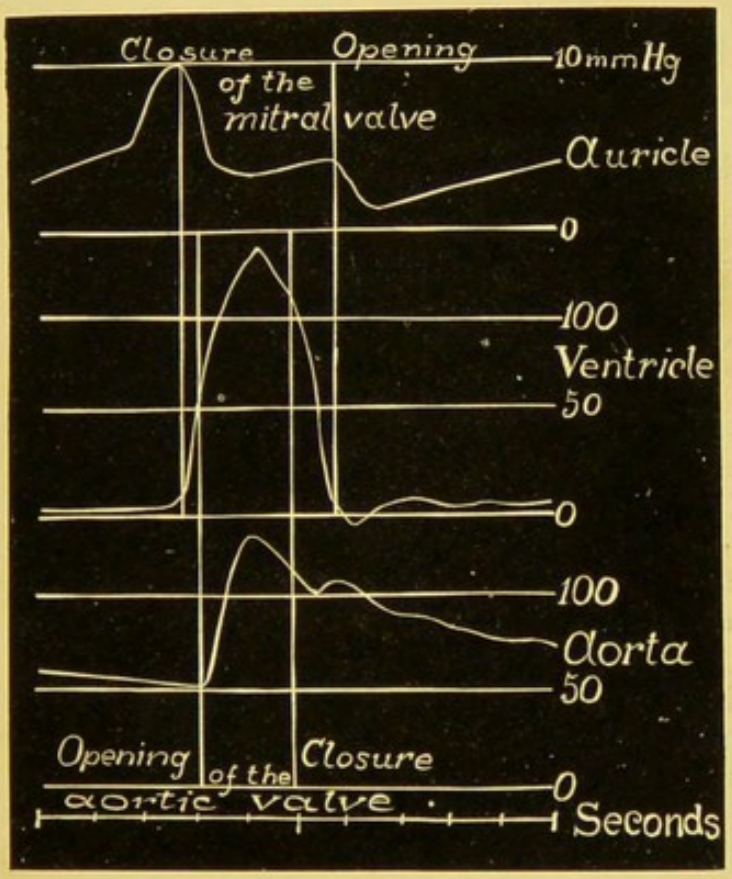


FIG. 24.—COMPARISON OF PRESSURE-CURVES OF LEFT AURICLE, LEFT VENTRICLE, AND AORTA. (V. FREY.)

Recorded by elastic manometers with air transmission. The ventricular curve shows a 'peak.'

portion of it has been expelled. This conclusion is essentially in accordance with the results of Chauveau and Marey, obtained long ago by means of their 'cardiac sound,' which was in principle an elastic manometer, though of somewhat faulty pattern (Fig. 25).

It consisted of an ampulla of indiarubber, supported on a framework, and communicating with a long tube, which was connected with a recording tambour. The ampulla was introduced into the heart through the jugular vein or carotid artery in the way already

described. Sometimes a double sound was employed, armed with two ampullæ, placed at such a distance from each other that when one was in the right ventricle the other was in the auricle of the same side. Each ampulla communicated by a separate tube in the common stem of the instrument with a recording tambour, and the writing points of the two tambours were arranged in the same vertical line. When any change in the blood-pressure takes place, the degree of compression of the ampullæ is altered, and the change is transmitted along the air-tight connections to the recording tambours. Simultaneous records of the changes in the blood-pressure in the right auricle and ventricle obtained in this way indicate a sudden rise of the auricular pressure corresponding with the auricular systole, followed by a sudden fall (Fig. 20). This is represented on the ventricular curve by a smaller elevation, which shows that the pressure in the ventricle has been raised somewhat by the blood driven into it from the auricle. Then follows immediately a great and abrupt increase of ventricular pressure, the result of the systole of the ventricle.

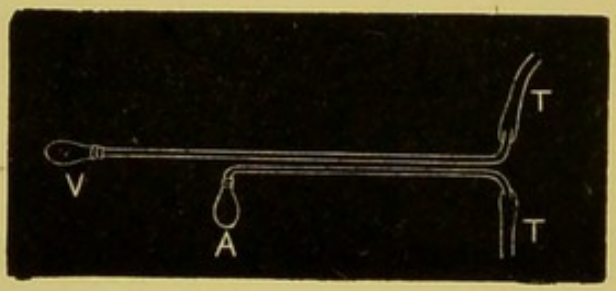


FIG. 25.—DIAGRAM OF CARDIAC SOUND FOR SIMULTANEOUS REGISTRATION OF ENDOCARDIAC PRESSURE IN AURICLE AND VENTRICLE.

A, elastic ampulla for auricle; V for ventricle; T, tubes connected with recording tambours.

The beginning of this elevation is synchronous with the beginning of the first sound; it remains for some time at the maximum, and then the curve suddenly sinks as the ventricle relaxes. On the descending limb there is a slight elevation, due, as Marey supposed, to the closure of the semilunar valves, which causes a better-marked and simultaneous elevation in the curve of aortic pressure when this is registered by means of a sound passed into the aorta through the carotid artery. Both the auricular and ventricular curves now begin again to rise slowly, showing a gradual increase of pressure as the blood flows from the great veins into the auricle, and through the tricuspid orifice into the ventricle. This slow rise continues till the next auricular systole.

It is probable that some of the smaller elevations on the curves of Chauveau and Marey, and particularly that which they associated with the closure of the semilunar valves, were due to the oscillations of their apparatus. For it is a remarkable fact that on most of the endocardiac pressure tracings of the best modern manometers, whether

the curves belong to the type of the peak or of the plateau, no sudden change of curvature, no nick, or crease, or undulation reveals the moment of opening or closure of any valve. But by experimentally graduating a pair of elastic manometers, and obtaining with them simultaneous records of the pressure in auricle and ventricle, we can calculate at what points of the ventricular curve the pressure is just greater than and just less than the pressure in the auricle. The first point, it is evident, will correspond to the instant at which the mitral or tricuspid valve, as the case may be, is closed, and the second to the instant at which it is opened. And in like manner, by comparing the pressure-curve of the aorta with that of the left ventricle, the moment of opening and closure of the semilunar valves may be determined (Figs. 23 and 24). According to the best observations, the closure of the semilunar valves takes place at a time corresponding to a point on the upper portion of the descending limb of the intraventricular curve.

The study of the curves of endocardiac pressure enables us to add precision in certain points to the description of the events of the cardiac cycle which we have already given, and, as regards the ventricles, to divide the cycle into four periods:

(1) *A period during which the pressure is lower in the ventricles than either in the auricles or the arteries, and the auriculo-ventricular valves are consequently open, and the semilunar valves closed. This is the period of 'filling' of the heart.*

(2) *A period, beginning with the ventricular systole, during which the pressure is rising abruptly in the ventricles, while they are as yet completely cut off from the auricles on the one hand and the arteries on the other by the closure of both sets of valves. This is the period during which the ventricles are, to use a homely but expressive phrase, 'getting up steam.'*

(3) *A period during which the pressure in the ventricles overtops that in the arteries, and the semilunar valves are open, while the auriculo-ventricular valves remain shut. This is the period of 'discharge.'*

(4) *A period during which the pressure in the ventricles is again less than the arterial, while it still exceeds the auricular pressure,*

and both sets of valves are closed. This is the period of rapid relaxation.

Of the four periods, the second and fourth are exceedingly brief. The third is relatively long and constant, being but slightly dependent on either the pulse-rate or the pressure in the arteries. The duration of the first period varies inversely as the frequency of the heart; with the ordinary pulse-rate it is the longest of all.

We have already said that a **negative pressure** may be detected in the cardiac cavities by means of a special form of mercurial manometer. This is confirmed by an examination of the tracings written by good elastic manometers, for the curves of both ventricles may often descend below the line of atmospheric pressure. The cause of this negative pressure has been much discussed. In part it may be ascribed to the aspiration of the thoracic cage when it expands during inspiration (p. 209). But since the pressure in a vigorously-beating heart may still become negative, though not to the same extent as before, when the thorax has been opened, and the influence of the respiratory movements eliminated, we must conclude that the recoil of the somewhat narrowed, or at least distorted, auriculo-ventricular rings, and of elastic structures in the walls of the ventricles, exerts of itself a certain feeble suction upon the blood.

The Pulse.—At each contraction of the heart a quantity of blood, probably varying within rather wide limits (p. 127), is forced into the already-full aorta. If the walls of the bloodvessels were rigid, it is evident (p. 74) that exactly the same quantity would pass at once from the veins into the right auricle. The work of the ventricle would all be spent within the time of the systole, and only while blood was being pumped out of the heart would any enter it. Since, however, the vessels are extensible, some of the blood forced into the aorta during the systole is heaped up in the arteries, beyond which, in the capillary tract, with its relatively great surface, the chief resistance to the blood-flow lies. The arteries are accordingly distended to a greater extent than before the systole, and, being elastic, they keep contracting upon their contents until the next systole over-distends them again. In this way, during the pause the walls of the arteries are executing a kind of elastic systole, and driving the blood on into the capillaries. The work done by the ventricle is, in fact, partly stored up as

potential energy in the tense arterial wall, and this energy is being continually transformed into work upon the blood during the pause, the heart continuing, as it were, to contract by proxy during its diastole. Thus, the blood progresses along the arteries in a series of waves, to which the name of 'blood-waves' or 'pulse-waves' may be given. Wherever the pulse-wave spreads it manifests itself in various ways—by an increase of blood-pressure, an increase in the mean velocity of the blood-flow, an increase in the volume of organs, and by the visible and palpable signs to which the name of pulse is commonly given in a restricted sense. The intermittence in the flow with which the pulse-wave is necessarily associated is at its height at the beginning of the aorta. In middle-sized arteries, such as the radial, it is still well marked, but it dies away as the capillaries are reached, and only under special conditions passes on into the veins.

The pulse was well known to the Greek physicians, and used by them to a certain extent as an indication in practical medicine. Harvey demonstrated with some clearness the relation of the pulse to the contraction of the heart, but Thomas Young was the first to form a proper conception of it as the outward token of a wave propagated from heart to periphery.

When the finger is placed over a superficial artery like the carotid, the radial or the temporal, a throb or beat is felt, which, without measurement, seems to be exactly coincident with the cardiac impulse. In certain situations the pulse can be seen as a distinct rhythmical rise and fall of the skin over the vessel. The throbbing of the carotid, especially after exertion, is familiar to everyone, and the beat of the ulnar artery can be easily rendered visible by extending the hand sharply on the wrist. When the pulse is felt by the finger, it is not the expansion, but the hardening of the wall of the vessel, due to the increase of arterial pressure, that is perceived; and even a superficial artery when embedded in soft tissues so that it cannot be compressed, gives no token of its presence to the sense of touch. Sometimes an artery is longitudinally extended by

the pulse-wave, and this extension may be far more conspicuous than the lateral dilatation. This is particularly seen when one point of the vessel is fixed and a more distal point offers some obstruction to the blood-flow, as at a bifurcation, or in an artery which has been ligatured and divided.

By means of the **sphygmograph**, the lateral movements of the arterial wall, or, rather, in man, the movements of the skin and other tissues lying over the bloodvessel, can be magnified and recorded. It would be very unprofitable to enumerate all the sphygmographs which ingenuity has invented and found names for. The first rude attempt to magnify the movements of the pulse was made by loosely

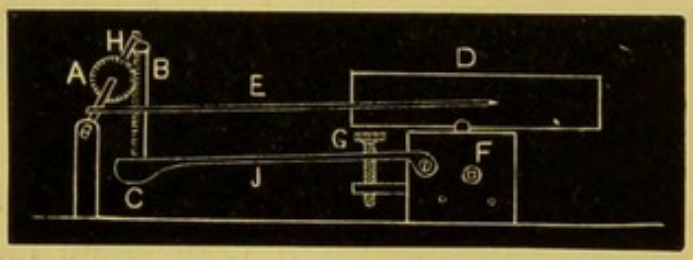


FIG. 26.—SCHEME OF MAREY'S SPHYGMOGRAPH.

A, Toothed wheel connected with axle H, and gearing into toothed upright **B**; C, ivory pad which rests over bloodvessel and is pressed on it by moving G, a screw passing through the spring J; E, writing-lever attached to axle H, and moved by its rotation; E writes on D, a travelling surface moved by clockwork F.

attaching a thin fibre of glass or wax to the skin with a little lard, in order to demonstrate the venous pulse which appears under certain conditions. Vierordt improved on this by using a counterpoised lever writing on a blackened surface. But the inertia of the lever was so great that the finer features of the pulse were obscured. In all modern sphygmographs there is a part, usually button-shaped, which is pressed over the artery by means of a spring, as in Marey's and Dudgeon's sphygmographs, or by a weight, or by a column of liquid. In Marey's instrument, the button acts upon a toothed rod gearing into a toothed wheel, to which a lever, or a system of levers, is attached. The lever has a writing-point which records the movement on a smoked plate, or a plate covered with smoked paper, drawn uniformly along by clockwork. Brondgeest's pansphygmograph is a particular application of Marey's tambours, for receiving

and registering the movement of the pulse, as is Marey's own 'sphygmograph of transmission.'

In a normal pulse-tracing (Fig. 27) the ascent is abrupt and unbroken; the descent is more gradual, and is interrupted by one, two, or even three or more, secondary wavelets. The most important and constant of these is the one marked 3, which has received the name of the dicrotic wave. Usually less marked, and sometimes absent, is the wavelet 2 between the dicrotic elevation and the apex of the curve. It is generally termed the predicrotic wave. Following the dicrotic wave are sometimes seen one or more ripples, which have been called by some elastic elevations.

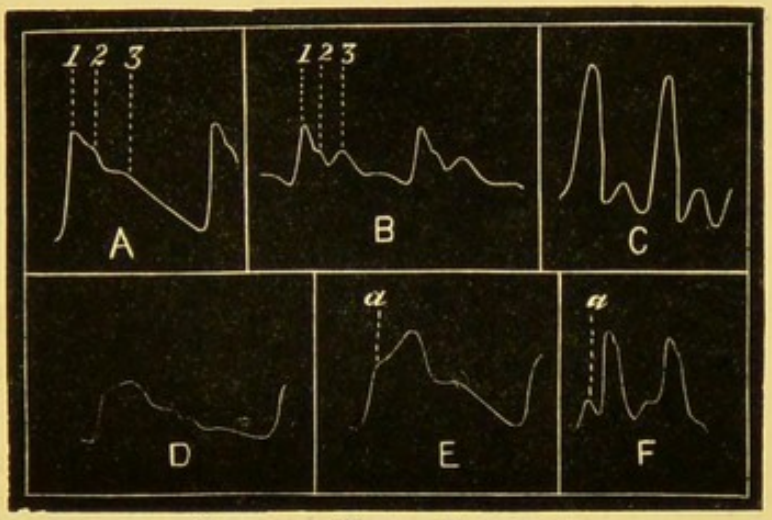


FIG. 27.—PULSE TRACINGS.

1, Primary elevation; 2, predicrotic or first tidal wave; 3, dicrotic wave. The depression between 2 and 3 is the dicrotic or aortic notch; 3 is better marked in B than in A. C, dicrotic pulse with low arterial pressure; D, pulse with high arterial pressure—summit of primary elevation in the form of an ascending plateau. E, systolic anacrotic pulse; the secondary wavelet *a* occurs during the upstroke corresponding to the ventricular systole. F, presystolic anacrotic pulse; *a* occurs just before the systole of the ventricle. In this rarer form of anacrotism, *a* may sometimes be due to the auricular systole when the aortic valves are incompetent.

In the explanation of the pulse-tracing, a fundamental fact to be borne in mind is the elasticity of the vessels. When an incompressible fluid like water is injected by an intermittent pump into one end of an elastic tube a wave is set up, which is transmitted to the other end of the tube. It is a positive wave—that is, it causes an increase of pressure and an expansion of the tube wherever it arrives; and if a series of levers be placed in contact with the tube, they will rise and sink in succession as the wave passes them. After the passage of this *primary wave* the walls of the tube, instead of coming instantly to rest in their original position, regain it by a series of oscillations, first shrinking too much, then expanding too much, but at each movement coming nearer to the position of equilibrium. Each vibration of the elastic wall is of course accompanied by a change of pressure in the contents of the tube. This change of pressure runs along the tube as a wave; and such waves, succeeding the primary one, may be called *secondary waves of oscillation.* These secondary waves will be set up in an elastic system whether the distal end of the system

be closed or open. But if it is closed, or sufficiently obstructed without being actually closed, secondary waves of another kind may also be generated, the primary wave on arriving at the distal end being reflected there. The reflected wave running back towards the central end may there again undergo reflexion, and pass out once more towards the distal end as a centrifugal, twice-reflected wave. When the liquid ceases to enter the tube at the end of the stroke, a wave of diminished pressure—a negative wave—is generated at the central end, and is propagated to the distal end, where it may be reflected just like the positive wave.

Although under certain conditions **the dicrotic wave** is so marked that the double beat of the pulse was discovered and named by physicians long before the invention of any sphygmograph, perhaps no physiological question has been more discussed or is less understood than the mechanism of its production. Two points, however, seem to be clear: (1) That it is a centrifugal, and not a centripetal, wave—that is to say, it travels away from, and not towards, the heart; (2) that the aortic semilunar valves have something to do with its origin.

It is not a centripetal wave, for in tracings taken at all parts of the arterial path, no matter what the distance from the heart and the capillaries (*e.g.*, the origin of the carotid and the radial at the wrist), the dicrotic wave is separated by the same interval from beginning of the primary elevation. This can only be explained by supposing that it has the same point of origin, and travels with the same velocity and in the same direction as the primary wave. It is not, then, a wave reflected directly from the peripheral distribution of the artery from which the pulse-tracing is taken. Nor does the contention of v. Frey and v. Kries, that it is a centrifrugal twice-reflected wave, seem more likely, although they have indeed by experiments on newly-killed animals been able to detect the traces of such waves. They suppose that these, reflected first from peripheral points at which the blood-flow is particularly obstructed (the bifurcations of the larger arteries, and the small arteries and capillaries in general), run towards the heart, and are then again reflected outwards from the semilunar valves.

Perhaps the explanation that best takes account of the facts and renders most clear the rôle of the semilunar valves

is somewhat as follows: When the systole abruptly comes to an end and the outflow from the ventricle ceases, the column of blood in the aorta tends still to move on in virtue of its inertia, and a diminution of pressure, accompanied by a corresponding contraction of the aorta, takes place behind it, just as a negative wave is set up in the central end of the elastic tube when the stroke of the pump is over. At the same moment, and while the semilunar valves are still for an instant incompletely closed, the diminution of pressure in the beginning of the aorta is intensified by the aspiration of the relaxing ventricle, which sucks the blood back against the valves, and draws them a little way into its cavity. A negative wave, therefore—a wave of diminished pressure, represented in the pulse-curve by the 'aortic notch'—travels out towards the periphery. The diminution of pressure is quickly followed by a rebound, as always happens in an elastic system, the recoiling blood meets the closed semilunar valves, the aorta expands again, and the expansion is propagated once more along the arteries as the dicrotic elevation.

Of the origin and significance of the predicrotic wave we know so little that it would not be profitable to discuss it. It seems, however, to be a secondary wave of oscillation. The so-called elastic oscillations (Landois) are probably due, in large part at least, to vibrations of the recording apparatus.

When the semilunar valve becomes incompetent in disease, or is rendered insufficient in animals by the artificial rupture of one or more of its segments, the dicrotic wave, as will be readily understood from the manner in which it is produced, either disappears altogether or is markedly enfeebled. But apart from any anatomical lesion or functional defect in the aortic valves, the prominence of the wave varies with a great number of circumstances, some of which are in a measure understood, while others remain obscure. It varies in particular with the abruptness of discharge of the ventricle and the extensibility of the arteries. The conditions are usually favourable when the arterial pressure is low, for the blood then passes quickly from the ventricle into the arteries, which, already only moderately tense, are easily dilated by the primary wave, then sharply collapse, and are again abruptly distended when the dicrotic wave arrives. And, in fact, an exaggeration of the dicrotic wavelet may be artificially produced by nitrite of amyl (Fig. 70, p. 183), a drug which lessens the blood-pressure by dilating the small

arteries, or by muscular exercise (Fig. 69, p. 183), running, for instance, which is supposed to lower the arterial pressure, partly by dilatation of the muscular and cutaneous arterioles, and partly by accelerating the venous flow (p. 121). The increase in the pulse-rate may also have something to do in this case with the exaggeration of the dicrotism, which is very frequently, although by no means invariably, associated with a rapidly-beating heart, and therefore is often seen in fever. On the other hand, in certain diseases associated with a high arterial pressure the dicrotic elevation almost disappears. Atheromatous arteries, being very inextensible, do not allow a dicrotic pulse.

Since the pulse represents a periodical increase and diminution in the amount of distension of an artery at any point, the line joining all the minima of the pulse-curve will vary in its height above the base-line, or line of no pressure, according to the amount of permanent distension, *i.e.*, permanent blood-pressure, which the heart in any given circumstances is able to maintain. Any circumstance that tends to lessen the permanent distension will cause a fall of the line of minima, and any circumstance tending to increase the distension will cause that line to rise. If, for example, the arm be raised while a pulse-tracing is being taken from the wrist, the line of minima falls because the permanent pressure in the radial artery is diminished.

The **form of the pulse-curve** varies in the different arteries, and therefore in making comparisons the same artery should be used. When the wave of blood only enters an artery slowly, the ascending part of the curve will be oblique. This is normally the case in a pulse-curve of a distant artery, such as the posterior tibial. The height of the wave is also less than in an artery nearer the heart, such as the carotid, or even the axillary, where the primary elevation is relatively abrupt (Fig. 71, p. 183).

Anacrotic Pulse.—As a rule, the ascent of the tracing is unbroken by secondary waves, but in certain circumstances these may appear on it. This condition, which, when well marked at any rate, may be considered pathological, is called anacrotism (Fig. 27). It is seen when the discharge of the left ventricle into the aorta is slow and difficult—*e.g.*, in old people whose arteries have been rendered less extensible by the deposit of lime-salts in their walls (atheroma), and in cases where the orifice of the aorta has been narrowed from disease of the semilunar valves (aortic stenosis). Since these conditions are in general associated

with hypertrophy and dilatation of the left ventricle, the slow emptying of the ventricle is, perhaps, partly due to the greater quantity of blood which it contains.

In whatever way the delay in the emptying of the ventricle is brought about, the most probable explanation of the anacrotic pulse is that the delay affords time for one or more secondary waves to be developed in the arterial system before the summit of the curve has been reached, and that these are superposed upon the long-drawn primary elevation.

In aortic insufficiency, where the left side of the heart is never cut off entirely from the aorta, the auricular impulse is sometimes marked on the pulse-curve as a distinct elevation; and this gives rise to a peculiar kind of anacrotic pulse, especially in the arteries nearest the heart (Fig. 27, F).

Frequency of the Pulse.—In health, the working of the cardiac pump is so smooth and apparently so self-directed, that it needs a certain degree of attention to perceive that the rate of the stroke is not absolutely constant. It is, in reality, affected by many internal conditions and external influences.

At the end of fœtal life the rate is given as 144-133; from birth till the end of the first year, 140-123; from 10 to 15 years, 91-76; from 20 to 25 years, 73-69. It remains at this till 60 years, and increases again somewhat in old age.* At all ages the pulse is somewhat quicker in the female than in the male, the excess amounting to about 8 beats a minute. So that if we take the average rate for a man (in the sitting position) as 72, the average for a woman will be 80. The difference is partly due to the fact that the average man is taller than the average woman; and it is known that in persons of the same sex and age the pulse-rate has an inverse relation to the stature. But there may be, in

* It must be remembered that these numbers are merely averages. Some healthy individuals have a much slower pulse-rate than 72 per minute, and some a rate considerably greater. Thus, while the average pulse-rate (taken in the sitting position) of 87 healthy (male) students, whose ages ranged from 18 to 36 years, was 73, the extreme variation was from 54 to 98. In the standing position the average was 80, and the variations 64 to 105. In the supine position, average 69, and variations 48 to 98. After a short spell of muscular exercise (generally running up and down some flights of stairs) the average in the standing position was 119, the variations 75 to 164, and the average increase 32.

addition, a real sexual difference. The position of the body exercises a small, but relatively constant, influence on the rate, which is greater in the standing than in the sitting posture, and greater in the latter than in the recumbent position. And this is true even when muscular action is as far as possible eliminated by fastening the person to a board. The pulse is further affected by the respiratory movements, especially when they are exaggerated in forced breathing, being accelerated during each inspiration (p. 249). It is also increased by the taking of food, and especially of alcoholic stimulants, by muscular exercise, in fever and many other pathological conditions, and by a high external temperature. A warm bath, for example, causes a very distinct acceleration of the heart; and Delaroche found that in air at the temperature of 65° C. his pulse went up to 160. A cold bath may depress the pulse-rate to 60, or even less. During sleep it may fall to 50. It is greatly influenced by psychical events, and that in the direction either of an increase or a decrease. Finally, it ought to be remembered as of some practical importance that the pulse-rate in women and children, but particularly in the latter, is less steady than in men, and more apt to be affected by trivial causes. And it is a good general rule to let a short interval elapse after the finger is laid on the artery before beginning to count the pulse, so that the acceleration due to the agitation of the patient may have time to subside.

Various Characters of the Pulse.—Certain terms which have come down from the older medicine, and are still used clinically to describe various conditions of the circulation as investigated by feeling the pulse, must here be briefly touched on:

'Hard' pulse (*pulsus durus*). Here the mean blood-pressure is high, the vessels are considerably distended, and the pulse therefore feels hard. With a 'soft' pulse (*pulsus mollis*) the mean blood-pressure is low.

With a 'quick' pulse (*pulsus celer*) the artery is rapidly distended by the pulse-wave. With a 'slow' pulse (*pulsus tardus*) the distension is slow.

The terms 'strong' pulse (*pulsus fortis*) and 'weak' pulse (*pulsus debilis*) refer to the amount by which the pulse-wave increases the blood-pressure at the point.

'Large' pulse (*pulsus magnus*) and 'small' or 'thready' pulse

(*pulsus parvus*) refer to the increase in the quantity of blood which every pulse-wave causes in the vessel.

The 'force of the pulse' is a phrase which is often ambiguously used, sometimes apparently as synonymous with 'strength,' and sometimes with 'size,' as above defined. In fact, the quantitative information obtained by feeling the pulse with the finger, although more valuable for clinical purposes than anything that can be deduced from an ordinary sphygmographic record, is far inferior in precision to the qualitative notion which that time-honoured proceeding affords. The 'force of the pulse' does not necessarily correspond with the force of the heart. It depends partly on the suddenness with which the pulse-wave distends the artery, partly on the amount of this distension in relation to the previous permanent distension, and to some extent on the calibre of the vessel. Other things being equal, the pulse in a large vessel will feel stronger than that in a smaller vessel. This last factor accounts for the inequality in the force of the pulse which is not infrequently found between the two radials even of a healthy person.

Rate of Propagation of the Pulse-wave.—When pulse-tracings are taken simultaneously at two points of the arterial system unequally distant from the heart, by two sphygmographs whose writing-points move in the same vertical straight line, it is found that the ascent of the curve begins later at the more distant, than at the nearer point. Since waves like the pulse-wave travel with approximately the same velocity in different parts of an elastic system like the arterial 'tree,' this 'delay' must be due to the difference in the length of the two paths. The difference in length can be measured; the time-value of the 'delay' can be deduced from the rate of movement of the recording surface; dividing the length by the time, we arrive at the rate of propagation of the pulse-wave. The average rate has been found to be about 7 metres per second in man in the arteries of the upper limb, and 8 metres in those of the lower limb, the difference being due to the smaller distensibility of the latter. The mean velocity of the pulse-wave is about the same as the speed of a moderately fast Atlantic liner (say 17 miles an hour), but less than that of a wave of the sea in a strong gale. The velocity of the pulse-wave must not be confounded with that of the blood-stream itself, which is not one-thirtieth as great. A ripple passes over the surface of a river at its own rate—a

rate that is independent of the velocity of the current. The passage of the ripple is not a bodily transference of the particles of water of which at any given moment the wave is composed, but the propagation of a change of relative position of the particles. The mere fact that the ripple can pass up stream as well as down is sufficient to illustrate this. The pulse-wave does not, however, correspond in every respect to a ripple on a stream, for the bodily transfer of the blood depends upon the series of blood-waves which the heart sets travelling along the arteries. Every particle of blood is advanced, on the whole, by a certain distance with every pulse-wave in which for the time it takes its place. But no particle continues in the front of the pulse-wave from beginning to end of the arterial system. The 'delay' or 'retardation' of the pulse (the interval, say, between the beginning of the ascent of the carotid and radial curves) is practically constant in the same individual, not only in health, but also in most diseases. But the retardation is markedly increased when the pulse-wave has to pass through a portion of an artery whose lumen is either greatly widened (aneurism), or greatly constricted (endarteritis obliterans).

The velocity of the pulse-wave has sometimes been deduced by comparing a tracing of the cardiac impulse with a pulse-tracing taken at the same time from a distant artery. But, as we have seen in dealing with the action of the heart, the ventricle does not at the very beginning of its contraction acquire sufficient force to cause the opening of the semilunar valves. The pulse, therefore, even in the aorta, must lag behind the ventricular pulse; and the amount of this 'lag' must be subtracted from the total retardation. But since the aortic 'lag,' unlike the retardation between two arteries, varies greatly even in health, depending as it does on the arterial blood-pressure, this method of determining the velocity of the pulse-wave is not satisfactory.

The Blood-pressure Pulse.—In man it is only possible to trace the pulse-wave along the arteries by movements of the walls of the vessels transmitted through the overlying tissues. In animals the changes of pressure that occur in

the blood itself can be directly registered, and these changes may be spoken of as the blood-pressure pulse. At bottom, as already pointed out, the phenomenon is exactly the same as that we have been dealing with in our study of the external pulse. We are only now to follow, by a more direct, and in some respects a more perfect method, the same wave of blood along the same channel.

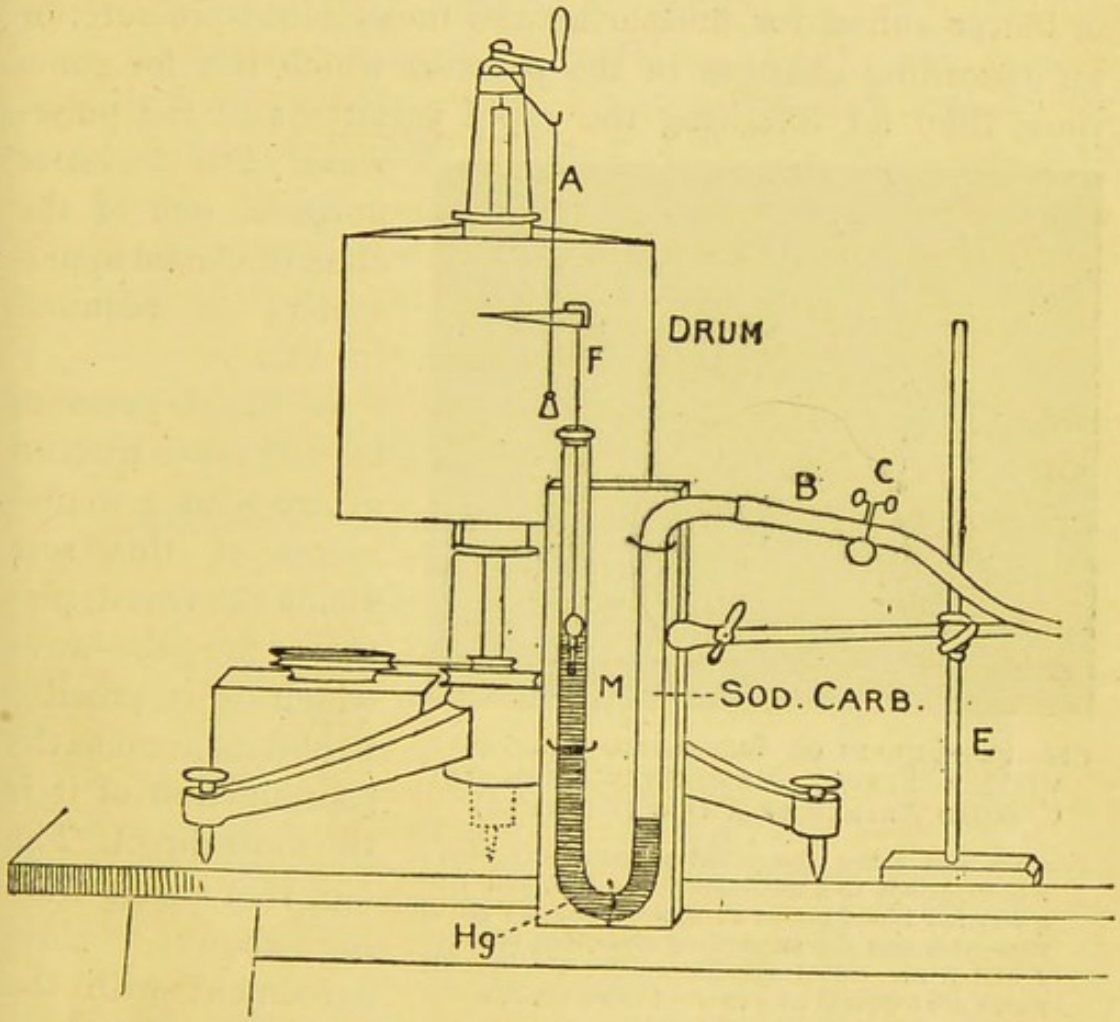


FIG. 28.—ARRANGEMENT FOR TAKING A BLOOD-PRESSURE TRACING.

M, manometer; Hg, mercury; F, float armed with writing-point; A, thread attached to a wire projecting from the drum and supporting a small weight—the thread keeps the writing-point in contact with the smoked paper on the drum; B is a strong rubber tube connecting the manometer with the artery; C, a pinchcock on the rubber tube, which is taken off when a tracing is to be obtained.

Measurement of the Blood-pressure.—Hales was the first to measure the blood-pressure. This he did by connecting a tall glass tube with the crural artery of a horse. The height to which the blood rose in the tube indicated the pressure in the vessel. Poiseuille, nearly half a century later, applied the mercury manometer, which had already been used in

physics, to the measurement of blood-pressure. Ludwig and others improved this method by making the manometer self-registering by means of a float in the open limb, supporting a style which writes on a revolving drum, the whole arrangement being called a kymograph. (For the method of taking a blood-pressure tracing, see p. 185.)

For reasons already mentioned the mercurial manometer is better suited for measuring the mean blood-pressure, or for recording changes in the pressure which last for some time, than for following the rapid variations of the pulse-wave. For the latter purpose, one of the class of elastic manometers is required (p. 82).

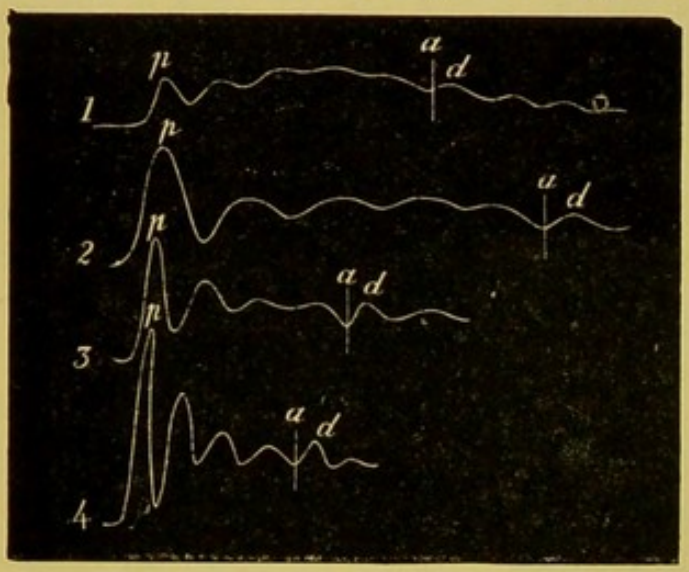


FIG. 29.—CURVES OF BLOOD-PRESSURE TAKEN WITH A SPRING MANOMETER FROM THE CAROTID ARTERY OF A DOG (HÜRTHLE).

When 1 was taken the blood-pressure was high; 2 corresponds to a medium, 3 to a low, and 4 to a very low blood-pressure; *p* is the primary elevation—this and the succeeding elevations between *p* and *a* are called systolic waves; the systolic waves are followed by a marked elevation *d*, which corresponds to the dicrotic wave.

A blood-pressure tracing taken from an artery with a manometer of this sort yields the truest picture of the pulse-wave which it is possible to obtain, because the reproduction of it is the most direct. The fact that such a tracing shows a close agreement with the trace of a good sphygmograph applied to the corresponding artery on the other side, is a striking proof of the general accuracy of the sphygmographic method for physiological purposes, and enables us to guide ourselves in transferring to man, in whom, of course, the sphygmograph can alone be used, the information derived from direct manometric observations in animals.

For the same reason it is unnecessary to discuss the manometric tracings, as regards the pulsatory phenomena, in all their details. It will be sufficient to say that while the form of the blood-pressure pulse-curve varies with the

mean blood-pressure, the dicrotic wave is always marked on it, preceded by one or more oscillations falling within the period of the systole, and followed by one or more within the period of the diastole. When the blood-pressure is low, the first or primary elevation is the highest of the whole curve (Fig. 29). When the blood-pressure is high, the maximum falls later, coinciding with one of the secondary systolic waves, but always preceding the dicrotic wave; and the curve assumes an anacrotic character.

That all the secondary oscillations, including the dicrotic wavelet, are of central, and not of peripheral origin, may be shown, just as in the sphygmographic method, by recording the blood-pressure simultaneously at two points of the arterial system at different distances from the heart—*e.g.*, in the crural and carotid arteries. The secondary waves are found, by measuring the tracings, to reach the more distal point later than the more central.

The increase of pressure during the systole, as indicated by the height of the primary elevation, is always very large, much larger than it appears in a tracing taken with a mercury manometer. In the rabbit this pulsatory variation is one-third to one-fourth of the minimum pressure. In the dog it is still greater, owing to the slower rate of the heart, and oftens amounts to 50 mm. of mercury, while under favourable conditions (low minimum pressure and slowly beating heart) the systolic increase of pressure may be actually more than double the minimum (Hürthle). Fick found also, by means of his spring manometer, that the pulsatory variations of blood-pressure were greater than the respiratory variations (p. 249), although in the records of the mercury manometer the reverse appears often to be the case. Landois, too, in the course of experiments in which a divided artery was allowed to spout against a moving surface, and to trace on it a sort of pulse-curve painted in blood (a hæmautogram as it is called), observed that the rate of escape of the blood was nearly 50 per cent. greater during the systole, than during the diastole, of the heart. The existence of the dicrotic wave on this tracing was long looked on as the best proof that it was not an artificial phenomenon.

The wave of increased pressure, as it runs along the arterial system, carries with it wherever it arrives an increase of potential energy. But this excess of potential energy is continually being worn down, owing to the friction of the vascular bed; and although in the comparatively

large arteries the loss of energy is not great, it rapidly increases as the arteries approach their termination, and begin to branch. For not only is the total surface, and therefore the friction, increased with every bifurcation, but the mere change of direction and division of the wave cannot take place without loss of energy. For this reason the fluctuations of blood-pressure are greater in the large arteries near the heart than in arteries smaller and more remote. In the wide and much-branched capillary bed the pulse-wave disappears altogether, and the blood-pressure becomes relatively constant or permanent. And it is for some purposes convenient to look upon the blood-pressure in the arteries as made up of a *permanent* element, with pulsatory oscillations superposed on it. Since no portion of the arterial system is more than partially emptied in the

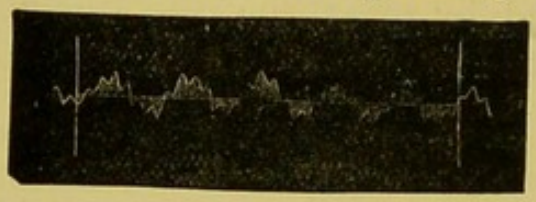


FIG. 30.—BLOOD-PRESSURE TRACING.
The horizontal straight line intersecting the curves is the line of mean pressure.

interval between two blood-waves, the minimum or permanent pressure is always positive—*i.e.*, always above that of the atmosphere. The only reason for this is that the beats of the heart succeed each other so rapidly that the successive waves overlap or 'interfere,' and are only separated at their crests.

If the heart is stopped while a blood-pressure tracing is being taken—and we shall see later on how this can be done (p. 134)—the minimum line of the tracing goes on falling towards the zero-line. When the heart begins beating again, the pressure-curve rises, not by a continuous ascent, but by successive leaps, each corresponding to a beat of the heart, and each overtopping its predecessor, till the old line of minimum or of mean pressure is again reached.

The **mean arterial blood-pressure** is the permanent pressure plus one-half of the average pulsatory oscillation. In a blood-pressure tracing the line of permanent pressure joins

all the minima ; the line of maximum pressure joins all the maxima ; the line of mean pressure is drawn between them in such a way that of the area included between it and the blood-pressure curve as much lies above as below it (Fig. 30). As has been said, a tracing taken with a mercury manometer gives approximately the mean blood-pressure. Each beat of the heart is represented on it by a single elevation of no great size, sometimes not amounting to more than one-twentieth of the height of the curve above the line of zero or atmospheric pressure. The small oscillations due to the heart-beat are superposed upon much longer, and often, as registered in this way, larger waves, caused by the movements of respiration. The line of mean pressure intersects the respiratory waves midway between crest and trough (Fig. 30).

So much having been said by way of definition, we have now to consider the amount of the mean arterial pressure, the variations which it undergoes, and the factors on which its maintenance depends.

As to its amount, it will be sufficiently accurate to say that in the systemic arteries of warm-blooded animals in general (including birds), and of man in particular, the mean pressure does not, under ordinary conditions, descend much below 100 mm. of mercury, nor rise much above 200 mm. ; while in cold-blooded animals it seldom exceeds 50 mm., and may fall as low as 20 mm.

It does not seem possible, at least with our present data, to further subdivide these two great groups ; nor do we know precisely whether the distinction depends mainly on morphological or mainly on physiological differences, whether, that is to say, the warm-blooded animal has a higher blood-pressure than the cold-blooded chiefly because its vascular system (and especially its heart) is anatomically more perfect, or because its heart beats faster and works harder. It may be that it is for both of these reasons that the birds, which in certain other respects are more nearly related to the reptiles than to the mammals, mount, as regards the pressure of the blood, into the mammalian class, and that a manometer in the carotid of a goose will rise as high, or almost as high, as in the carotid of a horse, a sheep, or a dog, while the pressure in the aorta of a tortoise is no higher than in the aorta of a frog. But we know that the mere average rate of the heart has of itself comparatively little influence on the blood-pressure within either group, for the heart of a rabbit

beats, on the average, very much faster than the heart of a dog, and yet the arterial pressure in the dog is certainly at least as great as in the rabbit. Nor does the size of the body seem to have any definite relation to the mean pressure, even in animals of the same species; and there is no reason to suppose that the pressure is materially less in the radial artery of a dwarf than in the radial artery of a giant.

In man the blood-pressure has been estimated by adjusting over an artery an instrument known as a sphygmomanometer or sphygmometer, which, in its most modern form, consists essentially of a hollow rubber pad or bag containing liquid or air, and connected with a metallic pressure gauge, graduated beforehand by comparison with a mercurial manometer. In using the sphygmometer of Hill and Barnard (Fig. 30*a*), the bag is inflated with air till the pulsation indicated by the index of the pressure gauge reaches a maximum. The mean pressure shown by the gauge at this point is approximately equal to the mean arterial pressure.

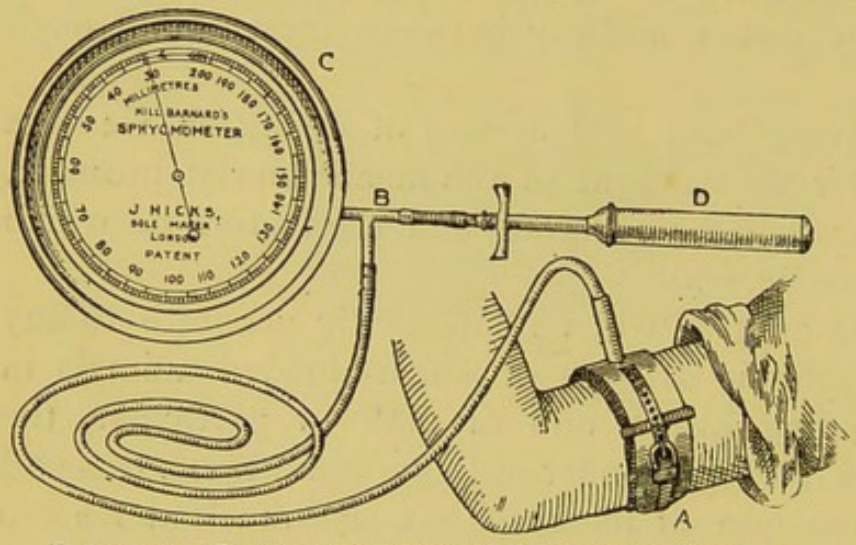


FIG. 30*a*.—SPHYGMOMETER OF HILL AND BARNARD.

It consists of a broad armlet, A, which is strapped round the upper arm. On the inside of the armlet is a thin rubber bag containing air, and connected by a T-tube, B, with a pressure gauge C, and a small compressing air-pump, D, fitted with a valve.

With this instrument it has been found that in the brachial artery the normal arterial pressure in most healthy young men is 110 to 130 mm. of mercury in the sitting posture. When the person is resting in the recumbent posture, the pressure may be as low as 95 mm. of mercury. Hard work and nervous strain may raise the pressure to 140 or 145 mm. of mercury. In the anterior tibial artery of a boy whose leg was to be amputated, the blood-pressure, measured by means of a manometer connected directly with the artery, was found to vary from 100 to 160 mm., according to the position of the body and other circumstances. In a woman sixty years old, in good health, the following readings were obtained with a sphygmomanometer:

June 28	126—130 mm. of mercury.	
,, 29	126—136	,,
Aug. 3	132—144	,,
,, 7	134—140	,,
,, 12	136—144	,, (ZADEK.)

Such measurements on man show that the mean blood-pressure under similar conditions in one and the same artery, and in one and the same individual, may vary for a considerable time only within comparatively narrow limits.

This relative constancy of the general arterial pressure is the result of a delicate adjustment between the work of the heart, the resistance of the vessels, and the volume of the circulating liquid. The quantity of the blood is tolerably steady in health, and considerable changes may be artificially produced in it (p. 165) without affecting the pressure in any great degree. On the other hand, the work of the heart and the peripheral resistance are highly variable and vastly influential. A narrowing of the arterioles throughout the body or in some extensive vascular tract increases the peripheral resistance; and if the heart continues to beat as before, the pressure must rise. If the arterioles are widened, while the heart's action remains unchanged, the pressure must fall. In like manner an increase or a decrease in the activity of the heart, in the absence of any change in the peripheral resistance, will cause a rise or a fall in the blood-pressure. But if a slowing of the heart is accompanied by an increase in the peripheral resistance, or a dilatation of the arterioles by an increase in the activity of the heart, the one change may be partially or completely balanced by the other, and the pressure may vary within narrow limits or not at all.

Not only is the mean pressure, as measured in a large artery, tolerably constant, but if recorded simultaneously in two arteries at different distances from the heart, it is seen to decrease very gradually so long as the arteries remain large enough to hold a cannula. It is nearly as high, for instance, in the crural artery of a dog as in the carotid. It is easy to see that this must be so, for the resistance of the arteries between the point where the arterioles are given off and the heart is only a small fraction of the total resistance of the vascular path; and we have said (p. 73) that the lateral pressure at any cross section of a system of tubes through which liquid is flowing is proportional to the resistance still to be overcome. This is also the reason why the pressure is always much lower in the pulmonary artery and right ventricle than in the aorta and left ventricle (only one-third to one-sixth as great), for the total resistance of the vascular path through the lungs is much less than that of the systemic circuit.

The Velocity-pulse.—We have seen that the blood is propelled through the arteries in a series of waves that travel from the heart towards the periphery. The particles in the front of the pulse-wave are constantly changing, but since every section of the arterial tree is successively distended,

every section contains more blood while the pulse-wave is passing over it than it contained immediately before. And since there is always a fairly free passage for this blood towards the periphery, there is a bodily transfer on the whole of a certain quantity with every wave.

The translation of the blood, instead of being entirely intermittent, as it would be in a rigid tube or in an elastic system with a slow action of the central pump, is to some extent constantly going on; for a portion of a blood-wave is always passing through every section of the arterial channel. Thus, we arrive at the same distinction as to the onward movement of the blood itself as we previously reached in regard to the blood-pressure, the distinction between the constant or permanent factor of the velocity and the periodic factor, which we may call the velocity-pulse.

The Velocity of the Blood.—By the velocity or rate of flow of a river we should mean, if the flow were uniform throughout the whole cross-section, the rate of movement of any given portion or particle of the water. If we could identify a portion of the water, we could determine the velocity by measuring the distance travelled over by that portion in a given time. If the velocity was uniform over the channel, we could predict the actual time which would be required to traverse any fractional part of the measured distance. If, however, the velocity of the current changed from point to point, then we could only deduce from our observation the *mean* rate of the river for the measured distance. To determine the actual rate for any given portion of this distance over which the rate was uniform, we should have to make a separate observation for this portion alone.

But as soon as we pass from an ideal frictionless river to an actual stream, in which the water at the bottom and near the banks flows more slowly than that in the middle and on the surface, we are in every case restricted to the notion of mean velocity. We may distinguish between the velocity of different parts of the current, between that of the mid-stream and the side current, the bottom and the surface layers; but when we consider the river as a whole, we take cognizance only of the mean or average velocity. And at any cross-section this may be defined as the volume of water passing per hour, or whatever the unit of time may be, divided by the cross-section of the current. It is evident that this does not enable us to determine the actual velocity of any given particle of the water at any given moment within a measured interval; nor does it tell us whether or not the average velocity of the current has itself undergone variations within the period of observation.

We have dwelt upon this point because the measurement of the velocity of the blood, to which we must now turn,

involves the same considerations. Within the smaller arteries, as the microscope shows us, and as we should in any case expect from what we know of fluid motion, the blood-current, apart from the periodical variations in its velocity, due to the action of the heart, varies in speed from point to point of the same cross-section. The layer next the periphery of the vessel, the so-called peripheral plasma-layer or Poiseuille's space, moves more slowly than the central portion, the axial stream. In fact, we must suppose that in the large as well as in the small vessels the layer just in contact with the vessel-wall is at rest, while the stratum internal to this slides on it and has its velocity diminished by the friction. The next layer again slides on the last, but since this is already in motion, its velocity is not so much diminished, and so on. The velocity must therefore increase as we pass towards the axis of the bloodvessel, and reach its maximum there (p. 168).

Again, the velocity must be altered wherever an alteration occurs in the width of the bed, that is, in the total cross-section of the vascular system; for since as much blood comes back in a given time to the right side of the heart as leaves the left side, the same quantity must pass in a given time through every cross-section of the circulation. Wherever the total section of the vascular tree increases, the blood-current must slacken; wherever it diminishes, the current must become more rapid. Now the total section increases as we pass from the heart along the branching arteries, and reaches its maximum in the capillary region. It gradually diminishes again along the veins, but never becomes so small as in the arterial tract. We must, therefore, expect the mean velocity to be greatest in the large arteries, less in the veins, and least in the arterioles, capillaries and venules. Although in strictness we are only at present concerned with the arteries, it will be well to consider here what a change of velocity at any part of the vascular channel really implies. To say that when the channel widens the velocity diminishes, is not to explain the meaning of this diminution. A diminution of velocity implies a diminution of kinetic energy, and it is necessary to know what becomes of the

energy that disappears. The stock of energy imparted by the contraction of the heart to a given mass of blood constantly diminishes as it passes round from the aorta to the right side of the heart, for friction is constantly being overcome and heat generated. This energy, as we have seen, exists in a moving liquid in two forms, potential and kinetic, the former being measured by the lateral pressure, the latter varying directly as the square of the velocity. Whenever the velocity, and therefore the kinetic energy, of a given mass of the blood is diminished without a corresponding increase in the potential energy, some of the total stock of energy must have been used up to overcome resistance (p. 73).

In a uniform, rigid, horizontal tube, as has been already remarked, the velocity (and consequently the kinetic energy) is the same at every cross-section of the tube, while the potential energy, represented by the lateral pressure, diminishes regularly along the tube. When the calibre of the tube varies, it is different. Suppose, for instance, that the liquid passes from a narrower to a wider part, the velocity must diminish in the latter. The kinetic energy of visible motion which has disappeared must have left something in its room. Here there are three possibilities: (1) The kinetic energy that has disappeared may be just enough to overcome the extra friction in the wider part of the tube due to eddies and consequent change of direction of the lines of flow; in this case the potential energy of a given mass of the liquid will be the same at the beginning of the wider part as in the narrower part. The lost kinetic energy will have been transformed into heat. (2) The kinetic energy which has disappeared may be greater than is enough to overcome the extra resistance; a portion of it must, therefore, have gone to increase the potential energy, and the lateral pressure will be greater in the wide than in the narrow part. (3) The lost kinetic energy may be less than enough to overcome the extra resistance; in this case both the lateral pressure and the velocity will be less in the wide than in the narrow part. It has been experimentally shown that when a narrow portion of a tube is succeeded by a considerably wider portion, and this again by a narrow part, case (2) holds; and the liquid may, under these conditions, actually flow from a place of lower to a place of higher lateral pressure.

In the vascular system the conditions are not the same. The widening of the bed which takes place as we proceed in the direction of the arterial current is not due to the widening of a single trunk, but to the branching of the channel into smaller and smaller tubes. In the larger arteries the increase of resistance is so gradual that both the potential

and the kinetic energy diminish only slowly, and the lateral pressure and velocity are not much less in the femoral artery than in the aorta or carotid. But in the capillary region the friction increases so much that although the velocity, and therefore the kinetic energy, is greatly less than in the arteries, the amount of kinetic energy lost is not upon the whole equivalent to the energy consumed in overcoming the extra resistance; the potential energy of the blood is also drawn upon, and the lateral pressure falls sharply in the capillary region, as well as the velocity. Where the capillaries open into the veins, the lateral pressure again sinks abruptly, while the velocity begins to increase, till in the largest veins it is probably about half as great as in the aorta.

Where does the extra kinetic energy of the blood in the veins come from? To say that the vascular channel again contracts as the blood passes from the capillaries into the veins, and that, since the same quantity must flow through every cross-section of the channel, the velocity must necessarily be greater in the narrower than in the wider part, does not answer the question. The greater portion of the kinetic energy of the arterial blood is, as we have seen, destroyed, or, rather, changed into an unavailable form, into heat, in the capillary region. The mean velocity of the blood in the capillaries is not more than $\frac{1}{500}$ to $\frac{1}{200}$ of the velocity in the aorta; the kinetic energy of a given mass of blood in the capillaries cannot therefore be more than $(\frac{1}{200})^2$, or $\frac{1}{40000}$ of its kinetic energy in the aorta. In the veins, taking the velocity at half the arterial velocity, the kinetic energy of the mass would be one-fourth of that in the aorta, or at least 10,000 times as great as in the capillary region. This extra kinetic energy comes partly from the transformation of some of the potential energy of the blood. The resistance in the veins is very small compared with that in the capillaries; less of the potential energy represented by the lateral pressure at the end of the capillary tract is required to overcome this resistance, and some of it is converted into the kinetic energy of visible motion, the lateral pressure at the same time falling somewhat abruptly. Contributory sources of kinetic energy in the veins are the aspiration caused by the

respiratory movements and the pressure caused by muscular contraction in general, which, thanks to the valves, always aids the flow towards the heart. From these two sources new energy is supplied, to reinforce the remnant due to the cardiac systole (p. 121).

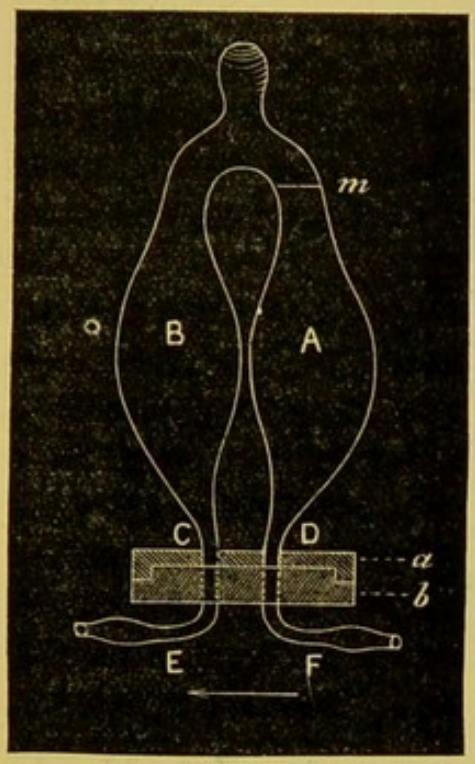


FIG. 31.—STROMUHR OF LUDWIG AND DOGIEL.

A, B, glass bulbs; *a*, a metal disc, to which A and B are attached, and which can be rotated on the disc *b*; E, F, cannulæ attached to *b*, and connected with the peripheral and central ends of a divided bloodvessel. At the beginning of the experiment, A and the junction between A and B are filled with oil; B is filled with normal saline or defibrinated blood: *a* being turned into the position shown in the figure, the blood passes through F and D into A, and the oil is forced into B. As soon as the blood has reached the mark *m*, the disc *a*, with the bulbs, is rapidly rotated, so that C is now opposite F. The blood now passes into B, and the oil is again driven into A. When the oil has reached D, reversal is again made, and so on.

Measurement of the Velocity of the Blood. — 1. *Direct Observation.*— (*a*) This method can be applied to transparent parts by observing the rate of flow of the corpuscles under the microscope. But it is only where the blood moves slowly, as in the capillaries, that the method is of use. (*b*) Part of the path of the blood through a large vessel may be artificially rendered transparent by the introduction of a glass tube, of approximately the same bore as the vessel (Volkmann). The tube is filled with salt solution, and the blood admitted by means of a stop-cock at the moment of observation. The time which the blood takes to pass from one end of the tube to the other is noted, and the length divided by the time gives the velocity of the blood in the tube. If the calibre of the tube is the same as that of the artery, this is also the velocity in the vessel; but if the calibre is different, a correction would have to be made. The method is not a good one, for the reason, among others, that the long tube introduces an extra resistance.

2. *Ludwig's Stromuhr.*—This instrument measures the quantity of blood which passes in a given time through the vessel at the cross-section where it is inserted. It consists of a U-shaped tube, with the limbs widened into bulbs, but narrow at the free ends, which are connected with a metal disc. By rotating the instrument, these ends can be placed alternately in communication with a cannula in the central, and another in the peripheral portion of a divided artery; or they can be placed so that none of the blood passes through the bulbs, but all goes by a short-cut. One limb of the instrument is

filled with oil, and the other with defibrinated blood. The limb containing the oil is first put into communication with the central end, and that containing the blood with the peripheral end of the artery. The blood from the artery rushes in and displaces the oil into the other limb, the defibrinated blood passing on into the circulation. As soon as the blood has reached a certain height, indicated by a mark, the instrument is reversed, and the oil is again displaced into the limb it originally occupied. This process is repeated again and again, the time from beginning to end of an experiment being carefully noted. The number of times the blood has filled a bulb in that period, the capacity of the bulb and the cross-section of the vessel being known, all the data required for calculating the velocity of the blood in the vessel have been obtained.

Suppose, for example, that the capacity of the bulb up to the mark is 5 c.c., and that it is filled twelve times in a minute, the quantity flowing through the cross-section of the artery is 1 c.c., or 1,000 cub. mm. per second. Let the diameter of the vessel be 3 mm., then its sectional area is $\pi \times \left(\frac{3}{2}\right)^2 = \frac{3{\cdot}14 \times 9}{4} = 7{\cdot}06$ sq. mm. The velocity is $\frac{1000}{7{\cdot}06} = 141$ mm. per second.

Various improvements in this method have been made, such as graphic registration of the reversals of the stromuhr.

3. A tube or box, in which swings a small pendulum, is inserted in the course of the vessel. The pendulum is deflected by the blood, and the amount of the deflection bears a relation to the velocity of the stream (Vierordt's *hæmatachometer;* Chauveau and Lortet's much more perfect *dromograph*) (Fig. 33).

4. *Pitot's Tubes.*—If two vertical tubes, *a* and *b*, of the form shown in Fig. 32, be inserted into a horizontal tube in which liquid is flowing in the direction of the arrow, the level will be higher in *a* than would be the case in an ordinary side-tube without an elbow; in *b* it will be lower. For the moving liquid will exert a push on the column in *a*, and a pull on that in *b*. The amount of this push and pull will vary with the velocity, so that a change in the latter will correspond to an alteration in the difference of level in the two tubes. Instruments on this principle have been constructed by Marey and Cybulski, the former registering the movements of the two columns of blood by connecting the tubes to tambours provided with writing levers, the latter by photography (Fig. 36).

5. *The electrical method*, described on p. 123, for the measurement of the circulation time, can also be applied to the estimation of the mean velocity of the blood between two cross-sections of the arterial path which are separated by a sufficient distance. For example, salt solution can be injected into the left ventricle or the beginning of the aorta, and the interval which it takes to reach a pair of electrodes in contact with, say, the femoral artery, determined. Knowing the distance between the point of injection and the electrodes, we can then calculate the mean velocity.

Of these methods, 3 and 4 are alone suited for the study of thevelocity -pulse, that is, the change of velocity occurring with every beat of the heart. The curves obtained by Chauveau's dromograph show a general agreement with blood-pressure tracings taken by a spring manometer, and with records of the external pulse obtained by a sphygmograph. There is a primary increase of velocity corresponding with the ventricular systole, and a secondary increase corresponding with the dicrotic wave (Fig. 37). Like all the other pulsatory phenomena, the velocity-pulse disappears in the capillaries, and is only present under exceptional circumstances in the veins.

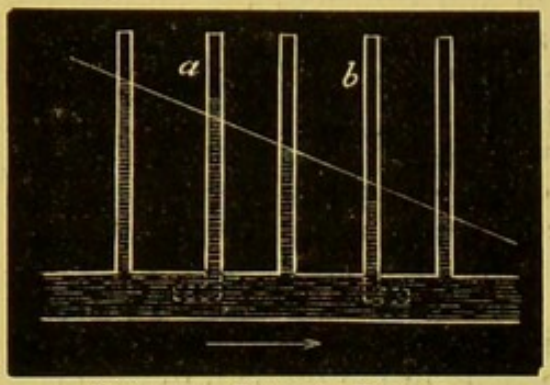


FIG. 32.—PITOT'S TUBES.

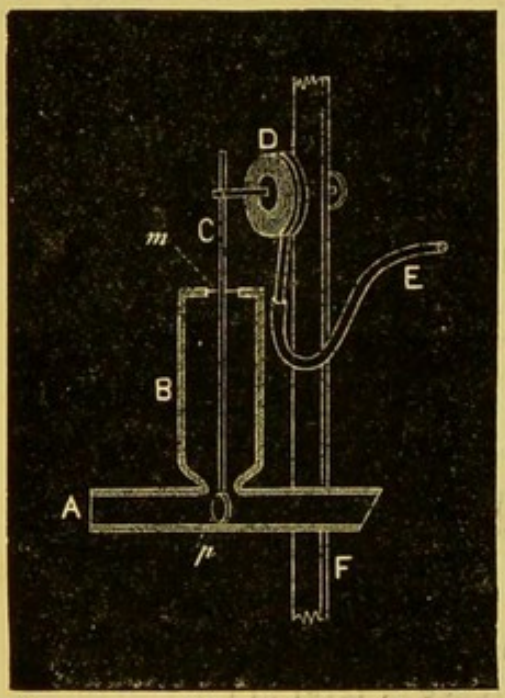


FIG. 33. — CHAUVEAU'S DROMOGRAPH.

A, tube connected with bloodvessel; B, metal cylinder in communication with A. The upper end of B has a hole in the centre, which is covered by a membrane, *m*, through which a lever, C, passes; C has a small disc *p*, at its end, which projects into the lumen of A, and is deflected in the direction of the blood-stream through A. The deflection is registered by a recording tambour in communication by the tube E with a tambour D, the flexible membrane of which is connected with the lever or pendulum C.

Fick, from a comparison of sphygmographic and plethysmographic tracings (p. 116), taken simultaneously from the radial artery and the hand, has demonstrated that in man the velocity-pulse exhibits the same general characters as in animals (Figs. 34 and 35). And v. Kries has confirmed Fick's conclusions by actual records of the velocity-pulse obtained by means of an arrangement called a gas tachograph (Fig. 38).

This consists of a plethysmograph connected with the tube of a gas-burner. When the part enclosed in the plethysmograph expands, air issues from the connecting tube, and

causes an increase in the height of the flame. When the part shrinks during diastole, air is drawn in from the flame, which is depressed. Since the speed of the blood in the

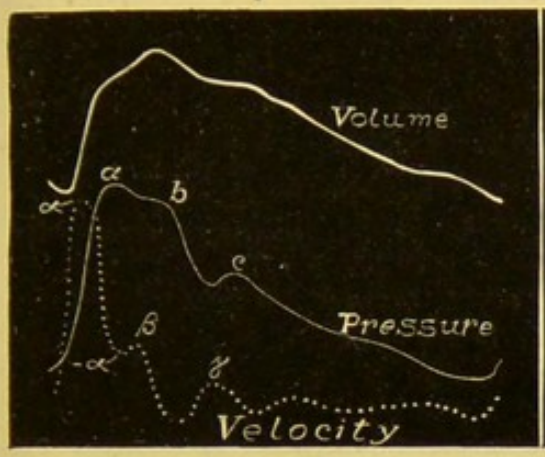


FIG. 34.

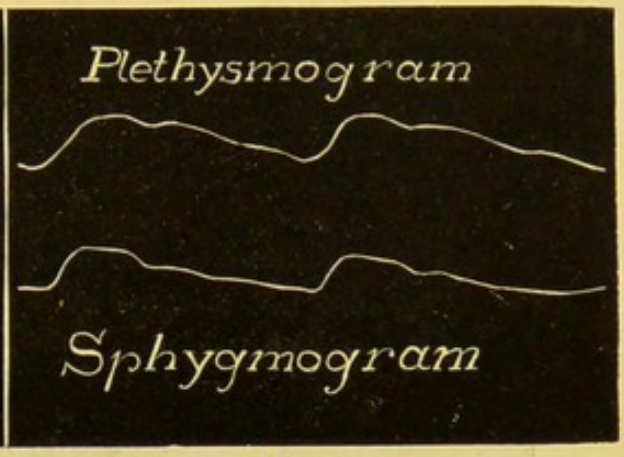


FIG. 35.

FIG. 34.—The highest of the three curves is a plethysmographic record taken from the hand; the second curve is a sphygmogram taken simultaneously from the corresponding radial artery; the lowest (interrupted) curve is the curve of velocity deduced from a comparison of the first two. (Fick.

FIG. 35.—Simultaneous plethysmographic and sphygmographic tracings.

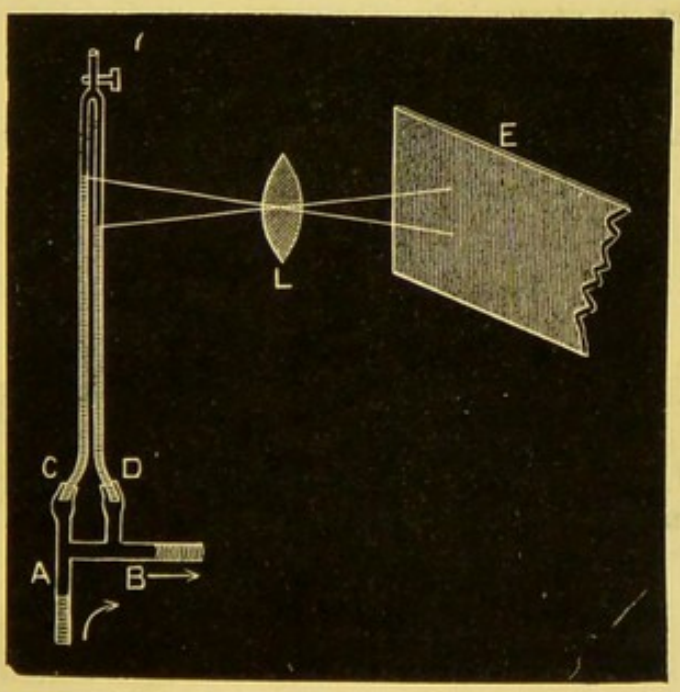


FIG. 36.—CYBULSKI'S ARRANGEMENT FOR RECORDING VARIATIONS IN THE VELOCITY OF THE BLOOD.

A, tube connected with central, B with peripheral end of divided bloodvessel. The blood stands higher in the tube C than in D. A beam of light passing through the meniscus in both tubes is focussed by the lens L on the travelling photographic plate E. The velocity at any moment is deduced from the height of the meniscus in the two tubes C and D.

veins may be considered constant during the time of an experiment, the rate at which the volume of the part alters

at any moment is a measure of the pulsatory change of velocity in the arteries of the part. And by photographing the movements of the flame on a travelling sensitive surface, the velocity-pulse is directly recorded.

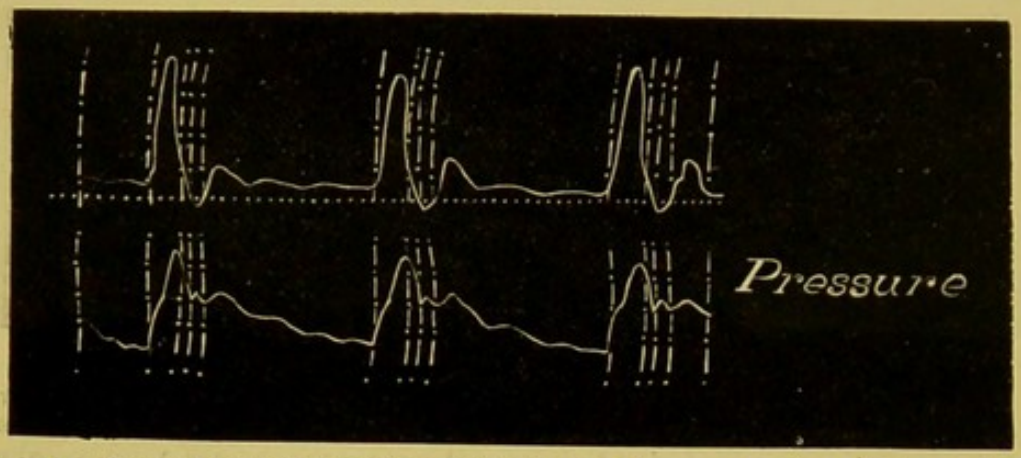


FIG. 37.—SIMULTANEOUS TRACINGS OF THE VELOCITY (UPPER CURVE) AND PRESSURE (LOWER CURVE). (LORTET.)

The tracings were taken from the carotid artery of a horse. The curve of velocity was obtained by the dromograph. The dicrotic wave is marked on it. The slightly curved ordinates drawn through the curves indicate corresponding points.

The mean velocity, like the mean blood-pressure, is more variable in the large arteries near the heart than in the smaller and more distant arteries. Dogiel found in measurements taken with the stromuhr (a good instrument for the

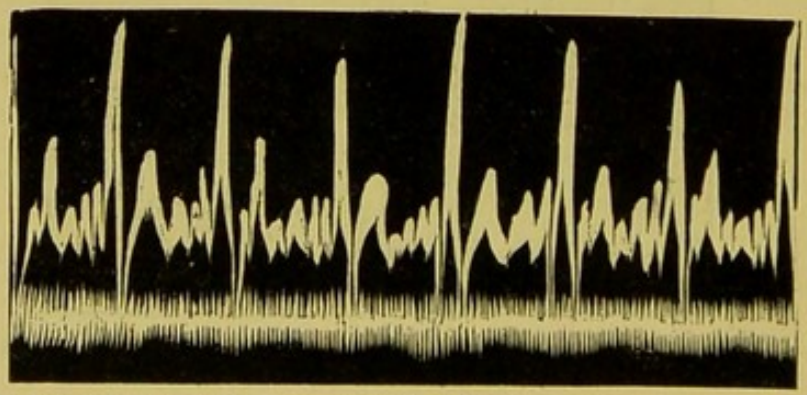


FIG. 38.—PHOTOGRAPHIC RECORD OF THE VELOCITY-PULSE OBTAINED BY THE GAS TACHOGRAPH (V. KRIES).

The upper curve is the photographic representation of the movements of the flame, and corresponds to the curve of velocity.

estimation of mean speed), within a period of two minutes, velocities ranging from over 200 mm. to under 100 mm. per

second in the carotid of the rabbit, and from over 500 mm. to less than 250 mm. in the carotid of the dog. Chauveau, with the dromograph, found the velocity in the carotid of a horse to be 520 mm. per second during systole, 150 mm. during diastole, 220 mm. during the period of the dicrotic wave.

It is probable, however, that if these numbers are at all accurate for bloodvessels in the immediate neighbourhood of the heart, there must be a rapid diminution in the velocity even while the arteries are still of considerable calibre. For it has been found by the electrical method that, in anæsthetized dogs at any rate, as is shown in the following table, the mean velocity between the origin of the aorta and the crural artery in the middle of the thigh is usually less than 100 mm. per second.

No. of experiment.	Body-weight in kilos.	Distance between point of injection and electrodes, in millimetres.	Average time between injection and arrival of the salt solution, in seconds.	Average pulse-rate per minute.	Average velocity per second, in millimetres.	Average distance traversed per heart-beat, in mm.
I.	34·55	420	4·62	105	90·9	51·9
II.	17·5	495	5·7	69	86·8	75·4
III.	14·99	400	5·0	102	80	47
IV.	10·32	470	7·12	74·5	72·9	58·7
V.	7·165	330	7·83	46·3 (weak beat)	42·1	54·5

In I. the injecting cannula was in the descending part of the thoracic aorta, in V. at the very origin of the aorta, and in II., III. and IV. in the left ventricle.

As to the speed of the blood in the arteries of man, our data are insufficient for more than a loose estimate. But it does not seem likely that the mean velocity of a particle of blood in moving from the heart to the femoral artery can exceed 150 mm. per second for the whole of its path. This would correspond to rather more than a third of a mile per hour. In the arch of the aorta the average speed may be twice as great. 'The rivers of the blood' are, even at their fastest, no more rapid than a sluggish stream. A red corpuscle, even if it continued to move with the velocity with which it set out through the aorta, would only cover

about 15 miles in twenty-four hours, and would require five years to go round the world.

The Volume-pulse.—When the pulse-wave reaches a part it distends its arteries, increases its volume, and gives rise to what may be called the volume-pulse. This may be readily recorded by means of a plethysmograph, an instrument consisting essentially of a chamber with rigid walls which enclose the organ, the intervening space being filled up with liquid (Fig. 39). The movements of the liquid are transmitted either through a tube filled with air to a recording tambour, or directly to a piston or float acting upon a writing lever. Special names have been given to plethys-

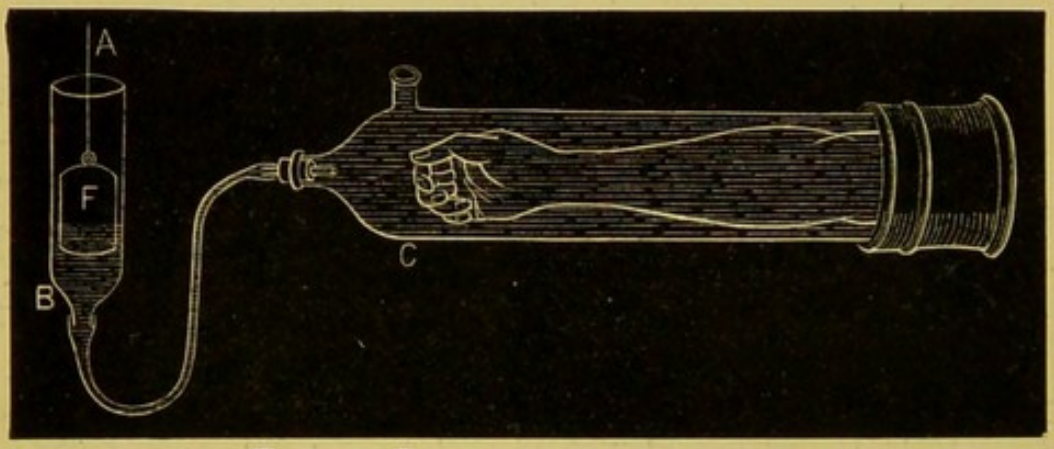


FIG. 39.—PLETHYSMOGRAPH FOR ARM.

F, float attached by A to a lever which records variations of level of the water in B, and therefore variations in the volume of the arm in the glass vessel C. Or the plethysmograph may be connected to a recording tambour. The tubulure at the upper part of C is closed when the tracing is being taken.

mographs adapted to particular organs; for example, Roy's oncometer for the kidney. The method has been successfully applied to the investigation of circulatory changes in man, a finger, a hand or an entire limb being enclosed in the plethysmograph. With a fairly sensitive arrangement, every beat of the heart is represented on the tracing by a primary elevation and a dicrotic wave. The general appearance of the curve is very similar to that of an ordinary pulse-tracing, though there are some differences of detail, especially in the time relations. A volume-pulse has been actually observed not only in limbs and portions of limbs, but also (in animals) in the spleen, kidney and brain, and other organs, and in the orbit. In the soft tissues of the mouth and

pharynx, too, a volume-pulse (the so-called cardio-pneumatic movement) can be detected by changes in the pressure of the air in the respiratory passages, which may even reveal themselves by a variation with each beat of the heart in the intensity of a note prolonged in singing, especially after fatigue has set in (Practical Exercises, p. 183).

Doubtless the weight of an organ would also show a pulse corresponding to the beat of the heart, if it could be isolated from the surrounding tissues (except for its vascular connections), and attached to a recording balance, as could probably be done with a kidney.

Further, it is possible that the temperature, at least of the superficial parts, is altered with every beat of the heart. For the amount of heat given off by the blood to the skin increases with its mean velocity, and, therefore, although the difference may not in general be measureable, more heat is presumably given off during the

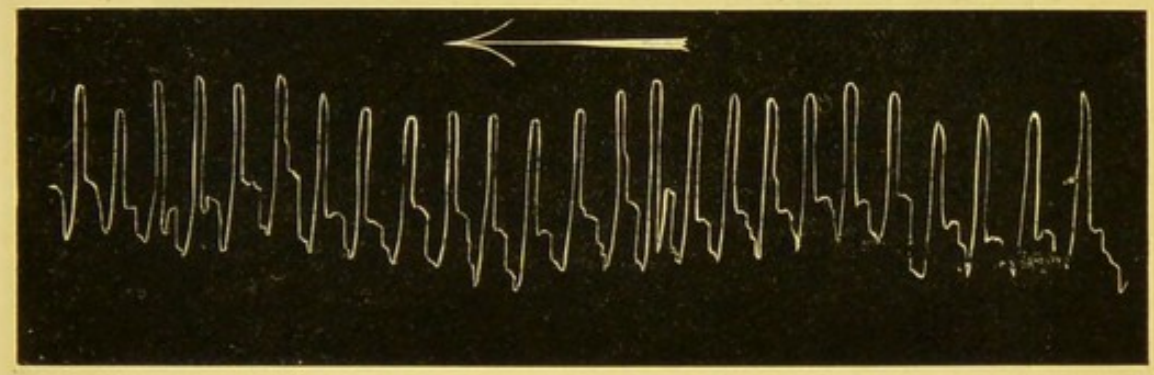


FIG. 40.—PLETHYSMOGRAPH TRACING FROM ARM.

The tracing was taken by means of a tambour connected with the plethysmograph. The dicrotic wave is distinctly marked.

systolic increase of velocity than during the diastolic slackening. In fact, with a very sensitive instrument (bolometer, or resistance thermometer, p. 479) applied directly to an exposed artery, indications of a change of temperature of the vessel-wall with each beat of the heart have been observed. And this, along with other considerations, suggests that, at any rate in certain situations and under certain conditions, there may even be a pulse of chemical change; that is, a slight and as yet doubtless inappreciable ebb and flow of metabolism corresponding to the rhythm of the heart.

The Circulation in the Capillaries.—From the arteries the blood passes into a network of narrow and thin-walled vessels, the capillaries, which in their turn are connected with the finest rootlets of the veins. Physiologically, the arterioles and venules must for many purposes be included in the capillary tract, but the great anatomical difference—

the presence of circularly-arranged muscular fibres in the arterioles, their absence in the capillaries—has its physiological correlative. The calibre of the arterioles can be altered by contraction of these fibres under nervous influences; the calibre of the capillaries, although it varies passively with the blood-pressure, and is possibly to some extent affected by active contraction of the endothelial cells, cannot be under the control of vaso-motor nerves acting on muscular fibres.

Harvey had deduced from his observations the existence of channels between the arteries and the veins. Malpighi was the first to observe the capillary blood-stream with the

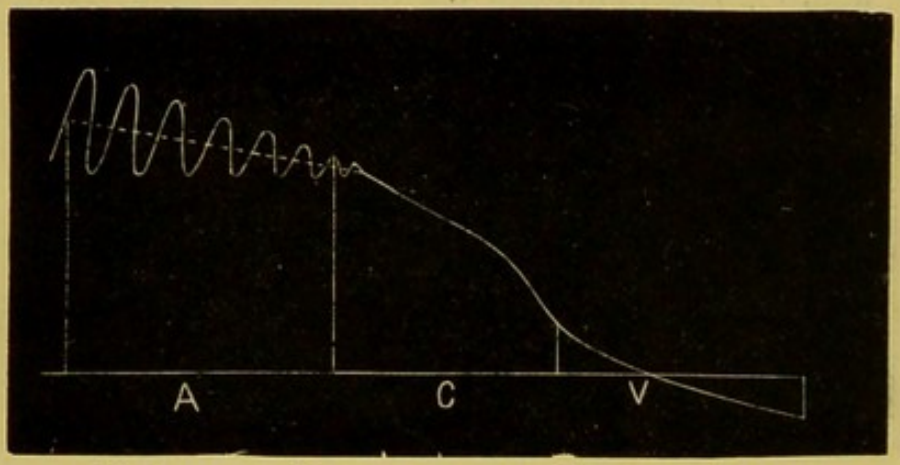


FIG. 41.—DIAGRAM TO ILLUSTRATE THE SLOPE OF PRESSURE ALONG THE VASCULAR SYSTEM.

A, arterial; C, capillary; V, venous tract. The interrupted line represents the line of mean pressure in the arteries, the wavy line indicating that the pressure varies with each heart-beat. The line passes below the abscissa axis (line of zero or atmospheric pressure) in the veins, indicating that at the end of the venous system the pressure becomes negative.

microscope, and thus to give ocular demonstration of the truth of Harvey's brilliant reasoning. He used the lungs, mesentery and bladder of the frog. The web of the frog, the tail of the tadpole, the wing of the bat, the mesentery of the rabbit and rat, and other transparent parts, have also been frequently employed for such investigations. From the apparent velocity of the corpuscles and the degree of magnification, it is easy to calculate the velocity of the capillary blood-stream. It has been estimated at from ·2 to ·8 mm. per second in different parts and different animals.

The comparative slowness of the current and the dis-

appearance of the pulse are the chief characteristics of the capillary circulation. The explanation we have already found in the great resistance of the narrow and much-branched vessels. Although the average diameter of a capillary is only about 10 μ (5 to 20 μ in different parts of the body), the number of branches is so prodigious that the total cross-section of the systemic capillary tract has been estimated at 500 to 700 times that of the aorta.

The total cross-section of the vascular channel gradually widens as it passes away from the left ventricle. In the capillary region it undergoes a great and sudden increase. At the venous end of this region the cross-section is again somewhat abruptly contracted, and then gradually lessens as the right side of the heart is approached; but the united sectional area of the large thoracic veins is greater than that of the aorta.

The blood-pressure in the capillaries has been measured by weighting a small plate of glass laid on the back of one of the fingers behind the nail, until the capillaries are just emptied, as shown by the paling of the skin (v. Kries), or by observing the height of a column of liquid that just stops the circulation in a transparent part (Roy and Graham Brown). The last-named observers found that a pressure of 100 to 150 mm. of water (about 7 to 11 mm. of Hg) was needed to bring the blood to a standstill in the capillaries and veins of the frog's web; that is, about a third of the blood-pressure in the frog's aorta. The pressure in the capillaries at the root of the nail in man varies from 30 to 50 mm. of mercury.

Under certain conditions the pulse-wave may pass into the capillaries and appear beyond them as a venous pulse. Thus, we shall see that when the small arteries of the submaxillary gland are widened, and the vascular resistance lessened, by the stimulation of the chorda tympani nerve, the pulse passes through to the veins. And, normally, a pulse may be seen in the wide capillaries of the nail-bed —especially when they are partially emptied by pressure— as a flicker of pink that comes and goes with every beat of the heart.

We have seen that the lateral pressure at any point of a uniform rigid tube through which water is flowing is proportional to the amount of resistance in the portion of the tube

between this point and the outlet. In any system of tubes the sum of the potential and kinetic energy must diminish in the direction of the flow; and although the problem is complicated in the vascular system by the branching of the channel and the variation in the total cross-section, yet theory and experiment agree that in the larger arteries the lateral pressure diminishes but slowly from the heart to the periphery, the resistance being small compared with the resistance of the whole circuit. In the capillary region the vascular resistance abruptly increases; the velocity (and therefore the kinetic energy) abruptly diminishes, and the

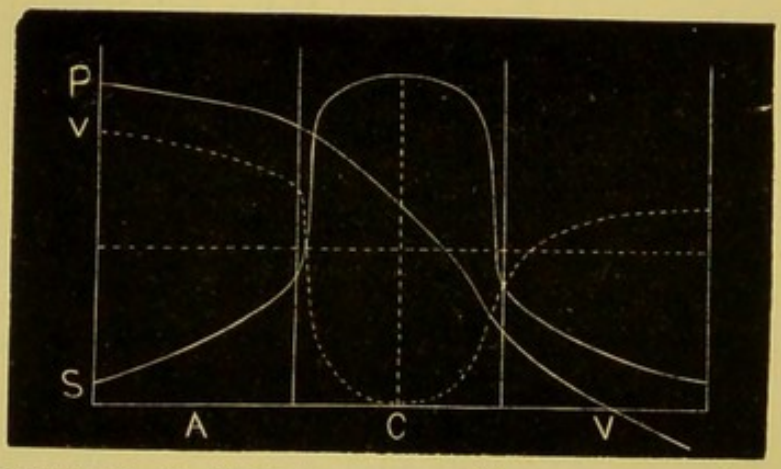


FIG. 42.—RELATION OF BLOOD-PRESSURE, VELOCITY, AND CROSS-SECTION.
The curves P, V and S represent the blood-pressure, velocity of blood, and total cross-section respectively in the arteries A, capillaries C, and veins V.

lateral pressure falls much more steeply between the beginning and the end of this region than between the heart and its commencement. In the veins only a small remnant of resistance remains to be overcome, and the lateral pressure must sink again rather suddenly about the end of the capillary tract. Fig. 42 shows by a rough diagram the manner in which the pressure, velocity and cross-section probably change from part to part of the vascular system.

The Circulation in the Veins.—The slope of pressure, as we have just explained, must fall rather suddenly near the beginning and near the end of the capillary tract. It continues falling as we pass along the veins, till the heart is again reached. In the right heart, and in the thoracic portions of the great veins which enter it, the pressure may be negative—that is, less than the atmospheric pressure.

And since nowhere in the venous system is the pressure more than a small fraction of that in the arteries, its measurement in the veins is correspondingly difficult, because any obstruction to the normal flow is apt to artificially raise the pressure. A manometer containing some lighter liquid than mercury, such as water or a solution of magnesium sulphate, is usually employed, in order that the difference of level may be as great as possible. In the sheep the pressure was found to be 3 mm. of mercury in the brachial, and about 11 mm. in the crural vein; in the dog's portal vein about 10 mm.

The venous pressure being so low, or, in other words, the potential energy which the systole of the heart imparts to the blood being so greatly exhausted before it reaches the veins, other influences begin here appreciably to affect the blood-stream:

1. *Contraction of the Muscles.*—This compresses the neighbouring veins, and since the blood is compelled by the valves, if it moves at all, to move towards the heart, the venous circulation is in this way helped.

2. *Aspiration of the Thorax.*—In inspiration the intrathoracic pressure, and therefore the pressure in the great thoracic veins, is diminished, and blood is drawn from the more peripheral parts of the venous system into the right heart (p. 250).

3. *Aspiration of the Heart.*—When the heart, after its contraction, suddenly relaxes, the endocardiac pressure becomes negative, and blood is sucked into it, just as when the indiarubber ball of a syringe is compressed and then allowed to expand. But we cannot attribute any great importance to this; and, of course, it is only the relaxation of the right ventricle which could directly affect the venous circulation.

4. Every change of position of the limbs, as in walking, aids the venous circulation (Braune), and this independently of the muscular contraction. When the thigh of a dead body is rotated outwards, and at the same time extended, a manometer connected with the femoral vein shows a negative pressure of 5 to 10 mm. of water. When the opposite movements are made, the pressure becomes positive.

It follows from the number of casually-acting influences which affect the blood-flow in the veins that it cannot be very regular or constant. We have seen that in the great arteries there is a considerable variation of velocity and of pressure with every beat of the heart; and although this variation is absent from the veins, since normally the pulse does not penetrate into them, the venous flow is, never-

theless, as a matter of fact, more irregular than the arterial. So that if it is difficult to give a useful definition of the term 'velocity of the blood' in the case of the arteries, it is still more difficult to do so in the case of the veins. Where voluntary movement is prevented, one potent cause of variation in the venous flow is eliminated; and in curarized animals certain observers have found but little difference between the mean velocity in the veins and in the corresponding arteries. Others have found the velocity in the veins considerably less, which is indeed what we should expect from the fact that the average cross-section of the venous system is greater than that of the arterial system.

To sum up, we may conclude that, upon the whole, the blood passes with gradually-diminishing velocity from the left ventricle along the arteries; it is greatly and somewhat suddenly slowed in the broad and branching capillary bed; but the stream gathers force again as it becomes more and more narrowed in the venous channel, although it never acquires the speed which it has in the aorta.

Venous Pulse.—To complete the account of the circulation in the veins, it must be added that in addition to the venous pulse described on p. 119, which travels through widened arterioles and capillaries from the arteries into the veins, a so-called venous pulse, travelling from the heart against the blood-stream and depending on variations of pressure in the right auricle, may be seen in the jugular vein in some healthy persons, but more frequently and more distinctly in cases of incompetence of the tricuspid valve. In animals a venous pulse of this nature has been demonstrated in the venæ cavæ, the jugular vein, and with a delicate manometer even in the large veins of the limbs. It moves with a speed of 1 to 3 metres a second (Morrow). The changes of pressure in the great veins due to the respiratory movements (p. 250) are also sometimes spoken of as a venous pulse, but they are produced in an entirely different way.

The Circulation-time.—Hering was the first who attempted to measure the time required by the blood, or by a blood-corpuscle, to complete the circuit of the vascular system. He injected a solution of potassium ferrocyanide into a vein (generally the jugular), and collected blood at intervals from the corresponding vein of the opposite side. After the blood had clotted, he tested for the ferrocyanide by addition of ferric chloride to the serum. The first of the samples that gave the Prussian blue reaction corresponded to the time when the injected salt had just completed the circulation. This method was improved by Vierordt, who arranged a number of cups on a revolving disc below the vein from which the blood was to be taken. In these cups samples of the blood were received, and the rate of rotation of the disc being known, it was possible to

measure the interval between the injection and appearance of the salt with considerable accuracy. Hermann made a further advance by allowing the blood to play upon a revolving drum covered with a paper soaked in ferric chloride, and by using the less poisonous sodium ferrocyanide for injection.

Even as thus modified, the method laboured under serious defects. It was not possible to make more than a single observation on one animal, at least without allowing a considerable interval for the elimination of the ferrocyanide, and, further, the method was unsuited for the estimation of the circulation time in individual organs. In both of these respects the more recently introduced **electrical method** presents considerable advantages; for by its aid we can not only obtain satisfactory measurements of the circulation time in such organs as the lungs, liver, kidney, etc., but we can repeat them an indefinite number of times on the same animal.

A cannula, connected with a burette (or a Mariotte's bottle, or a syringe), containing a solution of sodium chloride (usually a 1·5 to 2 per cent. solution), is tied into a vessel—say, the jugular vein. Suppose that the time of the circulation from the jugular to the carotid is required—that is, practically the time of the lesser or pulmonary circulation. A small portion of one carotid artery is isolated, and laid on a pair of hook-shaped platinum electrodes,* covered, except on the concave side of the hook, with a layer of insulating varnish. To further secure insulation, a bit of very thin sheet-indiarubber is slipped between the artery and the tissues. By means of the electrodes the piece of artery lying between them, with the blood that flows in it, is connected up as one of the resistances in a Wheatstone's bridge (p. 534). The secondary coil of a small inductorium, arranged for giving an interrupted current, and with a single Daniell cell in its primary, is substituted for the battery, and a telephone for the galvanometer, according to Kohlrausch's well-known method for the measurement of the resistance of electrolytes. It is well to have the induction machine set up in a separate room and connected to the resistance-box by long wires so that the noise of the Neef's hammer may be inaudible. The bridge is balanced by adjusting the resistances until the sound heard in the telephone is at its minimum intensity, the secondary coil being placed at such a distance from the primary that there is no sign of stimulation of muscles or nerves in the neighbourhood of the electrodes when the current is closed. A definite, small quantity of the salt solution is now allowed to run into the vein by turning the stop-cock of the burette. It moves on with the velocity of the blood, and reaching the artery on the electrodes causes a diminution of its electrical resistance (p. 34). This disturbs the balance of the bridge, and the sound in the telephone becomes louder. The time from the beginning of the injection to the alteration in the sound is

* The electrodes can easily be made by beating out one end of a piece of thick platinum wire to a breadth of 5 or 6 mm., and then bending the flattened part into a hook.

the circulation-time between jugular and carotid, and it can be read off by a stop-watch, or more accurately by an electric time-maker writing on a revolving drum. Instead of the telephone a galvanometer may be used, the equal and oppositely directed induction shocks being replaced by a weak voltaic current and the platinum by unpolarizable electrodes (p. 542). But this is less convenient.

The circulation-time of an organ like the kidney can be measured by adjusting a pair of electrodes under the renal artery and another under the renal vein, and reading off the interval required by the salt solution to pass from the point of injection first to the artery and then to the vein. The difference is the circulation-time through the kidney.

For certain purposes, and particularly for measurements on small animals like the rabbit, or on organs whose vessels are too delicate to be placed on electrodes without the risk of serious interference with the circulation, another method may be employed with advantage. It depends on the injection of a pigment, like methylene blue, which at first overpowers the colour of the blood and shows through the walls of the bloodvessels, but is soon reduced to a colourless substance, methylene white. The details of the method are given in the Practical Exercises (p. 192).

It may be said in general terms that in *one and the same animal the time of the lesser circulation is short as compared with the total circulation-time, relatively constant, and but little affected by changes of temperature. In animals of the same species it increases with the size, but more slowly, and rather in proportion to the increase of surface than to the increase of weight.*

Thus a dog weighing 2 kilogrammes had an average pulmonary circulation-time of 4·05 seconds, while that of a dog weighing 11·8 kilos was 8·7 seconds, and that of a dog with a body-weight of 18·2 kilos only 10·4 seconds. It is probable that in a man the pulmonary circulation-time is not usually much less than 12 seconds, nor much more than 15 seconds.

The circulation time in the kidney, spleen and liver is relatively long and much more variable than that of the lungs, being easily affected by exposure and changes of temperature (increased by cold, diminished by warmth).

In a dog of 13·3 kilos weight the average circulation-time of the spleen was 10·95 seconds; kidney, 13·3 seconds; lungs, 8·4 seconds. The circulation-time of the stomach and intestines is (in the rabbit) comparatively short, not exceeding very greatly that of the lungs, but it is lengthened by exposure. The circulation-time of the retina and that of the heart (coronary circulation) are the shortest of all.

The total circulation-time is properly the time required for the whole of the blood to complete the round of the pulmonary and systemic circulation. But there are many routes open to any given particle of blood in making its systemic circuit. If it passes from the aorta through the coronary circulation it takes an exceedingly short route. If it passes through the intestines and liver, or through the kidney, or through the lower limbs, it takes a long route. So that to determine the total circulation-time by direct measurement

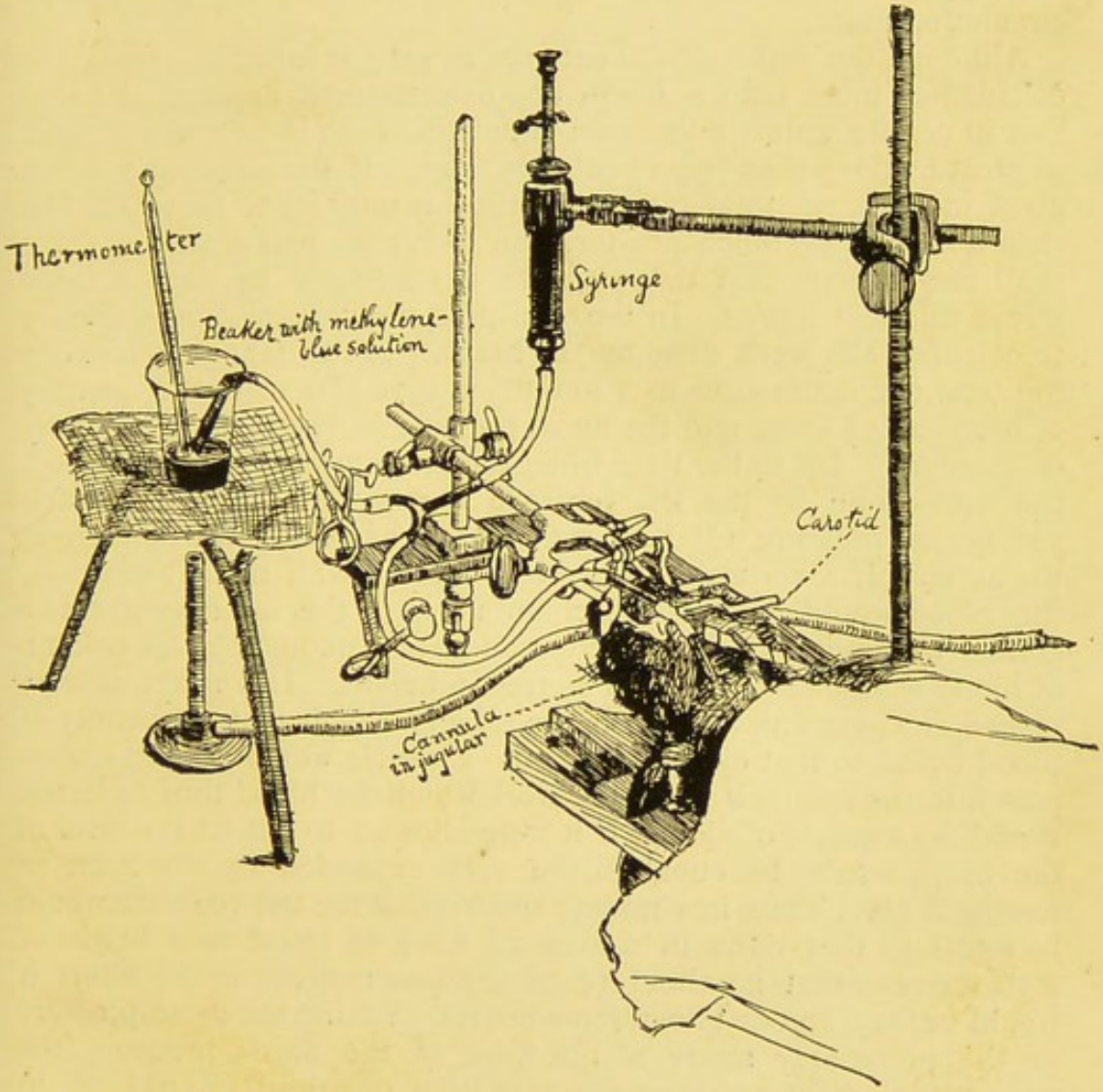


FIG. 43.—MEASUREMENT OF THE PULMONARY CIRCULATION-TIME IN RABBIT BY INJECTION OF METHYLENE BLUE.

we must know (1) the quantity of blood that passes on the average by each path in a given time, and (2) the average circulation-time of each path. If the average weight of blood in each organ be represented by w_1, w_2, w_3, etc.; and the average circulation-times by t_1, t_2, t_3, etc.; and t be the total systemic circulation-time; then $w_1\frac{t}{t_1}$, $w_2\frac{t}{t_2}$, $w_3\frac{t}{t_3}$, etc., will represent the quantity of blood passing through each organ in t seconds, since in the average circulation-

time of an organ the whole of the blood in it at the beginning of the period of observation will have been exchanged for fresh blood. But the whole of the blood in the body, which we may call W, passes once round the systemic circulation in t seconds. Therefore, $w_1\frac{t}{t_1} + w_2\frac{t}{t_2} + w_3\frac{t}{t_3}$, etc., = W. In this equation everything can be determined by experiment except t, and therefore t can be calculated. Adding t to the pulmonary circulation-time, we arrive at the total circulation-time.

Although our experimental data are as yet too meagre to make the calculation more than a rough approximation, it appears probable that in certain animals the total circulation-time is five or six times as great as the pulmonary circulation-time. If the same ratio holds good in man, the total circulation-time is unlikely to be much less than a minute or much greater than a minute and a quarter. We shall see directly that this estimate is confirmed by data derived from a different source. In the meantime, we may use it provisionally to calculate **the work done by the heart.** Let us take for simplicity the total circulation-time as 1 minute in a 70-kilo man, the quantity of blood as $5\frac{1}{2}$ kilos, and the mean pressure in the aorta as 200 mm. of mercury. Up to the time when the semilunar valves are opened, the work done by the left ventricle is spent in raising the intraventricular pressure till it is sufficient to overcome the pressure in the aorta. If a vertical tube were connected with the left ventricle, the blood would rise till the column was of the same weight as a column of mercury of equal section and 200 mm. high. This column of blood would be about 2.56 metres in height. If a reservoir were placed in communication with the tube at this height, a quantity of blood equal to that ejected from the ventricle would at each systole pass into the reservoir; and the work which the blood thus collected would be capable of doing, if it were allowed to fall to the level of the heart, would be equal to the work expended by the heart in forcing it up. Thus, in 1 minute the work of the left ventricle would be equal to that done in raising $5\frac{1}{2}$ kilos of blood to a height of 2·56 metres—that is, about 14 kilogramme-metres; in 24 hours it would be, say, 20,000 kilogramme-metres. Taking the mean pressure in the pulmonary artery at one-third of the aortic pressure (the estimates of different observers vary from one-third to one-sixth in different animals), we get for the daily work of the right ventricle about 7,000 kilogramme-metres. The work of the two ventricles is thus about 27,000 kilogramme-metres, which is enough to raise a weight of half a stone from the bottom of the deepest mine in the world to the top of its highest mountain, or to raise the man himself to more than twice the height of the spire of Strasburg Cathedral. By friction in the bloodvessels this work is almost all changed into its equivalent of heat, namely, about 63,000 small calories (p. 493). Further, since the contraction of the heart is always maximal (p. 131), and there is reason to believe that the quantity of blood ejected at a single systole by the left ventricle (being dependent upon the inflow

from the pulmonary veins, and therefore upon the inflow into the right side of the heart from the systemic veins) varies widely, some of the mechanical effect of the contraction must be wasted when the quantity is less than the ventricle is capable of expelling.

Output of the Heart.—If $5\frac{1}{2}$ kilos of blood pass through the heart in 1 minute with the average pulse-rate of 72 per minute, the quantity ejected by either ventricle with every systole will be $\frac{5500}{72} = 76$ grm., or about 72 c.c. This is much less than the amount assigned by Vierordt, which has gained the greatest vogue in physiological text-books, but all recent observers who have directly measured the output are agreed that Vierordt's estimate is too high. Thus, in a series of experiments on more than 20 dogs, ranging in weight from 5 to nearly 35 kilos, it has been shown that the output, or contraction volume, as it is sometimes called, of the left ventricle per kilo of body-weight diminishes as the size of the animal increases; and the relation between body-weight and output is such that in a man weighing 70 kilos we can hardly suppose that the ventricle discharges more than 105 grm. of blood per second, or 87 grm. (80 c.c.) per heart-beat with a pulse-rate of 72. Putting this result along with that deduced from the circulation-time, we can pretty safely conclude that the average amount of blood thrown out by each ventricle at each beat is not more than 70 or 80 c.c. Zuntz, from the quantity of oxygen absorbed by the blood in the lungs, has estimated the output at 60 c.c. But according to him this may be doubled during severe muscular work, when, as a matter of fact, by the aid of the X-rays or by percussion of the chest, the volume of the heart may be shown to be considerably increased. In the middle of last century, Passavant calculated the output at 46·5 grm., which is almost certainly too low.

The Relation of the Nervous System to the Circulation.

So far we have been considering the circulation as a purely physical problem. We have spoken of the action of the heart as that of a force-pump, and perhaps to a small extent that of a suction-pump too. We have spoken of the blood-vessels as a system of more or less elastic tubes through which the blood is propelled. We have spoken of the resistance which the blood experiences and the pressure which it exerts in this system of tubes, and we have considered the causes of this resistance, the interpretation of this pressure, and the physical changes in the vascular system that may lead to variations of both. But so far we have not at all, or only incidentally and very briefly, dealt with

the physiological mechanism through which the physical changes are brought about. We have now to see that although the heart is a pump, it is a living pump; that although the vascular system is an arrangement of tubes, these tubes are alive; and that both heart and vessels are kept constantly in the most delicate poise and balance by impulses passing from the central nervous system along the nerves.

In many respects, and notably as regards the influence of nerves on it, we may look upon the heart as an expanded, thickened and rhythmically-contractile bloodvessel, so that an account of its innervation may fitly precede the description of vaso-motor action in general.

The Relation of the Heart to the Nervous System.—A very simple experiment is sufficient to prove that the beat of the heart does not depend on its connection with the central nervous system, for an excised frog's heart may, under favourable conditions, of which the most important are a moderately low temperature, the presence of oxygen and the prevention of evaporation, continue to beat for days. The mammalian heart also, after removal from the body, beats for a time, and indeed, if defibrinated blood be artificially circulated through the coronary vessels, for several hours. But although this proves that the heart can beat when separated from the central nervous system, it does not prove that nervous influence is not essential to its action, for in the cardiac substance nervous elements, both cells and fibres, are to be found.

The Intrinsic Nerves of the Heart.—In the heart of the frog numerous nerve-cells are found in the sinus venosus, especially near its junction with the right auricle (Remak's ganglion). A branch from each vagus, or rather from each vago-sympathetic nerve (for in the frog the vagus is joined a little below its exit from the skull by the sympathetic), enters the heart along the superior vena cava (pp. 173, 174).

Running through the sinus, with whose ganglion cells the true vagus fibres, or some of them, are believed to make physiological junction (p. 141), the nerves pursue their course to the auricular septum. Here they form an intricate plexus, studded with ganglion cells. From the plexus nerve fibres issue in two main bundles,

which pass down the anterior and posterior borders of the septum to end in two clumps of nerve-cells (Bidder's ganglia), situated at the auriculo-ventricular groove. These ganglia in turn give off fine nerve-bundles to the ventricle, which form three plexuses, one under the pericardium, another under the endocardium, and a third in the muscular wall itself, or myocardium. From the last of these plexuses numerous non-medullated fibres run in among the muscular fibres and end in close relation with them. Similar plexuses of nerve-fibres exist in the mammalian ventricle. But while a few scattered ganglion cells are found in the upper part of the ventricular wall, neither in the mammal nor in the frog have any been as yet demonstrated in the apical half. In the rat's heart, according to the careful recent observations of Schwartz, true ganglion cells are confined to an area on the posterior surface of the auricles.

Cause of the Rhythmical Beat of the Heart.—It was long supposed that the presence of ganglion cells was the clue to the explanation of the automatic contraction of the heart, and by some they are still looked upon as centres from which impulses are sent out at regular intervals to the cardiac muscular fibres. Nor on a superficial view are arguments wanting in support of this opinion. We divide, in the frog, the sinus which contains ganglion cells from the lower portion of the heart, and it continues to pulsate. We cut off the apex, which contains no ganglion cells and it remains obstinately at rest. Further, if, without actually cutting off the apex, we dissever it physiologically from the heart by crushing a narrow zone of tissue midway between it and the auriculo-ventricular groove, we appear to abolish for ever its power of rhythmical contraction. The frog may live for many weeks, but in general the apex remains in permanent diastole. It can be caused to contract by an artificial stimulus, but it neither takes part in the spontaneous contraction of the rest of the heart, nor does it start an independent beat of its own. What can be simpler than to suppose that the sinus beats because it has ganglion cells in its walls, and that the apex refuses to beat because it has none? But if we pursue our investigations a little farther, we shall find that the matter is more complex. Let us inquire, for instance, what happens to the auricles and ventricle of the frog's heart when the sinus is cut off. The answer is that, as a rule, while the sinus goes on beating, the rest of the heart comes to a standstill, in spite of the

numerous ganglion cells in the auricular septum and the auriculo-ventricular groove. Not only so, but if the ventricle be now severed from the auricles by a section carried through the groove, it is the former, poor in nerve-cells though it be, which will usually first begin to beat. We shall again have to discuss this experiment (p. 142). It, at any rate, proves this, that the presence of ganglion cells is not the *only* condition on which the power of automatic rhythmical contraction depends. For a portion of the heart rich in ganglion cells may, under certain circumstances, refuse to beat. The converse is also true: rhythmical contraction, either spontaneous or artificially induced, may be observed in many organs that are free from nerve-cells, or in which, at least, no nerve-cells have ever been discovered. The embryonic heart, for instance, beats with a regular rhythm at a time when as yet no ganglion cells have grown into its walls. The isolated bulbus aortæ in the frog, which seems to contain no ganglion cells, and even the tiniest microscopic fragments of it, will pulsate spontaneously. A portion of the apex of a cat's ventricle, presumably ganglion-free, continues for a considerable time to beat with a rhythm of its own when connected with the rest of the heart by nothing but its bloodvessels. We know, further, that the ganglion-free apex of the frog's heart, lifeless as it seems when left to itself, can be caused to execute a long and regular series of pulsations when its cavity is distended with defibrinated blood, or serum, or certain artificial nutritive fluids, or even normal saline solution; that strips of the ventricle of the tortoise, also free from ganglia, can be made to beat rhythmically; that the rhythmical contraction of the smooth muscle of the ureter of the rabbit and dog is affected by distension much as that of the cardiac muscle is; and, finally, that even ordinary skeletal muscle can contract in a rhythmical manner under the stimulus of a certain tension and in certain saline solutions.

We can hardly doubt, in view of such facts—and others of like significance might easily be added—that the power of automatic rhythmical contraction possessed by the heart is essentially a property of the cardiac muscle, a property which belongs also, though in much smaller degree, to

muscular tissue in other parts of the vascular system, *e.g.*, in the central artery of the rabbit's ear, and the veins of the bat's wing. At the same time it must be remembered that full and formal proof of the myogenic origin of the cardiac beat has not yet been given. It is probable but not proven. It must also be borne in mind that when we have localized the essential mechanism of the rhythmical contraction in the muscle of the heart, we have still to ask whether this mechanism is not put into action by some stimulus external to the substance of the muscle. And, indeed, a certain amount of evidence has been brought forward that the normal stimulus (for the heart of the terrapin) depends on the presence of calcium and potassium salts in the blood (Howell).

We have seen that there is a normal order or sequence in which the different parts of the heart contract, the contraction beginning both in the frog and in the mammal at the base, and travelling more or less rapidly towards the apex. It would seem that the muscular tissue of the part of the heart in which the beat begins has a higher rhythmical power than the rest of the cardiac muscle, and that normally the contraction is only propagated, not originated, by the lower portion of the heart. But under certain conditions the normal sequence can be reversed. In the heart of the skate, it is easy by stimulating the bulbus arteriosus to cause a contraction passing from bulbus to sinus. Not only may the normal sequence be changed in the entire heart, but any part of the heart may apparently have its rhythmical power exalted by appropriate means, so that it can be brought to beat rhythmically when isolated from the rest of the heart. On the other hand, the power of propagating the contraction may be artificially interfered with—increased by heat, diminished by cold, abolished by pressure or fatigue. If, *e.g.*, a frog's heart is supported by a clamp fixed in the auriculo-ventricular groove, and the clamp is tightened or the ventricle cooled, while the auricle is at the ordinary temperature, or if the auricle is heated while the ventricle is at the ordinary temperature, only every second or third auricular beat will be followed by a ventricular beat (p. 172).

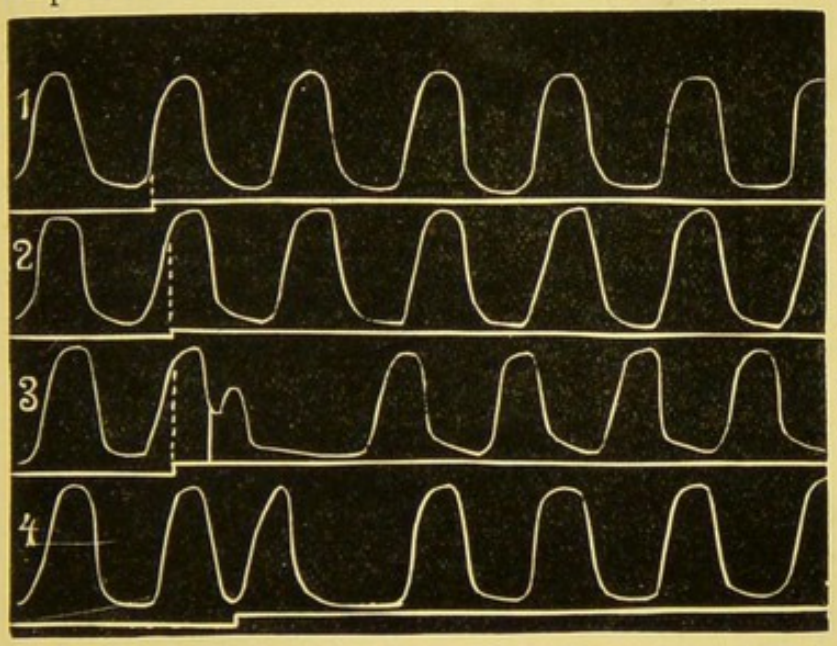
In addition to its marked power of rhythmical contraction, the cardiac muscle is distinguished from ordinary skeletal muscle by other peculiarities. The most striking of these is that 'it is everything or nothing with the heart'; in other words, the heart muscle, when it contracts, makes the best effort of which it is capable at the time; a weak stimulus, if it can just produce a beat, causes as great a contraction as a strong stimulus. Another peculiarity is that a true tetanus of the cardiac muscle cannot be obtained at all, or only under

very special conditions. When the ventricle of a normally beating frog's heart is stimulated by a rapid series of induction shocks, its rate is generally increased, but there is no definite relation between the number of stimuli and the number of beats. Many of the stimuli are ineffective. In the same way a portion of the heart, such as the apex of the ventricle, when stimulated in the quiescent condition by an interrupted current, responds by a rhythmical series of beats, and not by a tetanus. It is evident that the cardiac muscle, like ordinary striped muscle, is for some time after excitation incapable of responding to a fresh stimulus, *i.e.*, there is a **refractory period.** But this is immensely longer in cardiac than in skeletal muscle. When the phenomenon is analyzed, it is found that a stimulus falling into the heart muscle between the moment at which the contraction begins and the moment at which it reaches its maximum, produces no effect —is, so to speak, ignored. When the stimulus is thrown in at any point between the maximum of the systole and the beginning of the next contraction, it causes what is called an extra contraction. The extra contraction is followed by a longer pause than usual—a so-called compensatory pause —which just restores the rhythm, so that the succeeding systole falls in the curve where it would have fallen had there been no extra contraction (Fig. 44). The refractory period is shorter for strong than for weak stimuli, and is markedly diminished by raising the temperature of the heart. So that stimulation of the heated heart with a series of strong induction shocks may cause a tetaniform condition, if not a typical tetanus. The contraction of the normally beating heart is really a simple contraction, and not a tetanus. The capillary electrometer shows only the electrical changes corresponding to a single contraction (p. 622); and when the nerve of a nerve-muscle preparation is laid on the heart, the muscle responds to each beat by a simple twitch, and not by tetanus (p. 179).

Like ordinary skeletal muscle, the cardiac muscle is at first benefited by contraction, so that when the apex is stimulated at regular intervals, each contraction is somewhat stronger than the preceding one. To this phenomenon the name of

the staircase or 'treppe' has been given from the appearance of the tracings (p. 548).

The Extrinsic Nervous Mechanism of the Heart.—While, as we have seen, the essential cause of the rhythmical beat of the heart resides in the tissue of the heart itself, it is constantly affected by impulses that reach it from the central nervous system. These impulses are of two kinds, or, rather, produce two distinct effects: *inhibition*, or diminution in the rate or force of the heart-beat, and *augmentation*, or increase in the rate or force. Both the inhibitory and the augmentor impulses arise in the medulla oblongata, and perhaps a



A frog's heart was stimulated at a point corresponding to the nick in the horizontal line below each curve. In 1 and 2 there was no response; in 3 and 4 there was an extra contraction, succeeded by a compensatory pause.

FIG. 44.—REFRACTORY PERIOD AND COMPENSATORY PAUSE (MAREY).

narrow zone of the neighbouring portion of the cord; and they can be artificially excited by stimulation in this region. They pursue their course to the heart by fibres which may in certain animals be mingled together, but are anatomically distinct. We may, therefore, divide the extrinsic or external nervous mechanism of the heart into a cardio-inhibitory centre with its efferent inhibitory nerve-fibres, and a cardio-augmentor centre with its efferent augmentor nerve-fibres. Both of those centres, as we shall see, have also extensive relations with afferent nerve-fibres from all parts of the body, including the heart itself.

It was in the vagus of the frog that inhibitory nerves were first discovered by the brothers Weber more than fifty years

ago, and even now our knowledge of the cardiac nervous mechanism is more complete in this animal than in any other. We shall, therefore, first describe the phenomena of inhibition and augmentation as we see them in the heart of the frog, and then pass on to the mammal.

In the frog the inhibitory fibres leave the medulla oblongata in the vagus nerve. The augmentor fibres come off from the upper part of the spinal cord by a branch from the third nerve to the third sympathetic ganglion, and thence find their way along the sympathetic cord to its junction with the vagus, in which they run, mingled with the inhibitory fibres, down to the heart.

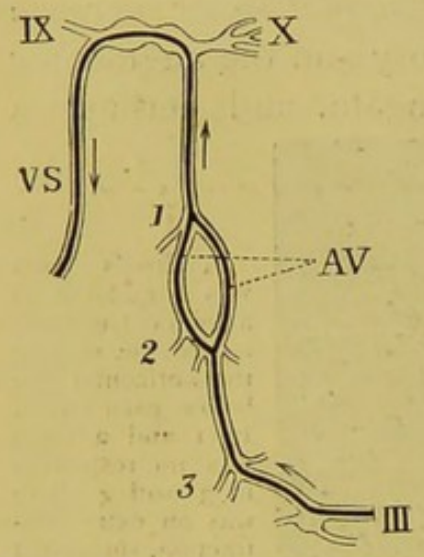


FIG. 45 (AFTER FOSTER).—DIAGRAM OF EXTRINSIC NERVES OF FROG'S HEART.

III, 3rd spinal nerve; AV, annulus of Vieussens; X, roots of vagus; IX, glosso-pharyngeal nerve; VS, combined vagus and sympathetic; 1, 2, and 3, the 1st, 2nd, and 3rd sympathetic ganglia. The dark line indicates the course of the sympathetic fibres. The arrows show the direction of the augmentor impulses.

When the vago-sympathetic in the frog or toad is cut, and its peripheral end stimulated, the heart in the vast majority of cases is stopped or slowed, or its beat is distinctly weakened without, it may be, any marked slowing. In other words, the rate at which the heart was working, before the stimulation, is greatly diminished, or reduced to zero. Such an effect, a diminution of the rate of working, we call *Inhibition*. What precise form the inhibition shall take, whether the stoppage shall be complete or partial, appears to depend partly upon the strength of the stimulus used, and partly upon the state of the heart itself. Some hearts it may be impossible to stop with weak stimulation, although other signs of inhibition may be distinct, while they are readily stopped by stronger stimulation. In other cases the strongest stimulation may not produce complete standstill. Again, a heated heart may be more readily brought to standstill by stimulation of the vagus than a heart at the ordinary temperature or a cooled heart.

But there are other points of importance to be noted in

regard to this inhibition: (1) It does not begin for a little time after stimulation has begun. In other words, there is a distinct latent period; and the length of this latent period is related to the phase of the heart's contraction at which the stimulus is thrown in, and to the rate at which the heart is beating. As a general rule, the heart makes at least one beat before it stops.

(2) The inhibition does not continue indefinitely, even if stimulation of the nerve is kept up. Sooner or later, and

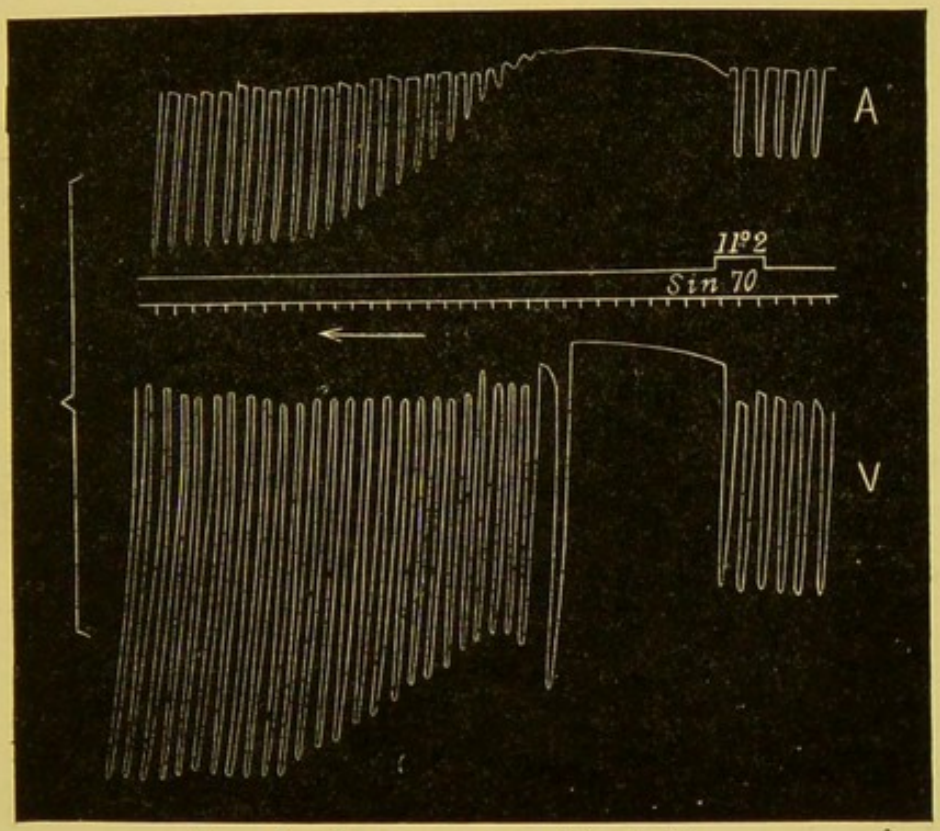


FIG. 46.—TRACING FROM FROG'S HEART.

A, auricular, V, ventricular tracing. Sinus stimulated (primary coil 70 mm. from secondary). Heart at temperature 11·2° C. Complete standstill. The time tracing between the curves marks intervals of two seconds.

usually, in fact, after an interval of a few seconds, the heart begins again to beat if it has been completely stopped, or to quicken its beat if it has only been slowed, or to strengthen it if the inhibition has only weakened the contraction, and it soon regains its old rate of working. Not only so, but very often there follows a longer or shorter period during which the heart works at a greater rate than it did before the inhibition, and this greater rate of working may be manifested by increased frequency of beat, or increased

strength of beat, or by both. When the temperature of the heart is low, increased frequency; when it is high, increased strength, is generally seen during this *period of secondary augmentation.** The cause of this secondary augmentation, and of the primary augmentation sometimes seen in fresh preparations and often in hearts that have been long exposed (Fig. 49), excited much speculation before it was known that sympathetic fibres existed in the vagus. There is no longer any doubt that it is due to the stimulation of these accelerator or, as it is better to call them (since mere acceleration is not the only consequence of their stimula-

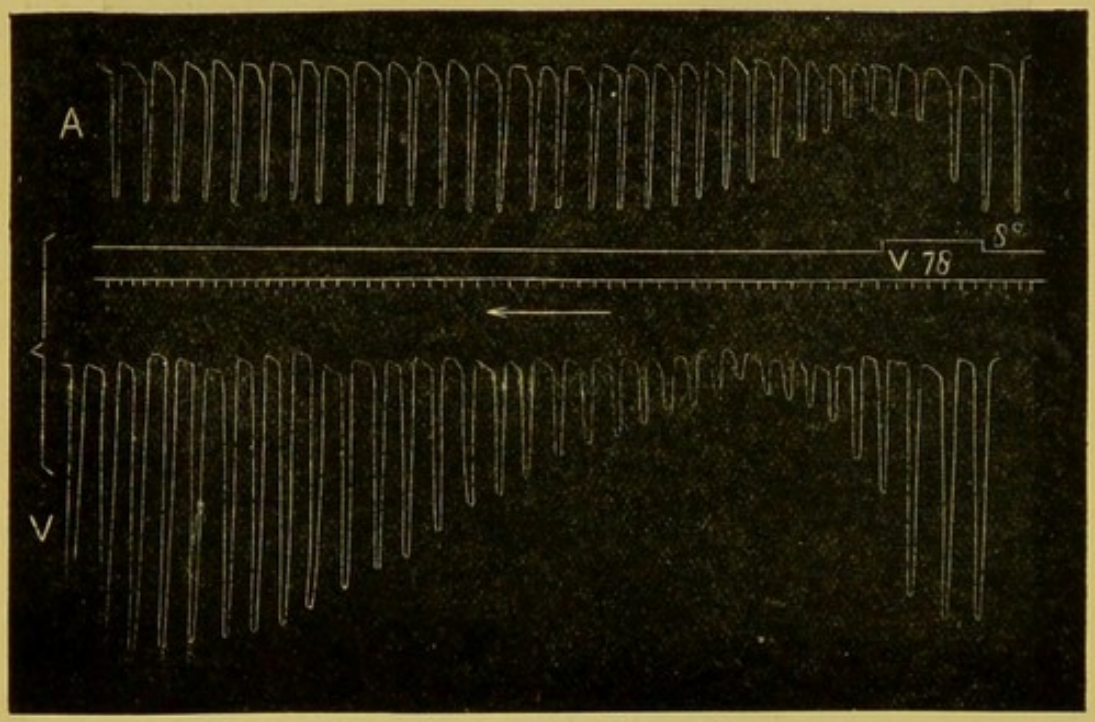


FIG. 47.—FROG'S HEART. VAGUS STIMULATED.

Temperature of heart 8° C., 78 mm. between the coils. Diminution in force of auricle and ventricle, but not complete standstill. Time tracing shows two-second intervals.

tion), *augmentor* fibres in the mixed nerve. For (1) excitation of the roots of the vagus proper within the skull, and therefore above the junction of the sympathetic fibres, causes no secondary augmentation, or very little, and the inhibition lasts far longer than when the mixed trunk is stimulated.

(2) Excitation of the upper or cephalic end of the sympathetic cord before it has joined the vagus causes, after a

* Augmentation is termed 'secondary' when it is preceded by inhibition, 'primary' when it is not so preceded.

relatively long latent period, marked augmentation. And if the contractions of the heart are registered, the tracing bears a close resemblance to the curve of secondary augmentation following excitation of the mixed nerve on the other side with an equally strong stimulus and for an equal time.

(3) When the vago-sympathetic is stimulated weakly there is little or no secondary augmentation. Now, it is known that the augmentor fibres require a comparatively strong stimulus to cause any effect when they are separately excited, whereas a weak stimulus will excite the inhibitory fibres.

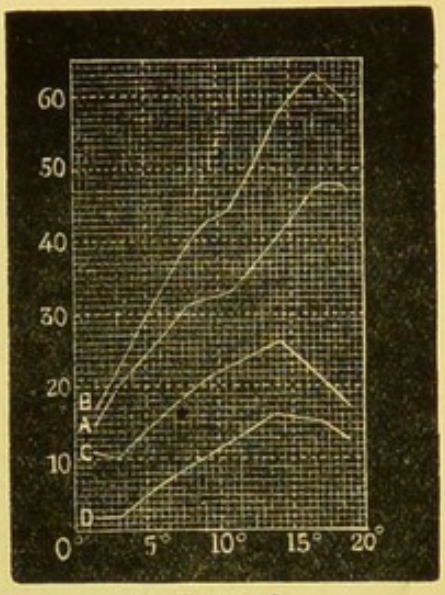


FIG. 48.

A is a curve representing in an experiment the rate of the heart before stimulation of the sympathetic, and B the maximum rate after stimulation, the number of beats per 100″ being laid off along the vertical, the temperature of the hearth along the horizontal axis. C is a curve showing the ratio of the frequency after, to that before stimulation of the sympathetic. D shows the absolute amount of acceleration at the various temperatures, the ordinates being the excess of the rate after, over that before stimulation.

The question arises at this point, why it is that, when the inhibitory and augmentor fibres are stimulated together in the mixed nerve (and the same is true when the sympathetic on one side and the vagus on the other are stimulated at the same time), the inhibitory effect always comes first, when there is any inhibitory effect, while the augmentation always has to follow. The answer has sometimes been given, that the latent period of the augmentor fibres is longer than that of the inhibitory fibres. But although this is certainly the case, the answer is insufficient. For the period of postponement may be much greater than the latent period of the sympathetic fibres when stimulated by themselves. The inhibition apparently runs its course without being affected by the simultaneous augmentor effect, which, lying latent until the end of the inhibition, then bursts out and completes its own curve. It is not like the passing of two waves through each other, but rather like the stopping of one wave until the other has passed by. It seems as if augmenta-

tion cannot develop itself in the presence of inhibition—at least, until the latter is nearly spent. In the frog, at any rate, the two processes can hardly be considered as antagonistic, in the sense that a definite amount of augmentor excitation can overcome a definite amount of inhibitory excitation. Nor is it the case that when the heart is played upon at the same time by impulses of both

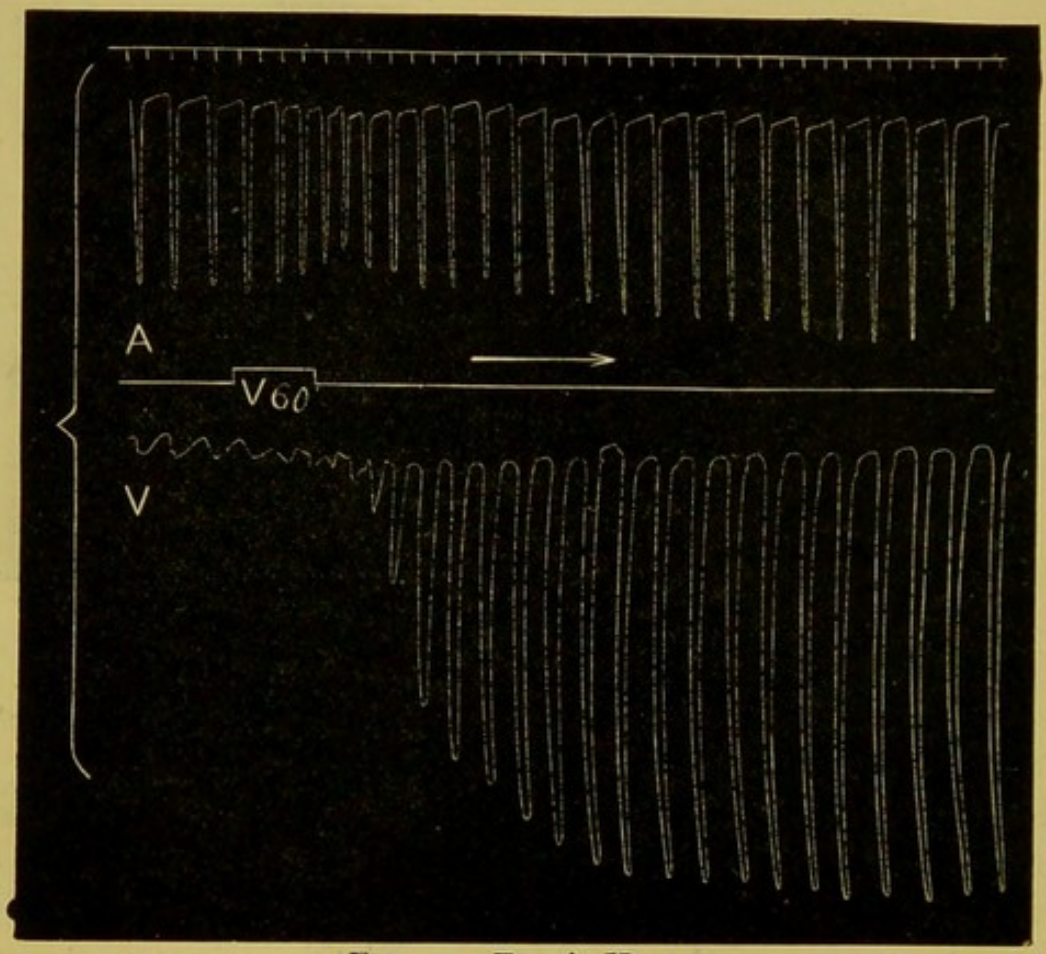


FIG. 49.—FROG'S HEART.

A, auricular; V, ventricular tracing. Ventricle beating very feebly. Vagus stimulated (60 mm. between coils). Marked augmentation of ventricular beat.

kinds, it pits them against each other and strikes the balance accurately between them. It is possible, however, that when the inhibitory fibres are very weakly, and the augmentor fibres very strongly stimulated, the amount of inhibition may be somewhat diminished. In mammals, on the other hand, a true antagonism seems to exist; and stimulation of the inhibitory nerves is less effective when the augmentors are excited at the same time.

In **mammals** (and in what follows we shall restrict ourselves to the dog, cat and rabbit, as it is in these animals that the subject has been chiefly studied) the *inhibitory* fibres run down the vagus in the neck and reach the heart by its cardiac branches. They are not, however, generally believed to be derived from the roots of the vagus itself, but from the inner branch of the spinal accessory, which joins the vagus. The *augmentor* fibres leave the spinal cord in the anterior roots of the second and third thoracic nerves, and possibly to some extent by the fourth and fifth. Through the corresponding white rami communicantes they reach the sympathetic cord, and running up through the stellate ganglion (first thoracic), and the annulus of Vieussens, which surrounds the subclavian artery, to the inferior cervical ganglion, they pass off to the heart by separate 'accelerator' branches, taking origin either from the annulus or from the inferior cervical ganglion.

In the dog the vagus and cervical sympathetic are, in the great majority of cases, contained in a strong common sheath, and pass together through the inferior cervical ganglion. After opening this sheath they may with care be separated, the fibres running in distinct strands, and not mixed together as in the vago-sympathetic of the frog. For some distance below the superior cervical ganglion the cervical sympathetic is not connected with the vagus, and here the nerves may be separately stimulated without any artificial isolation, but the electrodes must be very well insulated, as the available length of nerve is small.

In the rabbit, cat, horse, and some other mammals, the vagus and sympathetic run a separate course in the neck.

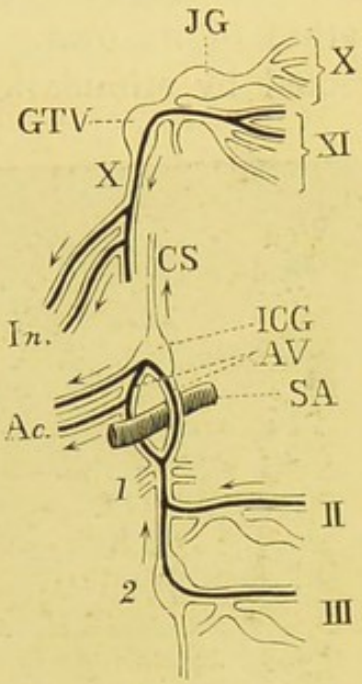


FIG. 50.—DIAGRAM OF CARDIAC NERVES IN THE DOG (AFTER FOSTER).

II, III, second and third dorsal nerves; SA, subclavian artery; AV, annulus of Vieussens; ICG, inferior cervical ganglion; CS, cervical sympathetic; 1, first thoracic or stellate ganglion of the sympathetic; 2, second thoracic ganglion; Ac., accelerator or augmentor fibres passing off towards the heart; X, roots of vagus; XI, roots of spinal accessory; JG, jugular ganglion; GTV, ganglion trunci vagi; In., inhibitory fibres passing off towards the heart.

The effects of stimulation of the vagus or vago-sympathetic in the mammal are very much the same as in the frog, except that secondary augmentation is far less marked or altogether absent, and that in the mammal the inhibitory fibres have no direct action on the ventricle. It indeed beats more slowly when the auricle is slowed, but this is

only because in the normally beating heart the ventricle takes the time from the auricle. The strength of the ventricular contractions is not at all diminished, even when the auricle is beating very feebly during inhibition. When the auricle is completely stopped, which does not occur so readily as in the frog, the ventricle also stops for a short time, but soon begins to beat again with an independent rhythm of its own. In the frog the ventricle is directly affected by stimulation of the vagus, and the force of its beats is diminished independently of the inhibitory effects in the auricles (Practical Exercises, pp. 178, 179).

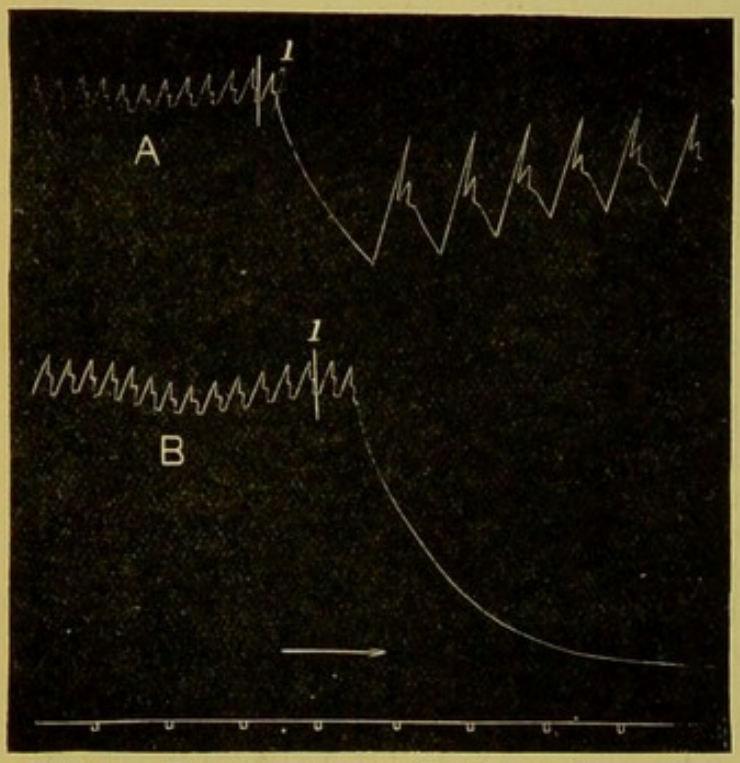


FIG. 51.—BLOOD-PRESSURE TRACING (RABBIT).

Vagus stimulated at 1. Stimulus stronger in B than in A (Hürthle's spring manometer).

Stimulation of the accelerator nerves in the dog causes an increase in the force of both the auricular and ventricular contraction, and, as a rule, in addition, some increase in the rate of the beat.

As to the **nature of the physiological linkage between the cardiac nerves and the muscular tissue** of the heart we know but little. It has been supposed that within the heart itself there may exist peripheral nervous mechanisms which mediate between the nerves and the muscle. We have already given reasons for denying to the ganglion cells any important share in the maintenance of the rhythmical beat, but we have not assigned them any function. It has been suggested that the ganglia may act as local inhibitory, or even as local augmentor, centres. Others, however, have inclined to the

view that the cells on the course of nerve-fibres in the heart are rather stations where the fibres lose their medulla, and where possibly other anatomical changes and rearrangements occur, than important intermediate mechanisms which essentially modify the physiological impulses falling into them, and shape the visible results that follow those impulses. In the discussions that have arisen over this question, appeal has frequently been made to the action of certain poisons on the heart.

Thus, after *nicotine* has been injected subcutaneously, or painted directly on the heart of a frog, stimulation of the vago-sympathetic causes no inhibition; it may cause augmentation. But stimulation of the junction of the sinus and auricle still causes inhibition, as in the normal heart. *Curara*, *conine*, and other drugs, resemble nicotine in this respect.

Atropia and its allies, such as *daturine*, not only abolish the inhibitory effect of stimulation of the vagus trunk, but also that of stimulation of the junction of sinus and auricle.

Muscarine, a poison contained in certain mushrooms (p. 174), causes diastolic arrest of the heart, which, when the circulation is intact, becomes swollen and engorged with blood. This action takes place in a heart already poisoned with nicotine or one of its congeners, but not in a heart under the influence of atropia or its allies. And a heart brought to standstill by muscarine can be made to beat again by the application of atropia, although not by nicotine.

These facts may be explained as follows: Nicotine paralyzes not the very ends of the vagus, but the ganglia through which its fibres pass. Stimulation of the sinus, which is practically stimulation of the vagus fibres between the ganglion cells and the muscular fibres, is therefore effective, although stimulation of the nerve-trunk is not (Langley). On the other hand, the atropia group paralyzes the nerve-endings themselves, so that neither stimulation of the sinus nor of the nerve-trunk can cause inhibition. Muscarine, on the contrary, stimulates the vagus fibres between the nerve-cells and the muscle, or the actual nerve-endings, or some other local nervous mechanism, and thus

keeps the heart in a state of permanent inhibition, which is removed when atropia cuts out the nerve-endings. It is quite in accordance with this, that muscarine has no effect on a heart whose vagus nerves, as occasionally happens, have no inhibitory power.

Some observers have supposed that although muscarine and pilocarpine in large doses do act on the nervous structures of the sinus, their primary and chief effect is to depress the rhythmical power of the muscle, which atropia, on the other hand, increases (Gaskell). And this view gains a certain amount of support from the facts that muscarine and atropia act very much in the same way on the heart of the mammalian embryo (rat, rabbit, etc.) before and after the development of its intrinsic nervous system, and that the passage of an interrupted current through the heart of very young embryos causes distinct inhibition. But, on the other hand, muscarine fails to affect the heart in many invertebrate animals—for instance, in the Daphnia (Pickering). So that the only conclusion to which it is possible to come is that we do not as yet thoroughly understand either the mode of action of these substances or their point of attack.

Stannius' Experiment.—Nor can much more be said of another series of phenomena that are intimately related to our present subject, and have excited, since they were first made known by Stannius, an enormous amount of discussion. The chief facts of this classical experiment we have already mentioned (p. 130), and they are also described in the 'Practical Exercises' (p. 175). They are easy to verify, but difficult to interpret. To Gaskell and his followers the most probable explanation of the standstill caused by the first ligature is that the lower portion of the heart, when cut off from the sinus in which the beat normally originates, needs some time for the development of its rhythmical power to the point at which an independent rhythm can be maintained. For in the heart of the tortoise, in which a similar temporary standstill of the auricles and ventricle occurs when the former are detached from the sinus, the circulation of a blood solution through the coronary vessels or the application of atropia, both of which, according to Gaskell, increase the rhythmical power of the cardiac muscle, prevents or removes the standstill. The effects following the second Stannius ligature are supposed to be due to stimulation of the muscular tissue by the ligature. But it is not easy to explain why the second ligature should stimulate the ventricle in preference to the auricles, and why the first ligature should apparently not stimulate the muscular tissue at all. Nor does the explanation become easier if we suppose, as is sometimes done, that it is the Bidder's ganglia which are stimulated by the ligature or by the knife, for there is no real evidence that they have motor functions.

Another view is that the first ligature stimulates the inhibitory mechanism (vagus fibres) at the junction of the sinus and right auricle, a position in which it is specially sensitive to stimuli. This causes inhibition of the whole of the heart below the ligature. The second

ligature cuts off the ventricle from the inhibitory impulses, while leaving the auricle still under their influence.

Nature of Inhibition and Augmentation.—So far we have been discussing the phenomena of inhibition and augmentation as ultimate facts. We have not attempted to go behind them, nor to ask what it is that really happens when inhibitory impulses fall into a heart, which from the first days of embryonic life has gone on beating with a regular rhythm, and in the space of a second or two bring it to a standstill. The question cannot fail to press itself upon the mind of anyone who has ever witnessed this most beautiful of physiological experiments; but as yet there is no answer except ingenious speculations. The most plausible of these is the trophic theory of Gaskell, who sees in the vagus a nerve which so acts upon the chemical changes going on in the heart as to give them a trophic, or anabolic, or constructive turn, and thus to lessen for the time the destructive changes underlying the muscular contraction. The augmentor nerves, on the other hand, are supposed to exert a katabolic influence, and to favour these destructive changes. And while, according to Gaskell, the natural consequence of inhibition is a stage of increased efficiency and working power when the inhibition has passed away, the natural complement of augmentation is a temporary exhaustion.

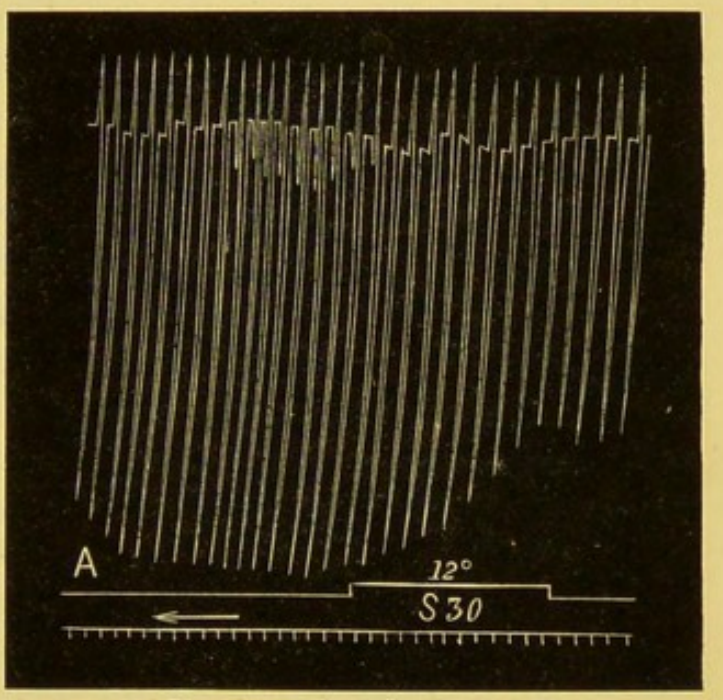


FIG. 52.—FROG'S HEART.

Sympathetic stimulated (30 mm. between the coils). Temperature 12°. Marked increase in force. Only auricular tracing reproduced. Time trace, two-second intervals.

But it must be remembered that this distinction is not as yet based upon any very solid foundation of actually-observed and easily-interpreted facts, while to some of the facts brought forward in its favour undue importance has been given. For instance, a positive electrical variation has been seen in the quiescent auricle of the tortoise on stimulating the vagus, and a negative variation in the quiescent frog's ventricle on stimulating the cardiac sympathetic, neither of these variations apparently being accompanied with any sensible mechanical change. It has been argued from this (on the assumption that the negative variation observed when most excitable tissues, muscle and nerve, for example, are stimulated, is the expression of destructive metabolic changes or katabolism), that the vagus has the power of causing constructive (anabolic) changes, and

the augmentor nerves the power of causing destructive (katabolic) changes, apart from mechanical effects. But all that we really know is that electrical changes and chemical changes can both be evoked in living tissues. We are quite ignorant of the relation between the two.

The Normal Excitation of the Cardiac Nervous Mechanism.—We have now to inquire how this elaborate nervous mechanism is normally set into action. And we may say at once that, striking as are the effects of experimental stimulation of the vagus trunk or the nervi accelerantes in their course, it is only under exceptional circumstances that the efferent nerve-fibres, at any rate before they have entered the heart, can be directly excited in the intact body. In certain cases the pressure of a tumour or an aneurism on the nerve-trunks, or, in the case of the accelerators, the progress of a pathological change in the sympathetic ganglia through which the fibres pass, has been thought to bring about by direct stimulation a slowing or a quickening of the pulse. In some individuals the vagus may be excited by compressing it against the vertebral column or against a bony tumour in the neck. But it is from the cardio-inhibitory and cardio-augmentor centres in the medulla oblongata that the impulses which regulate the activity of the heart are normally discharged. Inhibitory impulses seem to be constantly passing out from the medulla, for section of both vagi causes almost invariably an increase in the rate of the heart, at least in mammals, although the increase is less conspicuous in animals like the rabbit, whose normal pulse-rate is high, than in animals like the dog, whose pulse-rate is comparatively low. Section of one vagus usually causes only a comparatively slight increase, for the other is able of itself to control the heart. It is not certainly known whether the augmentor centre in like manner discharges a continuous stream of impulses, or is only roused to occasional activity by special stimuli. For the results of section of the nervi accelerantes, or the extirpation of the inferior cervical and stellate ganglia, are dubious and conflicting. But if it does exert a tonic influence on the heart, this is feebler than the tone of the inhibitory centre. As to the nature of this inhibitory tone, and the manner in which it is maintained,

we know but little. It may be that the chemical changes in the nerve-cells of the inhibitory centre lead of themselves to the discharge of impulses along the inhibitory nerves. But there is some evidence that, in the complete absence of stimulation from without, the activity of the centre would languish, and perhaps be ultimately extinguished. For when the greater number of the afferent impulses have been cut off from the medulla oblongata by a transverse section carried through its lower border, division of the vagi produces little effect on the rate of the heart. Be this as it may, we know that the activity of the inhibitory centre is profoundly influenced—and that both in the direction of an increase and of a diminution—by impulses that fall into it through afferent nerves and by stimuli directly applied to it. And we may assume that the same is true of the augmentor centre. When, for instance, the central end of one vagus is stimulated, the other being intact, the usual result is a slowing or weakening of the heart, which, however, is generally less marked than when the stimulation is applied to the peripheral end of the nerve. But sometimes the heart is accelerated without any preceding inhibition.

The depressor nerve, a branch of the vagus, which is easily found in the rabbit as a slender nerve running close to the sympathetic in the neck, and a little to its inner side, falls into the same category with the vagus itself as regards its reflex action on the heart, to which it bears an important relation. Stimulation of its peripheral end has no effect, for the cardiac fibres which it carries are afferent, not efferent. But excitation of its central end causes a marked fall of blood-pressure (p. 161), accompanied by, but not essentially due to, a distinct slowing of the heart. If the animal is not anæsthetized, there may be signs of pain, and for this reason the depressor has sometimes been spoken of, somewhat loosely, as the sensory nerve of the heart. Stimulation of the cephalic end of the cervical sympathetic in the dog often causes reflex slowing of the heart and general dilatation of the vessels, although sometimes the opposite effects. The abdominal sympathetic (of the frog) also contains afferent fibres, through which reflex inhibition of the heart can be

produced when they are excited mechanically by a rapid succession of light strokes on the abdomen with the handle of a scalpel (Goltz).

On the other hand, when the central end of an ordinary peripheral nerve like the sciatic is excited, the common effect is pure augmentation, which sometimes perhaps develops itself with greater suddenness than when the accelerator nerves are directly stimulated. Occasionally, however, the augmentation is abruptly followed by a typical vagus action. Here the reflex inhibitory effect seems to break in upon and cut short the reflex augmentor effect.

These examples show that certain afferent nerves are especially related to the cardio-inhibitory, and others to the cardio-augmentor, centre, or at least that the central connections of some nerves are such that inhibition is the usual effect of their reflex excitation, while the opposite is the case with other nerves. But it is improbable that the effect of a stream of afferent impulses reaching the cardiac centres by any given nerve is determined solely by anatomical relations. The intensity and the nature of the stimulus seems also to have something to do with the result. For when ordinary sensory nerves are weakly stimulated, augmentation is said to be more common than inhibition, and the opposite when they are strongly stimulated. And while a chemical stimulus, like the inhaled vapour of chloroform or ammonia, causes in the rabbit reflex inhibition of the heart through the fibres of the trigeminus that confer common sensation on the mucous membrane of the nose, the mechanical excitation of the sensory nerves of the pharynx and œsophagus when water is slowly sipped causes acceleration.* The stimulation of the nerves of special sense is followed sometimes by the one effect and sometimes by the other. To complete the catalogue of the nervous channels by which impulses may reach the cardiac centres in the medulla, we may add that there must be an extensive connection between them and the cerebral cortex, since every passing emotion leaves its trace upon the curve of cardiac action. It is a remarkable fact, too, and one

* In 78 healthy students the average pulse-rate (in the sitting position) was increased from 73 to 85 per minute by sipping water.

that can only be explained by such a connection, that although in the vast majority of individuals the will has no influence whatever on the rate or force of the heart, except, perhaps, indirectly through the respiration, some persons have the power, by a voluntary effort, of markedly accelerating the pulse. In one case of this kind it was noticed that perspiration broke out on the hands and other parts of the body when the heart was voluntarily accelerated. A rise of blood-pressure due to constriction of the vessels has also been observed. The effort cannot be kept up for more than a short time, and the pulse-rate quickly goes back to normal. It has been recently asserted that this peculiar power is more common than has been supposed, and that where it is present in rudiment, it can be cultivated, although it is a dangerous acquisition (Van de Velde).

As an example of the direct action of a chemical stimulus on a cardiac centre, we may cite the marked inhibition produced by injection of an extract of the suprarenal capsule into a vein (p. 475), and as an instance of the direct action of a physical change, the slowing of the heart in asphyxia as the blood-pressure rises (p. 163). The variation in the pulse-rate associated with changes in the position of the body, to which we have already referred (p. 96), has been attributed to direct stimulation of the inhibitory centre by the increase of blood-pressure in the medulla oblongata when a person who has been standing assumes the supine, or even the sitting, posture. But it may also be due in part to changes in the amount of muscular contraction.

Theoretically, quickening of the heart might be caused either by a diminution in the inhibitory tone or by an increase in the activity of the augmentor centre; and slowing of the heart might be due either to a diminution in the augmentor tone, if such exists, or to an increase in the activity of the inhibitory centre. So that it is not always easy to interpret such results as we have quoted above. But it would appear that under ordinary conditions the rate of the heart is mainly regulated by the inhibitory centre, which, within a considerable range, can produce variations in either direction. The augmentor mechanism is perhaps

merely auxiliary to the inhibitory, being called into action only in emergencies.

Vaso-motor Nerves.—Just as the muscular walls of the heart are governed by two sets of nerve-fibres, a set which keeps down the rate of working and a set which may increase it, the muscular walls of the vessels are under the control of nerves which have the power of diminishing their calibre (*vaso-constrictor*), and of nerves which have the power of increasing it (*vaso-dilator*). All nerves that affect the calibre of the vessels, whether vaso-constrictor or vaso-dilator, are included under the general name *vaso-motor*. These vaso-motor nerves, like the augmentor and inhibitory fibres of the heart, are connected with a centre or centres, which in turn are in relation with numerous afferent nerves. It is through this reflex mechanism that the blood-vessels are mainly influenced, although the endings of the vaso-motor nerves in the smooth muscular fibres or the muscular fibres themselves may sometimes be directly affected by substances circulating in the blood. Albumose, for instance, causes by peripheral action dilatation of the vessels and a fall of blood-pressure (p. 188), suprarenal extract constriction, with a rise of pressure (p. 189). Vaso-motor nerves control chiefly the small arteries. They have no direct influence on the capillaries. Nor has the existence of an effective vaso-motor regulation of the calibre of the veins, except in the portal system, been proved up to this time by any clear and unambiguous experiment, although there are grounds on which it has been surmised that the nervous system does influence the 'tone' of the whole venous tract. These grounds will be mentioned in the proper place. Meanwhile, before describing the distribution of the best-known tracts of vaso-motor fibres and defining the position of the vaso-motor centres, we must glance at the methods by which our knowledge has been attained.

(1) In translucent parts inspection is sufficient. Paling of the part indicates constriction; flushing, dilatation of the small vessels. This method has been much used, sometimes in conjunction with (2) in such parts as the balls of the toes of dogs or cats, the ear of the rabbit, the conjunctiva, the mucous membrane of the mouth and gums, the web of the frog, the wing of the bat, the intestines, etc.

(2) Observation of changes in the temperature of parts. This method has been chiefly employed in investigating the vaso-motor nerves of the limbs, the thermometer bulb being fixed between the toes. In such peripheral parts the temperature of the blood is normally less than that of the blood in the internal organs, because the opportunities of cooling are greater. The effect of a freer circulation of blood (dilatation of the arteries) is to raise the temperature; of a more restricted circulation (constriction of the arteries), to lower it.

(3) Measurement of the blood-pressure. If we measure the arterial blood-pressure at one point, and find that stimulation of certain nerves increases it without affecting the action of the heart, we can conclude that upon the whole the tone of the small vessels has been increased. But we cannot tell in what region or regions the increase has taken place; nor can we tell whether it has not been accompanied by diminution of tone in other tracts.

But if we measure simultaneously the blood-pressure in the chief artery and chief vein of a part such as a limb, we can tell from the changes caused by section or stimulation of nerves whether, and in what sense, the tone of the small vessels within this area has been altered. For example, if we found that the lateral pressure in the artery was diminished, while at the same time it was increased in the vein, we should know that the 'resistance' between artery and vein had been lessened, and that the blood now found its way more readily from the artery into the vein. If, on the other hand, the venous pressure was diminished, and the arterial pressure simultaneously increased, we should have to conclude that the vascular resistance in the part was greater than before. If the pressure both in artery and vein was increased, we could not come to any conclusion as to local changes of resistance without knowing how the general blood-pressure had varied.

It is also sufficient to measure the blood-pressure simultaneously at two points of the arterial path by which blood reaches the part, provided that there is a distinct difference in the pressure at the two points. The *ratio* of the two pressures will not be altered by any general change of blood-pressure due to changes in the action of the heart; any alteration in the ratio will indicate a change in the peripheral vascular resistance in the part beyond the more distal of the two manometers.

On this principle, Hürthle has studied the changes in the circulation of the brain by inserting manometers into the central end of the divided common carotid and the peripheral end of the internal carotid. The former shows the lateral pressure in the aorta, the latter that in the circle of Willis.

(4) The measurement of the velocity of the blood in the vessels of the part. This may be done by the stromuhr or dromograph, or by allowing the blood to escape from a small vein and measuring the outflow in a given time, or, without opening the vessels, by estimating the circulation time (p. 123). When changes in the general arterial pressure are eliminated, slowing of the blood-stream through a part

corresponds to increase of vascular resistance in it; increase in the rate of flow implies diminished vascular resistance. Sometimes the red colour of the blood issuing from a cut vein, and the visible pulse in the stream, indicate with certainty that the vessels of the organ have been dilated.

(5) Alterations in the volume of an organ or limb are often taken as indications of changes in the calibre of the small vessels in it. We have already seen how these alterations are recorded by means of a plethysmograph (p. 116). The brain is enclosed in the skull as in a natural plethysmograph, and changes in its volume may be registered by connecting a recording apparatus with a trephine hole.

(6) For the separation of the effects of stimulation of vaso-constrictor and vaso-dilator fibres when they are mingled together, as is the case in many nerves, advantage is taken of certain differences between them. For example, the vaso-constrictors lose their excitability sooner than the vaso-dilators when cut off from the nerve-cells to which they belong. So that if a nerve is divided, and some days

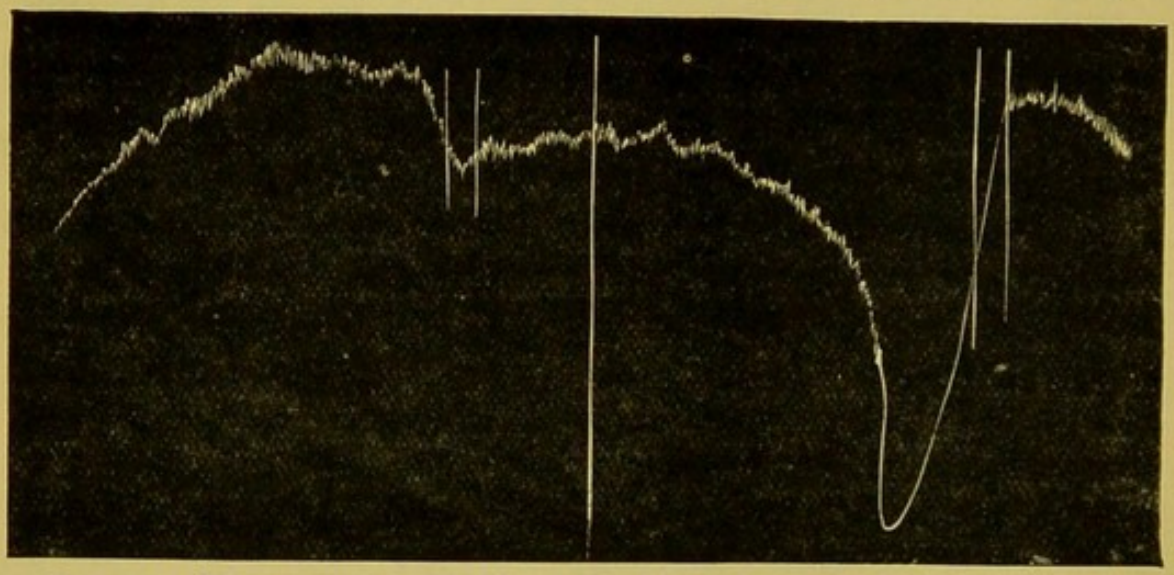


FIG. 53.—PLETHYSMOGRAMS (HIND LIMB OF CAT). (AFTER BOWDITCH AND WARREN.)

To be read from right to left. On the left hand is shown the effect of slow stimulation of the sciatic (1 per second); on the right hand the effect of rapid stimulation (64 per second).

allowed to elapse before stimulation, only the dilators will be excited. The vaso-dilators are more sensitive to weak stimuli repeated at long intervals than to strong and frequent stimuli, and the opposite is true of the constrictors. When a nerve containing both kinds of fibres is heated, the excitability of the vaso-constrictors is increased in a greater degree than that of the dilators; when the nerve is cooled, the dilators preserve their excitability at a temperature at which the constrictors have ceased to respond to stimulation (Fig. 53).

The Chief Vaso-motor Nerves.—The first discovery of vaso-motor nerves was made in the *cervical sympathetic*. When this nerve is cut, the corresponding side of the head, and especially the ear, become greatly injected owing to the

dilatation of the vessels. This experiment can be very readily performed on the rabbit, and the changes are most easily followed in an albino. The ear on the side of the cut nerve is redder and hotter than the other; the main arteries and veins are swollen with blood, and many vessels formerly invisible come into view. The slow rhythmical changes of calibre, which in the normal rabbit are very characteristically seen in the middle artery of the ear, disappear for a time after section of the sympathetic, although they ultimately again become visible (Practical Exercises, p. 190).

Stimulation of the cephalic end of the cut sympathetic causes a marked constriction of the vessels and a fall of temperature on the same side of the head. From these facts we know that the cervical sympathetic in mammals contains vaso-constrictor fibres for the side of the head and ear, and that these fibres are constantly in action. Certain parts of the eye, and the salivary glands, larynx, œsophagus, and thyroid gland, are also supplied with vaso-motor (constrictor) nerves from the cervical sympathetic.

It has been asserted that the cervical sympathetic contains some of the vaso-constrictor fibres that supply the corresponding half of the brain and its membranes, but this has been disputed, and some observers have even gone so far as to deny that the vessels of the brain have any vaso-motor nerves. Non-medullated nerve-fibres, however, may be seen in and around the walls of the cerebral bloodvessels (Huber), and it is difficult to believe that these have not a vaso-motor function, although this has not as yet been clearly demonstrated by experimental methods.

That the nerve contains some dilator fibres is proved by the fact that stimulation of the cephalic end in the dog causes flushing of the mucous membrane of the mouth on the same side. The vaso-motor fibres of the head run up in the cervical sympathetic, and then pass into various cerebral nerves, of which the fifth or trigeminus is the most important.

The *trigeminus nerve* contains vaso-constrictor nerves for various parts of the eye (conjunctiva, sclerotic, iris), and for the mucous membrane of the nose and gums, and section of it is followed by dilatation of the vessels of these regions.

The *lingual* branch of the trigeminus supplies vaso-motor fibres to the tongue, and apparently both vaso-constrictor and vaso-dilator.

In some animals, the rabbit for instance, the ear derives part of its vaso-motor supply directly from the cerebro-spinal system, through the great auricular nerve, as well as through the cervical sympathetic.

Another great vaso-motor tract, the most influential in the body, is contained in the *splanchnic* nerves, which govern the vessels of many of the abdominal organs. Section of these nerves causes an immediate and sharp fall of arterial pressure. The intestinal vessels are dilated and overfilled with blood. As a necessary consequence of their immense capacity, the rest of the vascular system is underfilled, and the blood-pressure falls accordingly. Stimulation of the peripheral end of the splanchnic nerves causes a great rise of blood-pressure, owing to the constriction of vessels in the intestinal area. We therefore conclude that in the splanchnics there are vaso-motor fibres of the constrictor type, and that impulses are constantly passing down them to maintain the normal tone of the vascular tract which they command. The presence of dilator fibres (for the intestines and the kidney, for example) has also been demonstrated in the splanchnic nerves, although the constrictors predominate, and special methods have to be employed for the detection of the dilators.

The same is true of *the nerves of the extremities*, which certainly contain vaso-dilator fibres in addition to vaso-constrictors, although the difficulty of demonstrating the presence of the former is fully as great as it is in the splanchnics. For the investigation is complicated by the fact that such nerves as the sciatic supply with vaso-motor fibres two leading tissues—skin and muscle; and these are not necessarily affected in the same direction or to the same extent by stimulation of their vaso-motor fibres. The vaso-constrictors under ordinary conditions preponderate, so that section of the sciatic or the brachial is generally followed by flushing of the balls of the toes and rise of temperature, stimulation by paling and fall of temperature. By taking advantage, however, of the unequal excitability of dilators

and constrictors in a degenerating nerve, and of the differences between the two kinds of fibres in their reaction to electrical stimuli (p. 150), it has been shown that vaso-dilators are also present, and come to the front when the conditions are rendered favourable for them and unfavourable for the constrictors.

The vaso-motor fibres for the fore-limb (dog) issue from the cord in the anterior roots of the third to the eleventh dorsal nerves, and for the hind-limb in the anterior roots of the eleventh dorsal to the third lumbar. Stimulation of most of these roots causes constriction of the vessels, but stimulation of the eleventh dorsal may cause dilatation (Bayliss and Bradford).

The Vaso-motor Nerves of Muscle.—When the motor nerve of the thin mylo-hyoid muscle of the frog, which can be observed under the microscope, is cut, the vessels are seen to dilate. On stimulation of the peripheral end of the cut nerve they dilate still more, and this effect is not abolished when contraction of the muscle is prevented by a dose of curara insufficient to paralyze the vaso-motor nerves (Gaskell). The dilatation on section of the nerve has been held to indicate the existence in it of vaso-constrictor fibres, and the dilatation on stimulation of the nerve, the existence of a larger number of vaso-dilators, which overcome the constrictors when both are excited. And it has been argued that this is of use to the contracting muscle, which requires a free flow of blood to supply it with food materials and to carry off its waste products. The average flow of blood through a mammalian muscle is also increased during contraction, apart from the initial increase due to the compression of the muscular veins. The outflow of blood from the main vein of one of the muscles used in mastication in the horse was found to be three times as great during voluntary work with it (in chewing) as in rest. And although no increase in the blood-flow through the skeletal muscles of a completely curarized mammal has ever been satisfactorily demonstrated, we can hardly doubt that they are provided with vaso-dilator fibres, and more scantily with vaso-constrictors. The existence in the vagus of vaso-constrictor, and in the annulus of Vieussens of vaso-dilator, fibres for the coronary arteries of the heart has also been asserted. It

has been suggested that the muscular vessels are widened in contraction, not through vaso-motor nerves, but by the direct action of the acid products of the active muscle itself, since it has been found that very dilute acids (lactic acid, *e.g.*) cause general dilatation of the small vessels. A similar explanation has been extended to the dilatation of the vessels of the brain during cerebral activity by some of those who deny the existence of vaso-motor nerves for that organ. But this ingenious speculation rests upon a very narrow basis of fact.

Vaso-motor Nerves of the Lungs.—There has been much discussion as to the course, and even as to the existence, of vaso-motor fibres for the lungs. The problem is perhaps the most difficult in the whole range of vaso-motor topography, for the pulmonary circulation is so related to other vascular tracts, that changes produced in the vessels of distant organs by the stimulation or section of nerves may affect the quantity of blood received by the right side of the heart, and therefore the quantity propelled through the lungs and the pressure in the pulmonary artery. All that we really know is that the lungs are supplied with vaso-constrictor fibres, although in all probability less richly than most other organs. Some of these fibres appear to pass out from the upper half of the dorsal spinal cord (Bradford and Dean), but perhaps others reach their destination by the vagus.

In most of the peripheral nerves **vaso-dilator** fibres are mingled with vaso-constrictors; but in certain situations, for an anatomical reason that will be mentioned presently, nerves exist in which the only vaso-motor fibres are of the dilator type. Of these, the most conspicuous examples are the *chorda tympani* and the *nervi erigentes;* and, indeed, it was in the chorda that vaso-dilators were first discovered by Bernard. The chorda tympani contains vaso-dilator and secretory fibres for the submaxillary and sublingual salivary glands. With the secretory fibres we have at present nothing to do; and the whole subject will have to be returned to, and more fully discussed in Chapter IV. But a most marked vascular change is produced by stimulation of the peripheral end of the divided chorda tympani nerve.

The glands flush red; more blood is evidently passing through their vessels. Allowed to escape from a divided vein, the blood is seen to be of bright arterial colour and shows a distinct pulse. The small arteries have been dilated by the action of the vaso-motor fibres in the nerve. The resistance being thus reduced, the blood passes in a fuller and more rapid stream through the capillaries into the veins, and on the way there is not time for it to become completely venous. These vaso-dilator fibres are apparently not in constant action, for section of the nerve, as a rule, produces little or no change. Vaso-constrictor fibres pass to the salivary glands from the cervical sympathetic, along the arteries, and stimulation of that nerve causes narrowing of the vessels and diminution of the blood-flow, sometimes almost to complete stoppage.

The *nervi erigentes* are the nerves through which erection of the penis is caused. When they are divided there is no effect, but stimulation of the peripheral end causes dilatation of the vessels of the erectile tissue of the organ, which becomes overfilled with blood. During stimulation of these nerves, the quantity of blood flowing from the cut dorsal vein of the penis may be fifteen times greater than in the absence of stimulation. It spurts out in a strong stream, and is brighter than ordinary venous blood (Eckhard). Stimulation of the peripheral end of the *nervus pudendus* causes constriction of the vessels of the penis, so that it contains vaso-constrictor fibres which are the antagonists of the nervi erigentes.

Vaso-motor Nerves of Veins.—Like arteries, veins have plexuses of nerve-fibres in their walls, and contract in response to various stimuli. In some cases, *e.g.*, in the wing of the bat, rhythmical contractions of the veins are strikingly displayed, but they do not seem to depend on the nervous system, as they persist after section of the brachial nerves. But up to a very recent date there was no clear proof of the existence of vaso-motor nerves for veins. In 1892, however, Mall showed that vaso-constrictor fibres for the portal vein exist in the splanchnic nerves. When these were stimulated, after the disturbing effect of changes in the

circulation through the intestines had been eliminated by compression of the aorta in the thorax, an actual shrinking of the vein could be observed. The fibres appear to issue from the spinal cord by the anterior roots of the third to the eleventh dorsal nerves, but chiefly in the fifth to the ninth dorsal (Bayliss and Starling). When the liver is enclosed in a plethysmograph of special construction, and the central end of an ordinary sensory nerve, like the sciatic, excited, reflex vaso-constriction takes place in the portal area, the volume of the organ diminishes, and the blood-pressure rises in the portal vein.

The vena portæ and its branches are in the physiological sense arteries rather than veins, since they break up into capillaries, and it was to be expected that the regulation of the blood-flow in them would be carried out in the same way as in ordinary arteries, namely, by means of vaso-motor nerves. But we must not, without special proof, extend the results obtained in the portal system to ordinary veins. A certain amount of evidence, however, exists that even such veins as those of the extremities are supplied, though scantily, with vaso-constrictor (veno-motor) fibres. After ligation of the crural artery or aorta, stimulation of the peripheral end of the sciatic has been seen to cause contraction of short portions of the superficial veins of the leg (Thompson, Bancroft).

Course of the Vaso-motor Nerves.—In the dog the vaso-constrictors pass out as fine medullated fibres (1·8 to 3·6 μ in diameter) in the anterior roots of the second dorsal to about the second lumbar nerves (Gaskell). They proceed by the white rami communicantes to the lateral sympathetic ganglia, where, or in more distal ganglia such as the inferior mesenteric, they lose their medulla, and their axis-cylinder processes (Chap. XII.) break up into fibrils that come into close relation with the nerve-cells of the ganglia. These ganglion cells in their turn send off axis-cylinder processes, which, acquiring a neurilemma, become non-medullated nerve fibres, and now pass by various routes to their final destination, the unstriped muscular fibres of the bloodvessels. Their course to the head has been already described. To the limbs they are distributed in the great nerves (brachial

plexus, sciatic, etc.), which they reach from the sympathetic ganglia by the grey rami communicantes.

The outflow of vaso-dilator fibres, which also takes place through the anterior roots, does not seem to be restricted to any particular part of the cord, although their existence has been most clearly demonstrated in nerves springing from those regions of the cerebro-spinal axis from which vaso-constrictor fibres do not arise, and where, therefore, we have not to contend with the difficulty of interpreting mixed effects. Some even emerge in the roots of origin of certain of the cranial nerves, as the trigeminus, although many of the vaso-dilator fibres contained in the trunk of this nerve distal to the Gasserian ganglion are derived from the cervical sympathetic, and originally come off from the upper dorsal portion of the spinal cord. The vaso-dilators appear upon the whole to pursue much the same course towards the periphery as the vaso-constrictors, although they often run for a greater distance after leaving the cord without losing their medulla. But eventually they too come into relation with ganglion cells, sometimes scattered along their course, or lying near or in the organs to which they are distributed; and as in the case of the vaso-constrictors, these ganglion cells with their axis-cylinder processes continue the nervous path to the periphery. It is believed that every vaso-motor fibre is interrupted by one, and only by one, ganglion cell between the cord and the bloodvessels.

Effect of Nicotine on Nerve-cells.—A method which has been found most fruitful in studying the relations of sympathetic ganglion cells to the vaso-motor fibres, as well as to the pilo-motor* and secretory fibres which in certain situations are so intricately mingled with them, must here be mentioned. It depends upon the fact that when a suitable dose of nicotine (10 milligrammes in a cat) is injected into a vein, or a solution is painted on a ganglion with a brush, the passage of nerve-impulses through the ganglion is blocked for a time (Langley). The seat of the 'block' is probably the felt-work of fibrils in which the central nerve-fibres terminate around the ganglion cells (Cushny and Huber). The nerve-fibres peripheral to the ganglion are not affected. The question whether efferent fibres are connected with nerve-cells between a given point and their

* Pilo-motor nerves supply the smooth *arrector pili* muscles, whose contraction causes the hair to 'stand on end.'

peripheral distribution can, therefore, be answered by observing whether any effect of stimulation is abolished by nicotine. If, for instance, the excitation of a nerve caused constriction of certain bloodvessels before, and has no effect after, the application of nicotine to a ganglion, its vaso-constrictor fibres, or some of them, must be connected with nerve-cells in that ganglion.

We have thus traced the vaso-motor nerves from the cerebro-spinal axis to the bloodvessels which they control; it still remains to define the portion of the central nervous system to which these scattered threads are related, which holds them in its hand and acts upon them as the needs of the organism may require.

Vaso-motor Centres.—Now, experiment has shown that there is one very definite region of the spinal bulb which has a most intimate relation to the vaso-motor nerves. If while the blood-pressure in the carotid is being registered, say, in a curarized rabbit, the central end of a peripheral nerve like the sciatic is stimulated, the pressure rises so long as the bulb is intact, this rise being largely due to the reflex constriction of the vessels in the splanchnic area. If a series of transverse sections be made through the brain, the rise of pressure caused by stimulation of the sciatic is not affected till the upper limit of the bulb is almost reached. If the slicing is still carried downwards, the blood-pressure sinks, and the rise following stimulation of the sciatic becomes less and less. When the medulla has been cut away to a certain level, only an insignificant rise or none at all can be obtained. The portion of the medulla the removal of which exerts an influence on the blood-pressure, and its increase by reflex stimulation, extends from a point 4 to 5 mm. above the point of the calamus scriptorius to within 1 to 2 mm. of the corpora quadrigemina (Owsjannikow). Other observers give narrower limits. Stimulation of the medulla causes a rise, destruction of this portion of it a fall, of general blood-pressure. There is evidently in this region a nervous 'centre' so intimately related, if not to all the vaso-motor nerves, at least to such very important tracts as to deserve the name of a vaso-motor centre. Experiment has shown that this is much the most influential centre, and it is usually called the chief or general vaso-motor centre. But

there are subsidiary centres all along the cord, and while a very large number of the constrictor fibres are related to the chief centre in the medulla, some are either normally under the control of subordinate centres, or may in special circumstances come to be dominated by them.

Thus, in the frog it is possible to go on destroying more and more of the cord from above downwards, and still to obtain reflex vaso-motor effects, as seen in the vessels of the web, by stimulating the central end of the sciatic nerve. Although these effects indeed diminish in amount as the destruction of the cord proceeds, yet a distinct change can be caused when only a small portion of the cord remains intact.

Similarly, in the mammal evidence has been obtained of the existence of 'centres' at various levels of the cord, capable of acting as vaso-motor centres after the chief centre in the bulb has been cut off. For example, after section of the cord at the upper limit of the lumbar region, erection of the penis, which is known to be due to a reflex dilatation of its arteries through the nervi erigentes, can still be caused by mechanical stimulation of the glans penis, so long as the afferent fibres of the reflex arc contained in the nervus pudendus are intact. Destruction of the lumbar cord abolishes the effect. It is impossible to avoid the conclusion that a vaso-dilator or erection centre, which is in relation on the one hand with the nervi erigentes, and on the other with the nervus pudendus, exists in the lower portion of the spinal cord. Vaso-motor centres for the hind-limbs have also been located in the same region. And such centres appear to exist even beyond the limits of the central nervous system. For when the lower portion of the cord is completely destroyed, the dilatation of the vessels of the hind-limbs, which is at first so conspicuous, passes away after a time; and the only plausible explanation seems to be that the functions of vaso-motor centres have been assumed by some of the peripheral (sympathetic) ganglia (Goltz and Ewald).

Of the anatomical relations of the nerve-cells that make up the bulbar and spinal vaso-motor centres, little more is known than may

be deduced from the physiological facts we have been reciting. It has been surmised that certain cells of small size scattered up and down the cord in the anterior horn and intermedio-lateral tract, and cropping out also in the bulb, are vaso-motor cells. It must be assumed that their axis-cylinder processes are connected with the vaso-motor fibres which we have already discovered emerging from the brain in certain cranial nerves and from the cord in the anterior spinal roots. And, indeed, there is reason to believe that, in the case of the spinal vaso-motor cells at any rate, the connection is made without the intervention of any other nerve-cells, and that the axis-cylinders of these vaso-motor fibres are the axis-cylinder processes of the vaso-motor cells. So that the simplest efferent path along which vaso-motor impulses can pass may be considered as built up of two neurons, one with its cell-body in the central nervous system, and the other in a sympathetic ganglion. But since it would appear that the spinal vaso-motor centres are under the control of the chief centre in the bulb, it is necessary to suppose that the axis-cylinder processes of some of the cells of the bulbar centre come into relation with the spinal vaso-motor cells, and that impulses passing, let us say, from the bulb to the vessels of the leg, would have to traverse three neurons (see Chap. XII.).

Vaso-motor Reflexes.—We have already seen that the cardiac centres are constantly influenced by afferent impulses, and that in the direction either of augmentation or inhibition. The vaso-motor centre in the bulb is equally sensitive to such impulses. They reach it for the most part along the same nerves, and by increasing or diminishing its tone cause sometimes constriction and sometimes dilatation of the vessels, the result depending partly upon the anatomical connection of the afferent fibres, but apparently in part also upon the state of the centre.

Of the afferent nerves that cause vaso-dilatation, the most important is the depressor, whose reflex inhibitory action on the heart has been already described. The fall in the arterial pressure is due chiefly, not to the inhibition of the heart, but to the inhibition of the portion of the vaso-motor centre that presides over the great area ruled by the splanchnic nerves, and the consequent dilatation of the vessels of the abdominal viscera. For if these nerves have been previously cut, stimulation of the depressor is ineffective, while it produces its usual result after section of the vagi. It has been suggested that the function of the depressor is to act as an automatic check upon the blood-pressure in the

interest of the heart, its terminations in the ventricular wall being mechanically stimulated when the pressure tends to rise towards the danger limit. In rare cases, efferent inhibitory fibres for the heart have been found in the depressor of the rabbit.

Many of the peripheral nerves contain fibres whose stimulation is followed by dilatation of the bloodvessels in special regions, usually the areas to which they are themselves distributed, accompanied by constriction of distant and, it may be, more extensive vascular tracts. Thus, the usual local effect of stimulating the afferent fibres of the

FIG. 54.—DIAGRAM OF DEPRESSOR NERVE IN RABBIT.

X, vagus; SL, superior laryngeal branch of vagus; D, depressor fibres. The arrows show the course of the impulses that affect the blood-pressure.

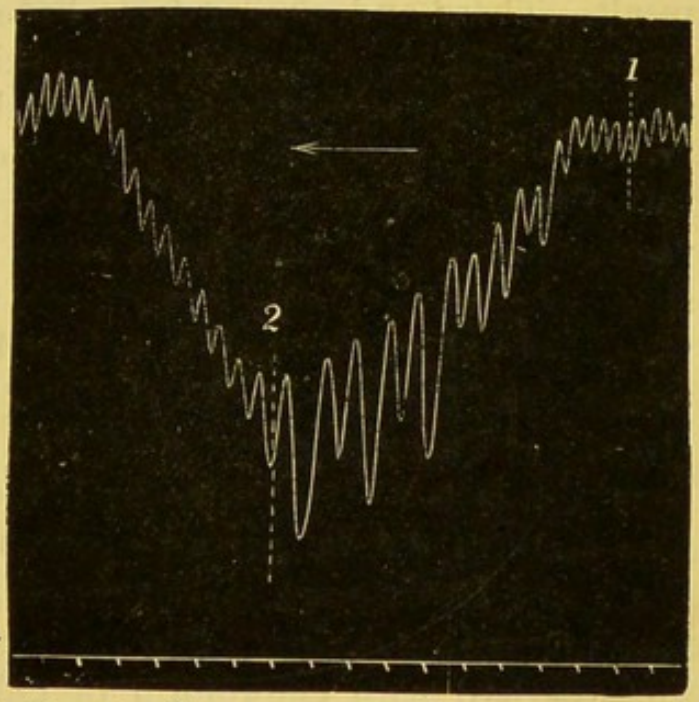


FIG. 55.—BLOOD-PRESSURE TRACING (RABBIT). (MERCURY MANOMETER.)

Central end of depressor stimulated at 1; stimulation stopped at 2. Time trace seconds.

lowest three thoracic nerves, in whose anterior roots run the vaso-motor fibres for the kidney, is a dilatation of the renal vessels (Bradford), and the usual local effect of stimulating the infra-orbital or supra-orbital nerve a dilatation of the external maxillary artery. But the general effect in both cases is vaso-constriction in other regions of the body, which more than compensates the local dilatation, so that the arterial blood-pressure rises. It is not difficult to see that both of these changes render it easier for the part to obtain an increased supply of blood.

The kind of stimulus seems to have something to do with the direction of the reflex vaso-motor change, for while electrical stimulation of every muscular nerve, even of the very finest twigs that can be isolated and laid on electrodes, provokes always, whether the shocks follow each other rapidly or slowly, a rise of general blood-pressure, mechanical stimulation of a muscle, as by kneading or massage, causes a fall. The condition of the afferent fibres also exerts an influence. For example, excitation of the central end of a sciatic nerve that has been cooled is followed by vaso-dilatation and fall of pressure, the opposite of the ordinary result. These and similar facts have led to the idea that most afferent nerves contain two kinds of fibres, whose stimulation can affect the activity of the vaso-motor centres, 'reflex vaso-constrictor,' or 'pressor' fibres, and 'reflex vaso-dilator,' or 'depressor' fibres. The branch of the vagus, however, to which the name 'depressor' has been specially given, is the only peripheral nerve the excitation of which is in all circumstances followed by a general diminution of arterial pressure. If specific 'depressor' fibres exist elsewhere, they are so mingled with 'pressor' fibres that their action is masked when both are stimulated together. The state of the vaso-motor centre is a third factor, which has some importance in determining the result of reflex vaso-motor stimulation. For instance, in an animal deeply anæsthetized with chloroform or chloral, excitation of an ordinary sensory nerve may cause, not a rise, but a fall of blood-pressure.

An interesting illustration of the reciprocal relation between different parts is found in the opposite behaviour of the vessels of the skin and those of the internal organs, which is often observed during reflex stimulation of the vaso-motor centres. For example, stimulation of the cut end of the sciatic causes, as we have already seen, a notable rise in the blood-pressure and extensive vaso-constriction. This certainly involves the splanchnic area; but superficial parts, as the lips, may be seen to be flushed with blood. In asphyxia, when the vaso-motor centres are directly stimulated by the venous blood, this antagonism is still better

marked: the cutaneous vessels are widely dilated and engorged, the face is livid, but the abdominal organs are pale and bloodless (Heidenhain). The blood-pressure rises rapidly, reaches a maximum, and then gradually falls as the vaso-motor centre becomes paralyzed (Figs. 56 and 57).

These facts enable us to some extent to understand the manner in which the distribution of the blood is adjusted to the requirements of the different parts of the body, so that to a certain degree of approximation no organ has too much, and none too little. The blood-supply of the organs is always shifting with the calls upon them. Now, it is the actively-digesting stomach and the actively-secreting glands of the alimentary tract which must be fed with a full stream

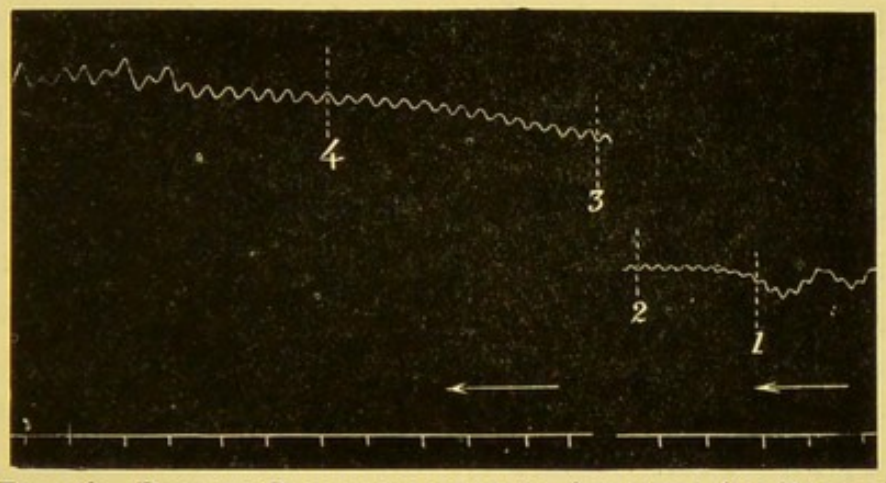


FIG. 56.—RISE OF BLOOD-PRESSURE IN ASPHYXIA (IN RABBIT).

Respiration stopped at 1. Interval between 2 and 3 (not reproduced) 44 seconds, during which the blood-pressure steadily rose. At 4, respiration resumed. Time tracing marks seconds.

of blood, to supply waste and to carry away absorbed nutriment. Again, it is the working muscles of the legs or of the arms that need the chief blood-supply. But wherever the call may be, the vaso-motor mechanism is able, in health, to answer it by bringing about a widening of the small arteries of the part which needs more blood, and a compensatory narrowing of the vessels of other parts whose needs are not so great.

It is also through the vaso-motor system, and especially by the action of that portion of it which governs the abdominal vessels, and of the nerves that regulate the work of the heart, that in animals to which the upright position

is normal (monkey) and in man the influence of changes of posture on the circulation is almost completely compensated.* The pressure in the upper part of the human brachial artery has been measured by Hill with the sphygmometer, first in the horizontal and then immediately afterward in the standing posture, and in health it has been found to remain practically unchanged. But if the person was over-worked or out of sorts, the compensation was less complete. In such animals as the rabbit this compensation is totally inefficient. When a domesticated rabbit, which has been kept in a hutch, is suspended vertically with the feet down, the blood drains into the abdominal vessels, syncope speedily ensues, and in a period that ranges from less than a quarter to three-quarters of an hour the animal dies in the convulsions of acute cerebral anæmia (Salathé, Hill). The head-down position has no ill effects. In wild rabbits, whose abdominal wall is more tense and elastic, these fatal symptoms are not easily produced, and the same is true of cats and dogs. But in all animals, when the compensation is destroyed, as in paralysis of the vaso-motor centre by chloroform, the circulation may be profoundly influenced by the position of the body: elevation of the head may lead to cerebral anæmia, syncope, and even death; elevation of the legs, and particularly the abdomen, may restore the sinking pulse by filling the heart and the vessels of the brain. If a chloralized dog be fastened on a board which can be rotated about a

* Two factors may be distinguished in the blood-pressure, the hydrostatic and the hydrodynamic elements. The hydrostatic portion of the pressure is due to the weight of the column of blood acting on the vessel; the hydrodynamic portion of the pressure is due to the work of the heart. If a dog be securely fastened to a holder arranged in such a way that the animal can be placed vertically, with the head up or down, and the mean blood-pressure in the crural artery be measured in the two positions, there will be a considerable difference. For when the legs are uppermost the heart has to overcome the weight of the column of blood rising above it to the crural artery; when the head is uppermost the action of the heart is reinforced by the weight of the blood. And if no change were produced in the action of the heart, or in the general resistance of the vascular path, by the change of position, this difference would be equal to the pressure of a column of blood twice as high as the straight-line distance between the cannula and the point of the arterial system at which the pressure is the same with head up as with head down (indifferent point).

horizontal axis passing under the neck, the blood-pressure in the carotid artery falls greatly when the animal is made to assume the vertical position with the head up, and either rises a little or remains practically unchanged when the head is made to hang down. So great may the fall of pressure be in the former position that death may occur if it be long maintained (Practical Exercises, p. 187).

Finally, it is in virtue of the amazing power of accommodation possessed by the vascular system, as controlled by the vaso-motor and cardiac nerves, that so long as these are

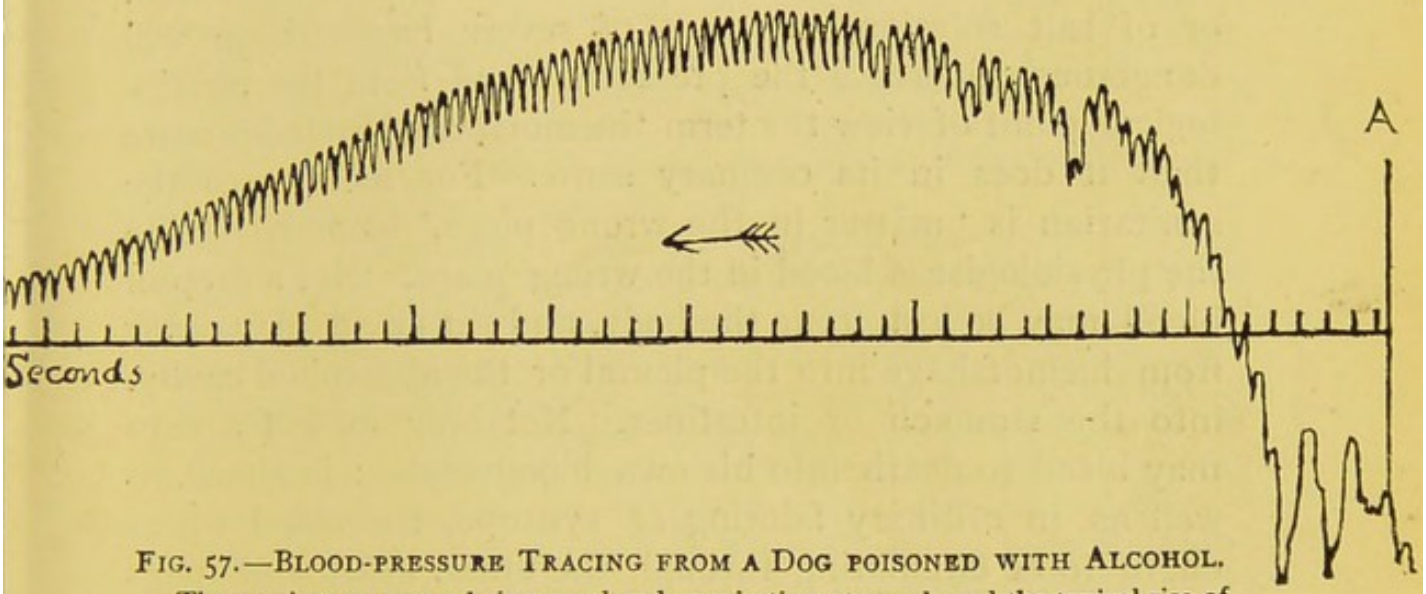


FIG. 57.—BLOOD-PRESSURE TRACING FROM A DOG POISONED WITH ALCOHOL.

The respiratory centre being paralyzed, respiration stopped, and the typical rise of blood-pressure in asphyxia took place. The pressure had again fallen, and total paralysis of the vaso-motor centre was near at hand, when at A the animal made a single respiratory movement. The quantity of oxygen thus taken in was enough to restore the vaso-motor centre, and the blood-pressure again rose. This was repeated five or six times.

not disabled the total quantity of blood may be greatly diminished or greatly increased, without endangering life, or even causing more than a transient alteration in the arterial pressure. It is not until at least a quarter of the blood has been withdrawn that there is any notable effect on the pressure, for the loss is quickly compensated by an increase in the activity of the heart and a constriction of the small arteries. An animal may recover after losing considerably more than half its blood.* Conversely, the volume

* It is not usually possible to obtain quite two-thirds of the total blood by bleeding a dog from a large artery. In seven dogs bled from the carotid, the ratio of the weight of the blood obtained to the body weight was 1 : 24·7, 1 : 21·7, 1 : 20·7, 1 : 20·6, 1 : 18·6, 1 : 16, 1 : 13·5. In the last case, the blood clotted with abnormal slowness, and the animal died in a few minutes.

of the circulating liquid may be almost doubled by the injection of blood or normal saline solution without causing death, and increased by 50 per cent. without any marked increase in the pressure. The excess is promptly stowed away in the dilated vessels, especially those of the splanchnic area; the water passes rapidly into the lymph, and is then more gradually eliminated by the kidneys.

From these facts we can deduce the practical lesson, that blood-letting, unless copious, is useless as a means of lowering the general arterial pressure, while it need not be feared that transfusion of a considerable quantity of blood, or of salt solution, in cases of severe hæmorrhage will dangerously increase the pressure. And from the physiological point of view the term 'hæmorrhage' includes more than it does in its ordinary sense. For as dirt to the sanitarian is 'matter in the wrong place,' hæmorrhage to the physiologist is blood in the wrong place. Not a drop of blood may be lost from the body, and yet death may occur from hæmorrhage into the pleural or the abdominal cavity, into the stomach or intestines. Not only so, but a man may bleed to death into his own bloodvessels; in shock, as well as in ordinary fainting or syncope, the blood which ought to be circulating through the brain, heart and lungs may stagnate in the dilated vessels of the splanchnic area.

The Lymphatic Circulation.—As has already been mentioned, some of the constituents of the blood, instead of passing back to the heart from the capillaries along the veins, find their way by a much more tedious route along the lymphatics. The blood-capillaries are everywhere in very intimate relation with lymph-capillaries, which are simply irregular spaces, more or less completely lined with epithelioid cells, in the connective-tissue that everywhere accompanies and supports the bloodvessels. The constituents of the blood-plasma are filtered through, or, as some say, secreted by the capillary walls into the lymph spaces, and there form the clear liquid known as lymph, from which the cells of the tissues take up food, and into which they discharge waste products. The lymph spaces are connected with more regular lymphatic vessels, with lymphatic glands at intervals on their course. These fall into larger trunks, and finally the greater part of the lymph reaches the blood again by the thoracic duct, which opens into the venous system at the junction of the left subclavian and internal jugular veins. The lymph from the right side of the head and neck, the right extremity, and the right side of the thorax with its viscera, is collected by the right

lymphatic duct, which opens at the junction of the right subclavian and internal jugular veins. The openings of both ducts are guarded by semilunar valves, which prevent the reflux of blood from the veins. Serous cavities like the pleural sacs are really large lymph spaces, and they are connected through small openings, called stomata, with lymphatic vessels.

The rate of flow of the lymph in the thoracic duct is very small compared with that of the blood in the arteries—only about 4 mm. per second, according to one observer. Nevertheless, a substance injected into the blood can be detected in the lymph of the duct in four to seven minutes (Tschirwinsky). The factors which contribute to the maintenance of the lymph flow are:

(1) The pressure under which it passes from the capillaries into the lymph spaces. The pressure in the thoracic duct of a horse may be as high as 12 mm. of mercury; in the dog it may be less than 1 mm. The difference is probably due, in part at least, to a difference in the experimental conditions, dogs being usually anæsthetized for such measurements, horses not. The pressure in the lymph spaces must, of course, be higher than in the thoracic duct, how much higher we do not know.

(2) The contraction of muscles increases the pressure of the lymph by compressing the channels in which it is contained, and the valves, with which the lymphatics are even more richly provided than the veins, hinder a backward and favour an onward flow. The contractions of the intestines, and especially of the villi, are an important aid to the movement of the chyle. By the contraction of the diaphragm, substances may be sucked from the peritoneal cavity into the lymphatics of its central tendon, through the stomata in the serous layer with which its lower surface is clad. It is even possible by passive movements of the diaphragm in a dead rabbit to inject its lymphatics with a coloured liquid placed on its peritoneal surface. Passive movements of the limbs and massage of the muscles are also known to hasten the sluggish current of the lymph, and are sometimes employed with this object in the treatment of disease.

(3) The movements of respiration aid the flow. At every inspiration the pressure in the great veins near the heart becomes negative, and lymph is sucked into them.

(4) In some animals rhythmically-contracting muscular sacs or hearts exist on the course of the lymphatic circulation. The frog has two pairs, an anterior and a posterior, of these lymph hearts, which pulsate, although not with any great regularity, at an average rate of sixty to seventy beats a minute, and appear to be governed by motor and inhibitory centres situated in the spinal cord. Such hearts are also found in reptiles. It is possible that in animals without localized lymph hearts the smooth muscle, which is so conspicuous an element in the walls of the lymphatic vessels, may aid the flow by rhythmical contractions.

PRACTICAL EXERCISES ON CHAPTER II.

1. **Microscopic Examination of the Circulating Blood.**—(1) Take a tadpole and lay it on a glass slide. Cover the tail with a large cover-slip, and examine it with the low power (Leitz, oc. III., obj. 3). Generally the tail will stick so closely to the slide, and the animal will move so little, that a sufficiently good view of the circulation can be obtained. If there is any trouble, destroy the brain with a needle.

Observe the current of the blood in arteries, capillaries and veins. An artery may be easily distinguished from a vein by looking for a place at which the vessel bifurcates. In veins the blood flows in the two branches of the fork *towards* the point of bifurcation, in arteries *away from* it.

Sketch a part of a field.

To Pith a Frog.—Wrap the animal in a towel, bend the head forwards with the index-finger of one hand, feel with the other for the depression at the junction of the head and backbone, and push a narrow-bladed knife right down in the middle line. The spinal cord will thus be divided with little bleeding. Now push into the cavity of the skull a piece of pointed lucifer match. The brain will thus be destroyed. The spinal cord can be destroyed by passing a blunt needle down inside the vertebral canal.

(2) Take a frog and pith its brain only, inserting a match to prevent bleeding. Pin the frog on a plate of cork into one end of which a glass slide has been fastened with sealing-wax. Lay the web of one of the hind-legs on the glass and gently separate two of the toes, if necessary by threads attached to them and secured to the cork plate. Put the plate on the microscope-stage and fasten by the clips (see pp. 26, 107).

2. **Anatomy of the Frog's Heart.**—Expose the heart of a pithed frog by pinching up the skin over the abdomen in the middle line, dividing it with scissors up to the lower jaw, and then cutting through the abdominal muscles and the bony pectoral girdle. The external abdominal vein, which will be observed on reflecting the skin, can be easily avoided. The heart will now be seen enclosed in a thin membrane, the pericardium, which should be grasped with fine-pointed forceps and freely divided. Connecting the posterior surface of the heart and the pericardium is a slender band of connective tissue, the frænum. A silk ligature may be passed around this with a threaded curved needle and tied, and then the frænum may be divided posterior to the ligature. The anatomical arrangement of the various parts of the heart should now be studied. Note the single ventricle with the bulbus arteriosus, the two auricles, and the sinus venosus, turning the heart over to see the latter by means of the ligature. Observe the whitish crescent at the junction of the sinus venosus and the right auricle (Fig. 58).

3. **The Beat of the Heart.**—Note that the auricles beat first, and then the ventricle. The ventricle becomes smaller and paler during its systole, and blushes red during diastole. Count the number of beats of the heart in a minute. Now excise the heart, lifting it by means

of the ligature, and taking care to cut wide of the sinus venosus. Place the heart in a small porcelain capsule on a little blotting-paper moistened with normal saline. Observe that it goes on beating. Put a little ice or snow in contact with the heart, and count the number of beats in a minute. The rate is greatly diminished. Now remove the ice and blotting-paper, cover the heart with normal saline, and heat, noting the temperature with a thermometer. Observe that the heart beats faster and faster as the temperature rises. At 40° C. to 43° C. it stops beating in diastole (heat standstill). Now at once pour off the heated liquid, and run in some cold normal saline. The heart will begin to beat again.

4. Cut off the apex of the ventricle a little below the auriculo-ventricular groove. The auricles, with the attached portions of the ventricle, go on beating. The apex does not contract spontaneously, but can be made to beat by stimulating it mechanically (by pricking it with a needle) or electrically. Divide the still contracting portion of the heart by a longitudinal incision. The two halves go on beating.

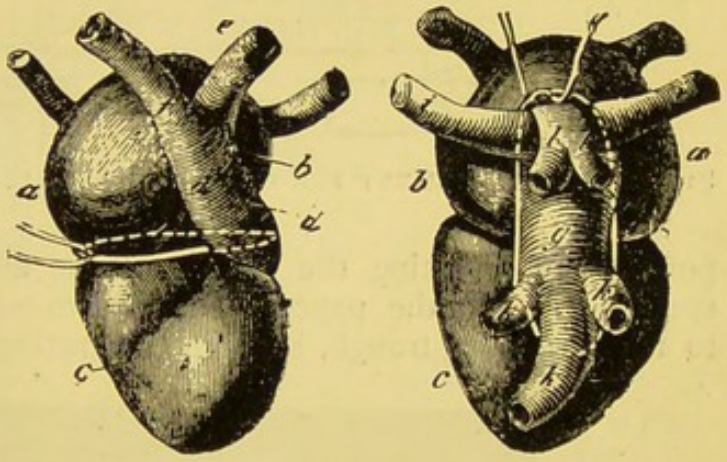


FIG. 58.—FROG'S HEART WITH STANNIUS LIGATURES IN POSITION (CYON).

Anterior surface of heart shown on the left, posterior surface on the right. *a*, right auricle; *b*, left auricle; *c*, ventricle; *d*, bulbus arteriosus; *e*, *f*, aortæ; *g*, sinus venosus.

5. **Heart-tracings.**—(1) Fasten a myograph-plate (Fig. 59) on a stand. Take a long light lever consisting of a straw or a piece of thin chip, armed at one end with a writing-point of parchment-paper, supported near the other end by a horizontal axis, and pierced not far from the axis by a needle carrying on its point a small piece of cork or a ball of sealing-wax. A counterpoise is adjusted on the short arm of the lever in the form of a small leaden weight. Cover a drum with glazed paper and smoke it. The paper must be put on so tightly that it will not slip. To smoke the drum, hold it by the spindle in both hands over a fish-tail burner, depress the drum in the flame, and rotate rapidly. Avoid putting on a heavy coating of smoke, as a more delicate tracing is obtained when the paper is lightly smoked The speed of the drum can be varied by putting in or taking out a small vane. Arrange an electro-magnetic time-marker for writing seconds (Fig. 60). Pith a frog (brain only), expose the heart, and put under it a cover-slip to give it support. Pin the frog on the myograph-plate, and adjust the foot of the lever so that it rests on the ventricle or the auriculo-ventricular junction. Bring the writing-point of the lever and that of the time-marker vertically

under each other on the surface of the drum. Set off the drum at the slow speed (say, a centimetre a second). When the lever rests on the auriculo-ventricular junction, the part of the tracing corresponding to the contraction of the heart will be broken into two

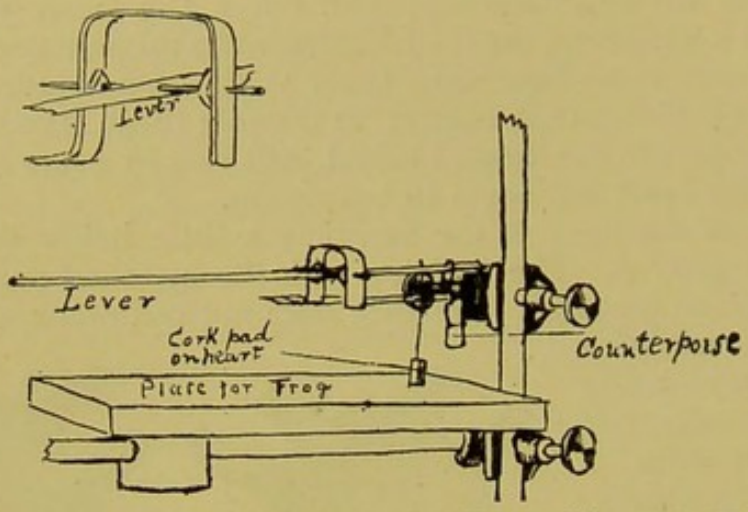


FIG. 59.—ARRANGEMENT FOR OBTAINING A HEART TRACING FROM A FROG.

portions, representing the systole of the auricles and ventricle respectively. Cut the paper off the drum with a knife and carry it to the varnishing-trough, holding the tracing by the ends with both

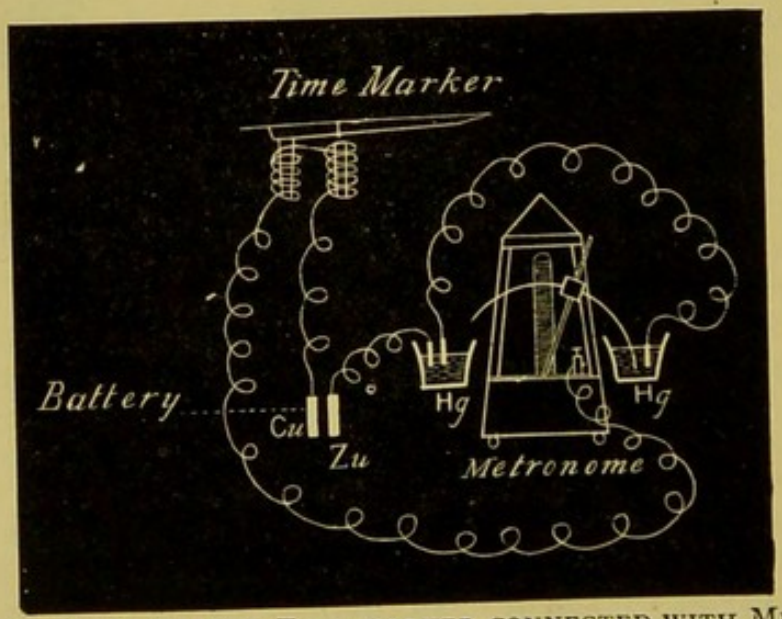


FIG. 60.—ELECTRO-MAGNETIC TIME-MARKER CONNECTED WITH METRONOME.

The pendulum of the metronome carries a wire which closes the circuit when it dips into either of the mercury cups, Hg.

hands, smoked side up. Immerse the middle of it in the varnish, draw first one end and then the other through the varnish, let it drip for a minute into the trough, and fasten it up with a pin to dry.

(2) *Heart Tracing, with Simultaneous Record of Auricular and*

Ventricular Contractions.—(*a*) For this purpose two levers may be arranged, one resting on the auricle, the other on the ventricle, the writing points being placed in the same vertical straight line on the drum. A convenient form of apparatus is shown in Fig. 61.

(*b*) *Gaskell's Method* (*a modification of*).—Attach a silk ligature to the very apex of the ventricle. Divide the frænum, cut the aorta across close to the bulbus, pinch up a tiny portion of the auricle and ligature it. Remove the intestines, liver, lungs, etc., care being taken in cutting away the liver not to injure the sinus. Then remove the lower jaw, and cut away the whole of the body except the head, part of the œsophagus, and the tissue connecting it with the heart. Fix the head in a clamp sliding on an ordinary stand. The heart is held at the auriculo-ventricular junction in a Gaskell's clamp supported on

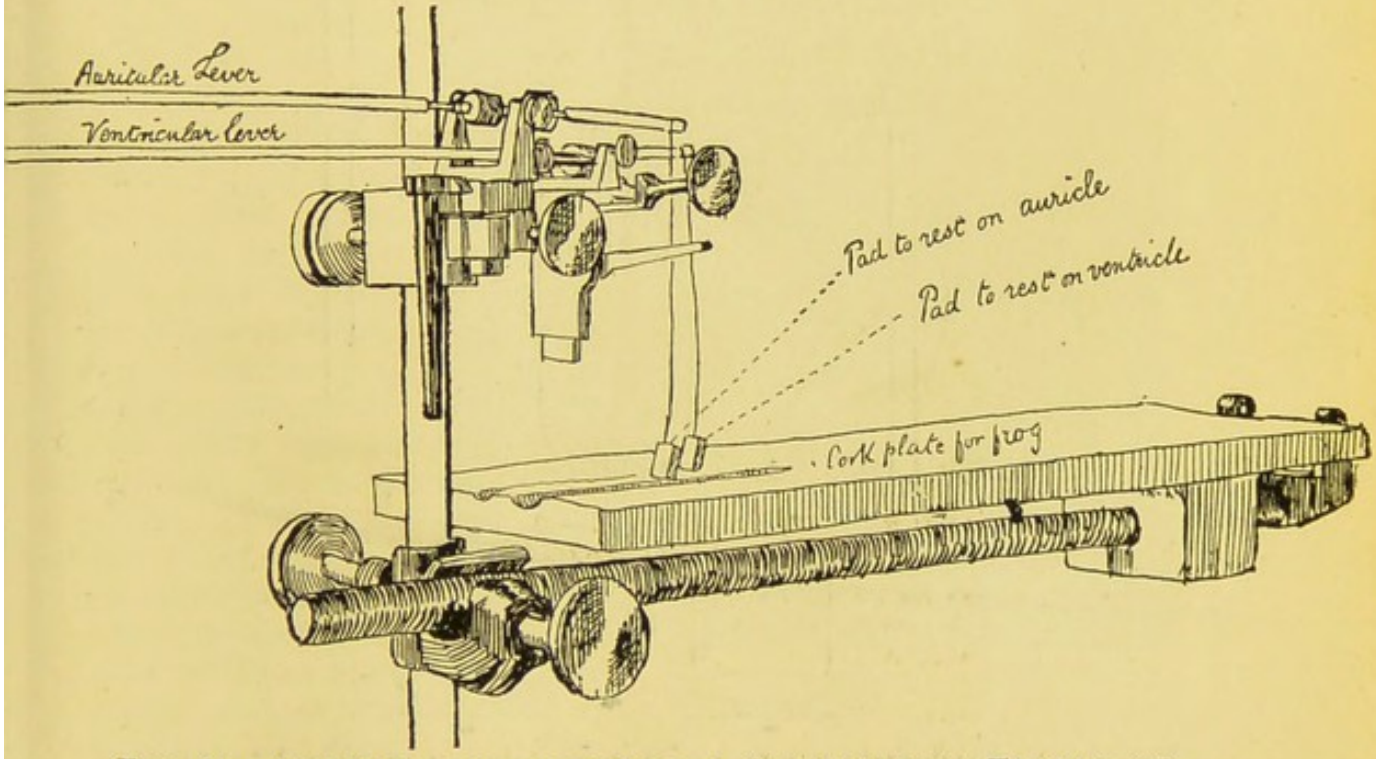


FIG. 61.—APPARATUS FOR OBTAINING A SIMULTANEOUS TRACING OF AURICULAR AND VENTRICULAR CONTRACTIONS.

a separate stand. The thread connected with the ventricle is brought round a pulley and attached to a lever above the heart. The auricle is connected with another lever. The writing points of the two levers are arranged in a vertical line on the drum. The small pulley must be oiled from time to time to lessen the friction (Fig. 62).

6. **Dissection of the Vagus and Cardiac Sympathetic Nerves in the Frog.**—(1) Put the tissues in the region of the neck on the stretch by passing into the gullet a narrow test-tube or a thick glass rod moistened with water, and by pinning apart the anterior limbs. Expose the heart by cutting through the pectoral girdle in the way described in 2 (p. 168). On clearing away a little connective tissue and muscle with a seeker, three large nerves will come into view. The upper is the glosso-pharyngeal, the lower the hypoglossal ; the

vagus crosses diagonally between them (Fig. 63). Above the vagus trunk, running parallel to it, and separated from it by a thin muscle and a blood-vessel (the carotid artery), lies its laryngeal branch. The vagus should be traced up to the ganglion situated on it near its exit from the skull.

(2) Then cut away the lower jaw, dividing and reflecting the membrane covering the roof of the mouth. At the junction of the

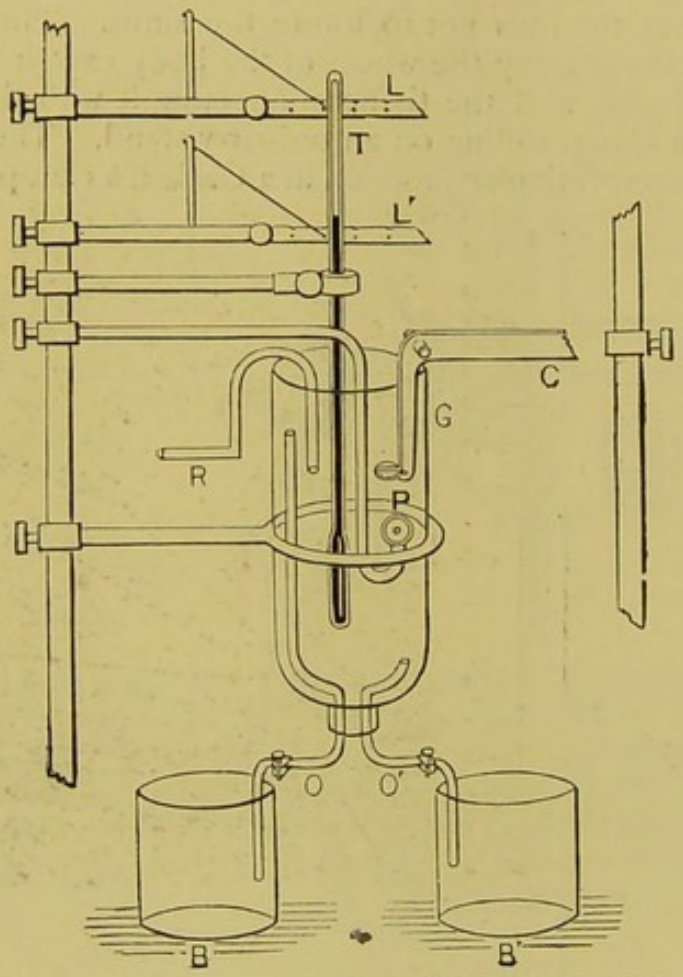


FIG. 62.—ARRANGEMENT FOR RECORDING AURICULAR AND VENTRICULAR CONTRACTIONS (AND STUDYING THE INFLUENCE OF TEMPERATURE ON THE HEART).

C, clamp holding the heart at the auriculo-ventricular groove. P, pulley round which a thread attached to the apex of the ventricle passes to the lever L'; L, lever connected with auricle. (The rest of the arrangement is for studying the influence of temperature on the heart and its nerves, G being a vessel filled with normal saline solution in which the heart is immersed; R, an inflow tube from a reservoir containing salt solution at the temperature required; O', an outflow tube by which G may be emptied into the beaker B'; O, a tube passing to the beaker B to prevent overflow from G; T, a thermometer.)

skull and the backbone will be seen on each side the levator anguli scapulæ muscle (Fig. 64). Remove this muscle carefully with fine forceps. Clear away a little connective tissue lying just over the upper cervical vertebræ, and the sympathetic chain, with its ganglia, will be seen. Pass a fine silk thread beneath the sympathetic about the level of the large brachial nerve, by means of a sewing-needle which has been slightly bent in a flame and fastened in a handle. Tie the

ligature, divide the sympathetic below it, and isolate it carefully with fine scissors up to its junction with the vagus ganglion.

Batteries.—*To set up a Daniell Cell.*—Fill the porous pot (Fig. 143, p. 517) previously well soaked in water, with dilute sulphuric acid (1 part of commercial acid to 10 or 15 parts of water) to within 1½ inches of the brim, and place in it the piece of amalgamated zinc. If the zinc is not properly amalgamated, leave it in the pot for a minute or two to clean its surface. Then lift it out, pour over it a little mercury, and rub the mercury thoroughly over it with a cloth. Put the pot into the outer vessel, which contains the copper plate, and is filled with a saturated solution of sulphate of copper, with some undissolved crystals to keep it saturated. After using the Daniell, it must always be taken down. The outer pot is left with the copper plate and the sulphate solution in it. The zinc is washed and brushed bright. The sulphuric acid is poured into the stock bottle, and the porous pot put into a large jar of water to soak.

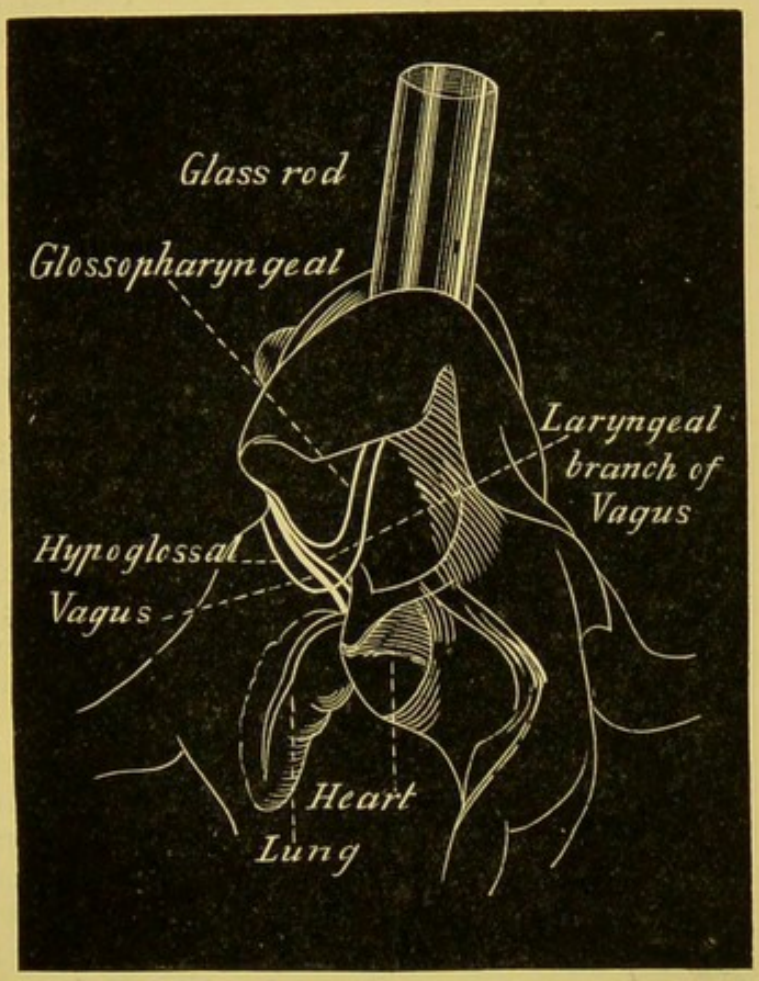


FIG. 63.—THE RELATIONS OF THE VAGUS IN THE FROG.

The Bichromate Cell contains only one liquid—a mixture of 1 part of sulphuric acid with 4 parts of a 10 per cent. solution of potassium bichromate. In this is placed one, or in some forms two, carbon plates and a plate of amalgamated zinc. After using the battery, take the zinc out of the liquid.

The Leclanché battery consists of a porous pot filled with a mixture of manganese dioxide and carbon packed around a carbon plate, which forms the positive pole. The pot stands in an outer jar of glass filled with a saturated solution of ammonium chloride, into which dips an amalgamated zinc rod, which constitutes the negative pole.

7. **Stimulation of the Vagus in the Frog.**—Make the same arrangements as in 5 (1) (p. 169), but, in addition, set up an induction machine arranged for an interrupted current (Fig. 65), with a Daniell,

a bichromate, or a Leclanché cell in the primary circuit, which should also include a simple key. Insert a short-circuiting key in the secondary circuit. Attach the electrodes to the short-circuiting key, push the secondary coil up towards the primary until the shocks are distinctly felt on the tongue when the Neef's hammer is set going and the short-circuiting key opened. Pith the brain of a frog, expose the heart, dissect out the vagus on one side, ligature it as high up as possible, and divide above the ligature. Fasten the electrodes on the cork plate by means of an indiarubber band, and lay the vagus on them. Set the drum off (at slow speed). After a dozen heart-beats have been recorded, stimulate the vagus for two or three seconds by opening the short-circuiting key. If the nerve is active, the heart will be slowed, weakened, or stopped. In the last case the lever will trace an unbroken straight line; but even if the stimulation is continued the beats will again begin.

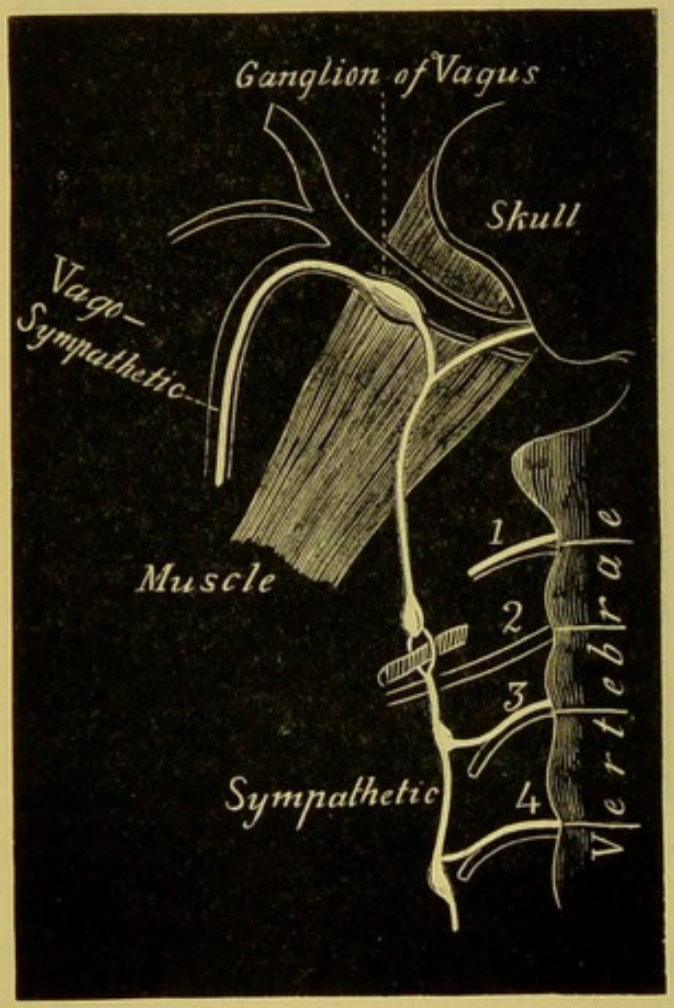


FIG. 64.—RELATION OF THE SYMPATHETIC TO THE VAGUS IN THE FROG.

1, 2, 3, 4 are spinal nerves.

8. **Stimulation of the Junction of the Sinus and Auricles.** — After a sufficient number of the observations described in 7 have been taken with varying time and strength of stimulation, take the writing-points off the drum, apply the electrodes directly to the crescent at the junction of the sinus venosus with the right auricle, and stimulate. The heart will be affected very much in the same way as by stimulation of the vagus, except that during the actual stimulation its beats may be quickened and the inhibition may only begin after the electrodes have been removed (Fig. 46, p. 135).

9. **Effect of Muscarine and Atropia.**—Paint on the sinus venosus with a small camel's-hair brush a very dilute solution of muscarine. The heart will soon be seen to beat more slowly, and will ultimately stop in diastole. Now apply a dilute solution of sulphate of atropia to the sinus. The heart will again begin to beat. Stimulation of the vagus will now cause no inhibition of the heart, because its endings have been paralyzed by atropia. (Muscarine has also been

applied to the heart, but it could be shown by a separate experiment that atropia by itself has the same effect on the vagus endings.) (P. 141.)

10. **Stannius' Experiment.**—Pith a frog. Expose the heart in the way described under 2 (p. 168). Ligature the frænum with a fine silk thread, and use the thread to manipulate the heart. With a curved needle pass a moistened silk thread between the aorta and the superior vena cava, and tie it round the junction of the sinus and right auricle (Fig. 58). The auricles and ventricle stop beating as soon as the ligature is tightened. The sinus venosus goes on beating. Now separate the ventricle from the rest of the heart by an incision through the auriculo-ventricular groove, or tie a second ligature in the groove. The ventricle begins to beat again, the auricle remaining quiescent in diastole (p. 142). Occasionally both auricle and ventricle, or only the auricle, may begin to beat.

11. **Stimulation of Cardiac Sympathetic Fibres in the Frog.**—(1) *In the vago-sympathetic after the inhibitory fibres have been cut out by atropia.*—Arrange everything as in 7 (p. 173). Assure yourself, by

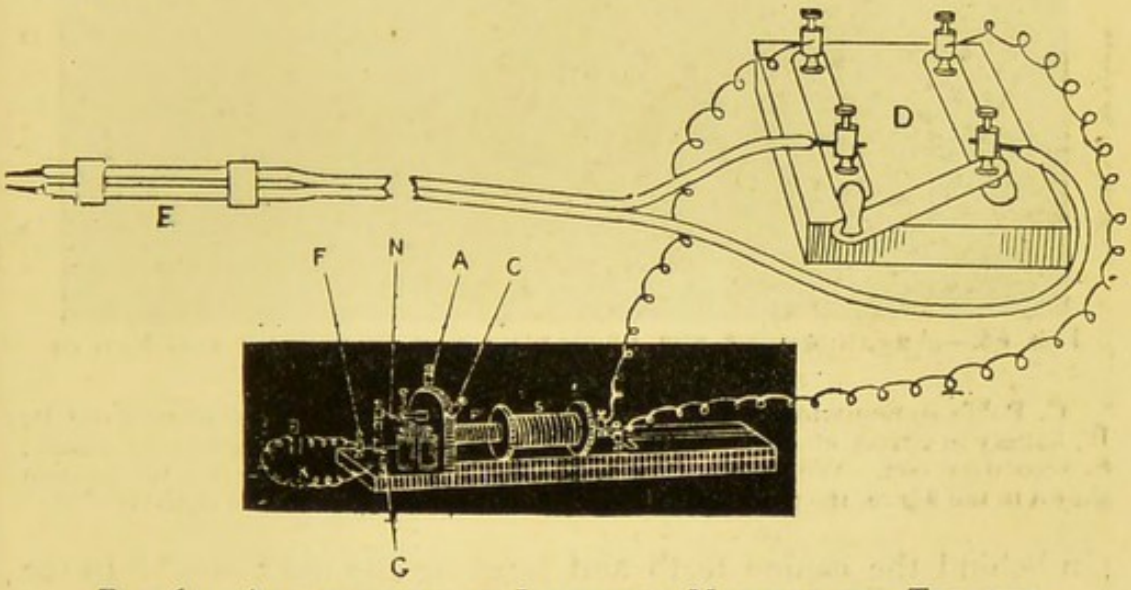


FIG. 65.—ARRANGEMENT OF INDUCTION MACHINE FOR TETANUS.

B, battery; K, simple key; P, primary coil; S, secondary coil; A, C, binding screws to be connected with battery for single shocks; F, G, binding screws for tetanizing current; N, Neef's hammer; D, short-circuiting key in secondary; E, electrodes. D and E are drawn to a much larger scale than the rest of the figure.

stimulating the vagus, that it inhibits the heart, and take a tracing during stimulation. Then paint a dilute solution of atropia on the sinus. Stimulation of the vagus, which is really the vago-sympathetic (see Fig. 64), will now cause, not inhibition, but augmentation (increase in rate or force, or both), since the endings of the inhibitory fibres have been paralyzed by atropia. The strength of the stimulating current required to bring out a typical augmentor effect is greater than that needed to stimulate the inhibitory fibres. Take a tracing to show augmentation produced by stimulating the nerve.

(2) *By direct stimulation of the cervical sympathetic.*—Make the same arrangements as in 11 (1), but, instead of isolating the vagus, dissect out the sympathetic on one side in the manner described in 6 (2) (p. 172), and do not apply atropia to the heart. Lay the upper

(cephalic) end of the sympathetic on very fine and well-insulated electrodes, and stimulate (Fig. 52, p. 143). (To insulate electrodes the points may be covered with melted paraffin. When the paraffin has cooled, a narrow groove, just sufficient to lay bare the wires on the upper side, is made in it, and the nerve is laid in this groove.)

Experiments 7, 11 (1) and 11 (2) will be rendered more exact by connecting a second electro-magnetic signal with a Pohl's commutator without cross-wires (Fig. 66), in such a way that the circuit is interrupted at the instant when stimulation begins.

12. **The Action of the Mammalian Heart.**—Inject under the skin of a dog (preferably a small one) 1 cc. of a 2 per cent. solution of morphia hydrochlorate for every kilogramme of body-weight. As soon as the morphia has taken effect (in 15-30 minutes), fasten the animal back down on a holder (as in Fig. 100), pushing the mouth-

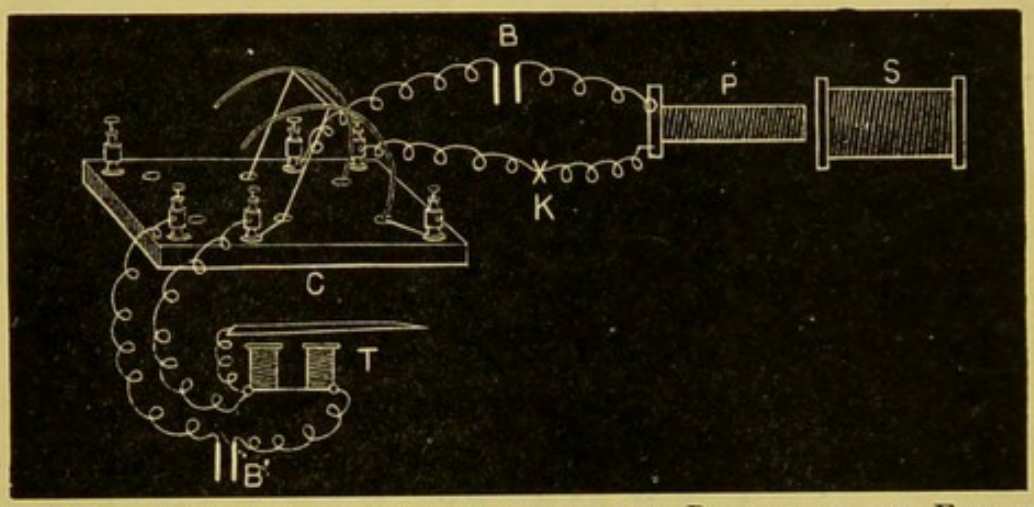


FIG. 66.—ARRANGEMENT FOR RECORDING THE BEGINNING AND END OF STIMULATION.

C, Pohl's commutator without cross-wires; B, battery in circuit of primary coil P; B', battery in circuit of electro-magnetic signal T; K, simple key in primary circuit; S, secondary coil. When the bridge of the commutator is tilted into the position shown in the figure, the primary circuit is closed and the circuit of the signal broken.

pin behind the canine teeth and screwing the nut home.* In the meantime select a tracheal cannula† of suitable size, and get ready

* A simple but efficient and convenient holder for a dog may be easily constructed as follows. Take a board of the length required (2½ to 5 feet, according to the size of the dog). At one end fasten two short upright wooden pins, with a clear space of 4 to 6 inches between them. These are pierced from side to side with four or five holes at different heights. An iron pin passing behind the canine teeth of the animal through two corresponding holes in the uprights, and tied over the muzzle by a cord arranged in a figure of eight, secures the head. For a large dog an upper pair of holes is used, for a small dog a lower pair. The feet are fastened by cords to staples inserted into the sides of the board, the fore-legs being drawn tailwards for all operations on the neck or head, headwards for operations on the thorax. A rabbit-holder can be made in exactly the same way.

† A tracheal cannula is easily made by heating a piece of glass tubing, about 6 inches long, a short distance from one end, and drawing it out slightly so as to form a 'neck.' The tubing is then bent about its middle to an obtuse angle, and the end next the neck is ground obliquely on a stone. The diameter of the cannula should be about the same as that of the trachea, into which it is to be inserted by its oblique end.

instruments for dissection—one or two pairs of artery-forceps, a pair of artery-clamps (bulldog pattern), two or three glass cannulæ of various sizes for bloodvessels, ten strong waxed ligatures, sponges, hot water, a towel or two, and a pair of bellows to be connected with the tracheal cannula when the chest is opened. Arrange an induction-coil and electrodes for a tetanizing current (Fig. 65, p. 175). With scissors curved on the flat clip away the hair from the front of the neck and the anterior surface of one thigh below Poupart's ligament. Put the hair carefully away, and remove all the loose hairs with a wet sponge so that they may not get into the wounds. If the animal is not fully anæsthetized, give ether. Insert a glass cannula, which should have a piece of indiarubber-tubing 2 to 3 inches in length on its wide end, into the central end of the femoral vein. Feel for the femoral artery, cut down over it, and with forceps or a blunt needle separate the femoral vein from it for about an inch. Pass two unwaxed ligatures under the vein, and tie a loose loop on each. Put a pair of bulldog forceps on the vein between the ligatures and the heart. Now tie the lower (distal) ligature, and cut one end short. The piece of vein between it and the bulldog forceps is thus distended with blood, and this facilitates the next step. With fine-pointed scissors make a snip in the wall of the vein. The cannula is now pushed through the slit in the vein, and the upper ligature tied firmly round its neck. By the aid of a pipette, made by drawing a piece of glass tubing out to a long point, the cannula and rubber tube are then completely filled with normal saline solution. Be sure to pass the point of the pipette right down to the point of the cannula, so as to dislodge any bubble of air that may tend to cling there. Then, holding up the open end of the rubber tube, close it, without allowing any air to enter, by means of a screw clamp or bulldog forceps, or a small piece of glass rod. 1 or 2 cc. of the 2 per cent. solution of morphia may be injected from time to time, when necessary, by pushing the needle of the hypodermic syringe through the rubber tube. When the needle is withdrawn the little hole closes completely, and nothing escapes from the cannula.

To put a Cannula in the Trachea.—The hair having been clipped in the middle line of the neck and the skin shaved, a mesial incision is to be made, beginning a little below the cricoid cartilage, which can be felt with the finger. The trachea is then cleared from its attachments by forceps or a blunt needle, and two strong ligatures are passed beneath it. A single loop is placed on each of those, but is not drawn tight. Raising the trachea by means of the upper ligature, the student makes a longitudinal incision through two or three of the cartilaginous rings, inserts the cannula, and ties the lower ligature firmly around its neck. It is well also, though not necessary, to now tie the upper ligature, and additional security may be obtained by tying together the ends of the two ligatures around the cannula.

Clip off the hair on each side of the sternum. Make an incision on each side through the skin and down to the costal cartilages about 2 inches from the edge of the breast-bone, and long enough to

expose about four costal cartilages (say, 3rd to 6th). With a curved needle pass waxed ligatures round the cartilages, and tie firmly to compress the intercostal vessels. Then pass a waxed ligature under the upper portion of the sternum, and tie it very tightly round that bone so as to occlude the internal mammary arteries. The bellows should now, or earlier if any symptoms of impeded respiration have appeared, be connected with one end of the horizontal limb of a glass T-piece, the other end of which is similarly connected with the tracheal cannula. The stem of the T-piece is provided with a short piece of rubber tubing, which, when artificial respiration is being carried on, is to be alternately closed and opened—closed during inflation of the lungs, and opened when the air is to be allowed to escape from them. Ether may, if necessary, be administered by passing this short tube through one neck of a Woulff's bottle containing the anæsthetic, and alternately compressing and opening it as described. If the cannula has a side-opening, as is usually the case with metal cannulæ, the T-piece may be dispensed with. One student should take sole charge of the artificial respiration, which ought to be begun as soon as the chest has been opened, and continued at the rate of about twenty inflations per minute. The costal cartilages and sternum are rapidly cut through with strong scissors just on the sternal side of the ligatures, and the sternum is divided below its ligature, the artificial respiration being suspended for an instant, as each cut is made, to avoid wounding the lungs. The lower part of the sternum is turned down like the lid of a box, tied out of the way or cut off altogether, and the heart, enclosed in the pericardium, comes into view. If the ligature round the sternum has not properly compressed the internal mammary arteries, hæmorrhage from the central ends may now occur. In this case they must be seized with artery-forceps and ligatured. A cotton thread is now passed with a suture-needle through each side of the pericardium, which is then stitched to the chest-wall and opened. The following observations and experiments should now be made:

(*a*) Note the various portions of the heart, right and left ventricles, right and left auricles, with the auricular appendices. Feel the heart with the hand, and observe that the right ventricle is softer and has thinner walls than the left, and that the auricles are softer than the ventricles. Note how all the parts of the heart harden in the hand during systole and soften during diastole (pp. 74-76).

(*b*) Dissect out the vago-sympathetic on one side in the neck of the dog. The guide to the nerve is the carotid artery. These two structures and the internal jugular vein lie side by side in a common sheath. Feel for the artery a little external to the trachea, cut down on it, open the sheath, isolate the vago-sympathetic for about an inch, pass two ligatures under it, tie them, and divide between the ligatures. The peripheral and central end of the nerve may now be successively stimulated. Stimulation of the peripheral end causes slowing of the heart or stoppage in diastole. Feel that it softens when it stops. It soon begins to beat again. Stimulation of the central end of the vago-sympathetic may or may not cause inhibition.

If it does, expose the other vago-sympathetic, divide it, and repeat the stimulation of the central end. There will now be no inhibition of the heart. Incidentally it may be seen that stimulation of the central end of the vago-sympathetic causes strong, though, of course, with opened chest, abortive, respiratory movements.

(*c*) Pith a frog (brain and cord), dissect out the sciatic nerve on one side up to the sacral plexus. Cut off the whole leg. Drop the cut end of the nerve on the heart, and hold the preparation so that the nerve touches the heart also by its longitudinal surface. At each cardiac beat the nerve is stimulated by the action current (Chap. XI.), and the muscles of the leg contract.

(*d*) Raise the board so that the head of the animal is down and the hind-feet up, and note whether there is any effect on the action and filling of the heart. Repeat the observation with head up and feet down.

(*e*) Compress the aorta with the fingers, and observe the effect on the degree of dilatation of the various cavities of the heart. Repeat the experiment with the inferior vena cava, and compare the results.

(*f*) Stop the artificial respiration, and observe the changes which take place in the auricles and ventricles, comparing particularly the right side of the heart with the left. Before the heart has stopped beating, recommence the artificial respiration.

(*g*) When the heart is again beating with a fair degree of regularity and strength, make a small penetrating wound with a scalpel in the left ventricle. Observe the course of the hæmorrhage, and note especially the difference in systole and diastole.

(*h*) Lay the electrodes on the heart, and stimulate it with a strong interrupted current. The character of the contraction soon becomes profoundly altered. Shallow irregular contractions flicker over the surface, with a kind of simmering movement suggestive of a boiling pot (delirium cordis, fibrillar contraction). Now kill the animal by stopping the artificial respiration. Observe how long the heart continues to beat, and which of its divisions stops last.

(*i*) Make a dissection of the cervical sympathetic up to the superior cervical ganglion, and down through the inferior cervical ganglion to the stellate or first thoracic ganglion. Make out the annulus of Vieussens and the cardiac sympathetic (accelerator) branches going off from the annulus or the inferior cervical ganglion to the cardiac plexus (Fig. 50, p. 139).

13. **Action of the Valves of the Heart.**—(1) Study the action of the valves of the ox-heart in the artificial scheme. Connect the ox-heart provided with the pump P and bottle B, as shown in Fig. 67. The cavity of the heart is illuminated by means of a small electric lamp, the wires of which pass in at A. When the piston of the pump is pushed down, water is forced through the aorta D along the tube T into the bottle, and flows back again into the left auricle by the tube T'. During each stroke of the pump the auriculo-ventricular valve is seen through the glass disc inserted into C to close, and the semilunar valve is seen through the glass in D to open. When

the piston is raised, the semilunar valve is seen to be closed and the auriculo-ventricular valve to be opened. For comparison a human heart with a valvular lesion might be used.

(2) With the sheep's or dog's heart provided, perform the following experiments:

(*a*) Open the pericardium and notice how it is reflected around the great vessels at the base of the heart. Distinguish the pulmonary artery, the aorta, the superior and inferior venæ cavæ, and the pulmonary veins. The trachea and portions of the lungs may also be attached. If so, remove them carefully without injuring the heart.

(*b*) Take two wide glass tubes, drawn slightly into a neck at one end. One of the tubes should be about 10 cm. long, and the other about 50 cm. Tie the short tube A firmly by its neck

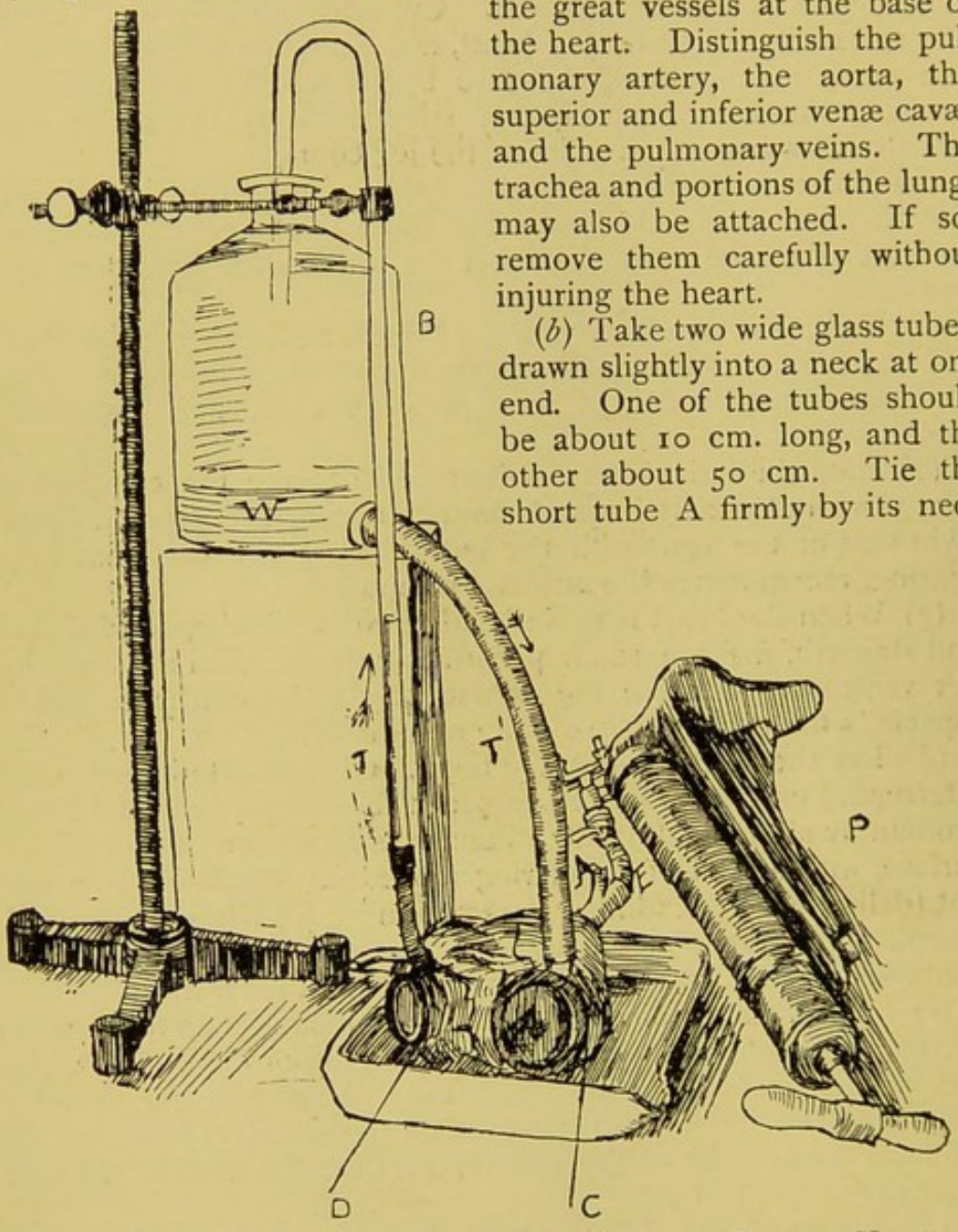


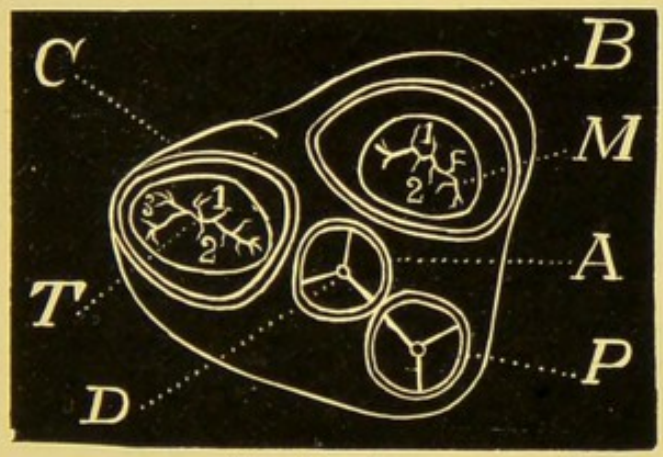
FIG. 67.—ARRANGEMENT TO ILLUSTRATE ACTION OF CARDIAC VALVES IN THE HEART OF AN OX (GAD).

C, glass window in left auricle; D, window in aorta; E, tube inserted through apex of heart into left ventricle and connected with pump P; A, side tube on E, through which wires are connected with a tiny incandescent lamp in the ventricle; W, water in bottle B; T, T′ tubes.

into the superior vena cava, the long tube B into the pulmonary artery. Ligature the inferior vena cava. Connect A by a small piece of rubber tubing with a funnel supported in a ring on a stand. Pour water into the funnel till the right side of the heart is full. It

will escape from the left azygos vein, which must be tied. Put on any additional ligatures that may be needed to render the heart water-tight. Support B in the vertical position by a clamp. Fill the funnel with water, and it will rise in B to the same level as in the funnel. Now compress the right ventricle with the hand, and the water will rise higher in B. Relax the pressure, and notice that the water remains at the higher level in B, being prevented by the semilunar valves from flowing back into the ventricle. By alternately compressing the ventricle and allowing it to relax, water can be pumped into B till it escapes from its upper end, and if this is so curved that the water falls into the funnel, a 'circulation' which imitates that of the blood can be established. Note that during the pumping the sinuses of Valsalva, behind the semilunar valves at the origin of the pulmonary artery, become prominent.

(*c*) Take out B and tear out one of the segments of the semilunar valve. Replace B, and notice that while compression of the ventricle has the same effect as before, the water no longer keeps its level on relaxation, but regurgitates into the ventricle. This illustrates the condition known as *insufficiency* or *incompetence* of the valves. But



The valves are supposed to be viewed from above, the auricles having been partially removed. *A*, aorta with semilunar valve; *D*, position of corpora Arantii; *P*, pulmonary artery; *B*, wall of left auricle; *M*, mitral valve, with 1 and 2, its posterior and anterior segments; *C*, wall of right auricle; *T*, tricuspid valve, with 1, its posterior, 2, its anterior, and 3, its external segment.

FIG. 68.—DIAGRAM OF VALVES OF HEART.

if the injury is not too extensive, it is still possible, by more vigorously and more rapidly compressing the heart, to pump water into the funnel. This illustrates the establishment of *compensation* in cases of valvular lesion.

(*d*) Now remove both tubes. Tie the pulmonary artery. Cut away the greater part of the right auricle. Pour water into the auriculo-ventricular orifice, and notice that the segments of the tricuspid valve are floated up so as to close the orifice. Invert the heart, and the ventricle will remain full of water. Open the right ventricle carefully, and study the papillary muscles, and the chordæ tendineæ, noting that the latter are inserted into the lower surface of the segments of the tricuspid valve, as well as into their free edges.

(*e*) Repeat (*b*), (*c*), and (*d*) on the left side of the heart, tying tube B into the aorta as far from the heart as possible, and A into the left auricle.

(*f*) Separate the aorta from the left ventricle, cutting wide of its origin so as not to injure the semilunar valves, and tie a short wide

tube into its distal end. Fill the tube with water, and notice that the valves support it. Cut open the aorta just between two adjacent segments of the valve, and notice the pockets behind the segments, and how they are related to each other, and connected to the wall of the vessel.

14. **Sounds of the Heart.**—(*a*) In a fellow-student notice the position of the cardiac impulse, the chest being well exposed. Use both a binaural and a single-tube stethoscope. Place the chest-piece of the stethoscope over the impulse, and make out the two sounds and the pause. (*b*) With the hand over the radial or brachial artery, try to determine whether the beat of the pulse is felt in the period of the sounds or of the pause. (*c*) Listen with the stethoscope over the junction of the second right costal cartilage with the sternum, and compare the relative intensity of the two sounds as heard here with their relative intensity as heard over the cardiac impulse.

15. **Cardiogram.**—Smoke a drum, and arrange a recording tambour and a time-marker beating half or quarter seconds to write on it (Fig. 60, p. 170). Apply the button of a

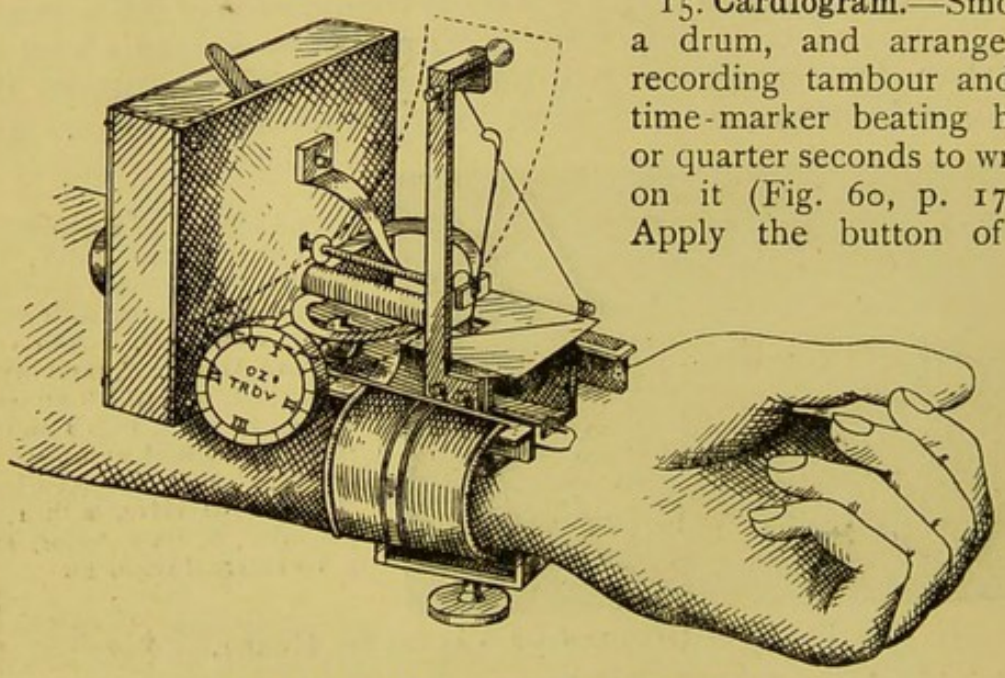


FIG. 68A.—DUDGEON'S SPHYGMOGRAPH.

cardiograph (Fig. 18, p. 79) over your own cardiac impulse, and fasten it round the body by the bands attached to the instrument. Connect the cardiograph by an indiarubber tube with a recording tambour. Set the drum off at a fast speed, take a tracing, and varnish it. Compare with Fig. 19 (p. 80), and measure out on the cardiogram the time-value of the various events in the cardiac revolution.

For the cardiograph, a small glass funnel, the stem of which is connected with the recording tambour, may be substituted, the broad end of the funnel being pressed over the apex-beat.

16. **Sphygmographic Tracings.**—Attach a Marey's sphygmograph (Fig. 26, p. 90) to the arm. Fasten a smoked paper on the plate D. Apply the pad C of the sphygmograph to the wrist over the point where the pulse of the radial artery can be most distinctly felt. Adjust the pressure by moving the screw G. The writing-point of the lever E will rise and fall with every pulse-beat. When everything is satis

factorily arranged, set off the clockwork which moves the plate D, and a pulse tracing will be obtained. Study the changes which can be produced in the pulse curve—(*a*) by altering the position of the body (sitting, standing, and lying down); (*b*) by exercise; (*c*) by inhalation of 2 drops of amyl nitrite poured on a handkerchief; (*d*) by raising the arm above the head and letting it hang at the side; (*e*) by compression of the brachial artery at the bend of the elbow; (*f*) by altering the pressure of the pad. Varnish the tracings after marking on them the conditions under which they were obtained.

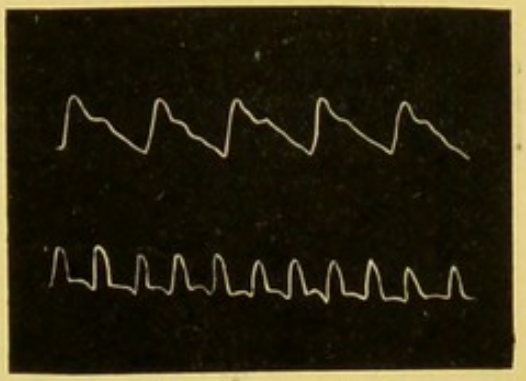


FIG. 69.—EFFECT OF EXERCISE ON THE PULSE (MAREY).

Upper tracing, normal; lower tracing, after running.

A Dudgeon's sphygmograph (Fig. 68A) may also be employed. Or a small glass funnel connected with a recording tambour may be pressed over the carotid artery. The lever of the tambour writes on a drum, on which at the same time half or quarter seconds are marked by an electro-magnetic signal.

17. **Plethysmographic Tracings.**—Connect the vessel C (Fig. 39, p. 116) with B, place the arm in it, and adjust the indiarubber band to make a watertight connection. Support C so that the arm rests

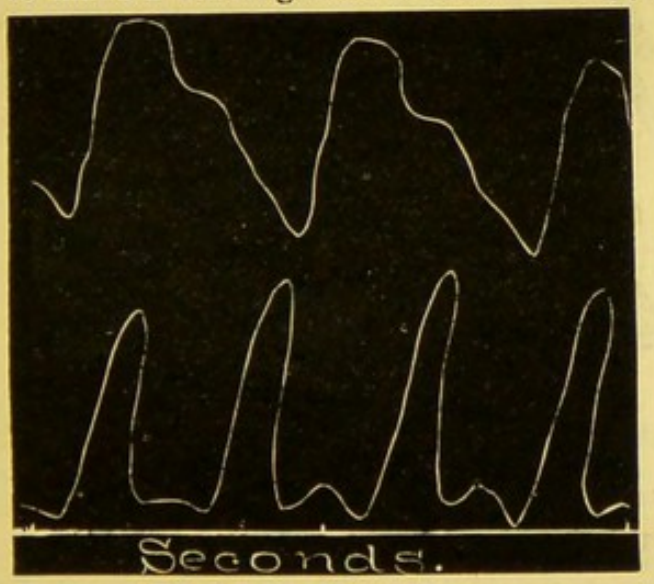


FIG. 70.—EFFECT OF AMYL NITRITE ON THE PULSE (MAREY).

Upper tracing, normal; lower, after inhalation of amyl nitrite.

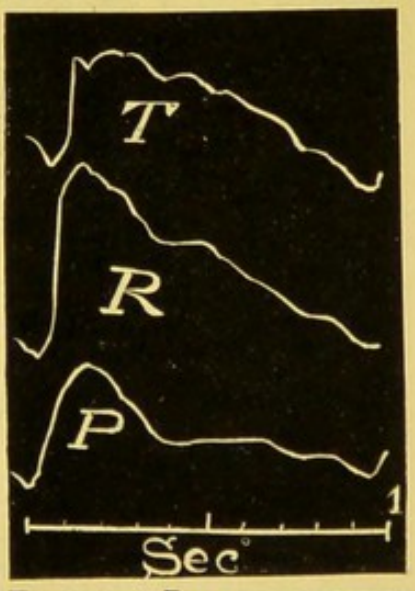


FIG. 71.—PULSE-TRACINGS FROM DIFFERENT ARTERIES.

T, temporal; *R*, radial; *P*, artery of foot. (v. Frey.)

easily within it, and fill it with water at body temperature. Adjust a writing-point, carried by the float A, to write on a drum, and close the upper tubulure of C with a cork. The quantity of blood in the arm is increased with every systole of the left ventricle, diminished in diastole. The float will therefore rise when the ventricle contracts, and sink when it relaxes. Or C may be connected by a rubber tube with a recording tambour writing on the drum. No water must get

into the tambour, and it is well to insert a piece of glass tubing in the connection between it and the plethysmograph, so that it may be seen when the water is rising too high. Adjust a time-marker to write half or quarter seconds (Fig. 60, p. 170). Mosso's plethysmograph (Fig. 72) may also be used.

(1) Take tracings with arm (*a*) horizontal, (*b*) hanging down.

(2) With the arm horizontal, take tracings to show the effect (*a*) of closing and opening the fist inside the plethysmograph;* (*b*) of applying a tight bandage round the arm a little way above the indiarubber band; (*c*) of inhaling 2 drops of amyl nitrite.

18. **Pulse-rate.**—(1) Count the radial pulse for a minute in the sitting, supine, and standing positions. Use a stop-watch, setting it off on a pulse-beat and counting the next beat as one. Make three observations in each position.

(2) Count the pulse in a person sitting at rest, and then again in the sitting position immediately after active muscular exertion. Note how long it takes before the pulse-rate comes back to normal.

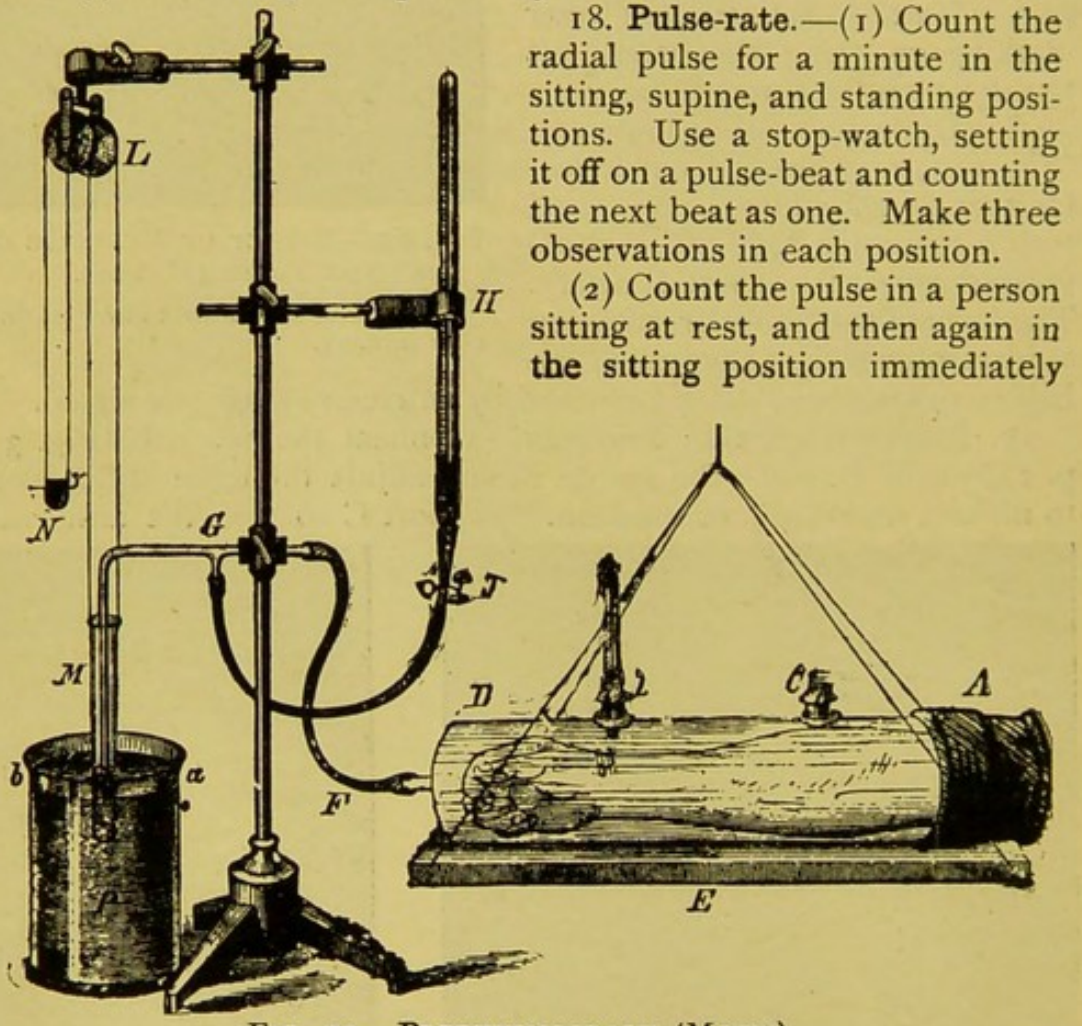


FIG. 72.—PLETHYSMOGRAPH (MOSSO).

M, balanced test-tube, in communication with *D*. When water passes from vessel *D* to *M*, or from *M* to *D*, *M* moves down or up, and its movements are recorded by the writing-point *N*. *M* is steadied by the liquid in *P*, into which it dips.

(3) Count the pulse in a person sitting at rest. Repeat the observation while water is being slowly sipped, and note any change.

(4) With one hand over the thorax of a rabbit, count its pulse. Then notice the effect (*a*) of suddenly closing its nostrils, (*b*) of bringing a small piece of cotton-wool sprinkled with ammonia or chloroform in front of the nose (*reflex inhibition of the heart*).

* Closing the fist causes a fall in the curve, *i.e.*, a diminution in the volume of the arm. On opening the hand, the curve regains its level.

19. **Blood-pressure Tracing.**—(*a*) Put a dog under morphia (p. 58). Set up an induction-machine arranged for an interrupted current (Fig. 65, p. 175). Fill the U-shaped manometer-tube (if this has not already been done) with clean mercury to the height of 10 to 12 c.m. in each limb. Put half an inch of oil above the mercury in the distal (straight) limb before putting in the float. This helps to keep the float from sticking. Then, tilting the tube carefully, fill the proximal limb (*i.e.*, the limb which is to be connected with the bloodvessel) with a saturated solution of sodium carbonate or a half-saturated solution of magnesium sulphate. This is easily done by means of a pipette furnished with a long point. Now attach a strong rubber tube to the proximal end of the manometer, and fill it also with the solution. All air must be got out of the manometer and its connecting-tube. Raise the end of the rubber tube and blow into it, so as to cause a difference of about 10 cm. in the height of the mercury in the two limbs of the manometer, and, without releasing the pressure, clamp the tube with a pinchcock or screw clamp (Fig. 28, p. 99).

Now smoke a drum, and arrange the writing-point of the manometer-float so that it will write on it. Suspend a small weight by a piece of silk thread from a support attached to the stand of the drum, so that it hangs down outside of the writing-point of the manometer-float and always keeps it in contact with the smoked surface without undue friction. Or a piece of glass rod drawn out to a fine thread in the blowpipe flame answers very well. Below the writing-point of the float, and in the same vertical line with it, adjust the writing-point of a time-marker beating seconds (Fig. 60, p. 170).

Next, fasten the animal on a holder, back down. Give ether and insert a tracheal cannula (p. 177). (The tracheal cannula is not absolutely required for the experiment, but it is convenient, as the animal is more under control, and artificial respiration can be begun at any moment, should this be necessary.) Insert a glass cannula, armed with a short piece of rubber tubing, into the central (cardiac) end of the carotid artery (p. 58). Leaving the bulldog forceps on the artery, fill the cannula and tube with the magnesium sulphate or sodium carbonate solution. Slip the rubber tube over a short glass connecting-tube. Fill this also with the solution, and connect it with the manometer-tube, seeing that both are quite full of liquid, so that no air may be enclosed. Now take off the bulldog forceps, and allow the drum to revolve at slow speed. The writing-point of the manometer-float will trace a curve showing an elevation for each heart-beat, and longer waves due to the movements of respiration.

(*b*) Isolate the vago-sympathetic nerve in the neck. Ligature doubly, and cut between the ligatures. Stimulate the peripheral (lower) end, the heart will be slowed or stopped, and the blood-pressure will fall. Stimulate the central (upper) end; there may be inhibition of the heart or acceleration, and the pressure may fall or rise.

(*c*) Expose and divide the other vago-sympathetic while a tracing is being taken. Again stimulate the central end of the nerve, and observe whether there is any effect.

(*d*) Expose the sciatic nerve in one leg, as follows. The leg having been loosened from the holder, the foot is seized by one hand and

lifted straight up, so as to put the skin of the thigh on the stretch. An incision is now made in the middle line on the posterior aspect of the thigh, through the skin and subcutaneous tissue. The muscles are separated in the line of the incision with the fingers, and the sciatic nerve comes into view lying deeply between them. Place a double ligature on it, and divide between the ligatures. Stimulate the upper (central end); the blood-pressure probably rises, and the heart may be accelerated. Stimulate the peripheral end of the nerve: there is little change in the blood-pressure and none in the rate of the heart.

(*e*) Note, incidentally, that stimulation of the central end of the sciatic or the upper (cephalic) end of the vago-sympathetic may cause increase in the rate and depth of the respiratory movements.

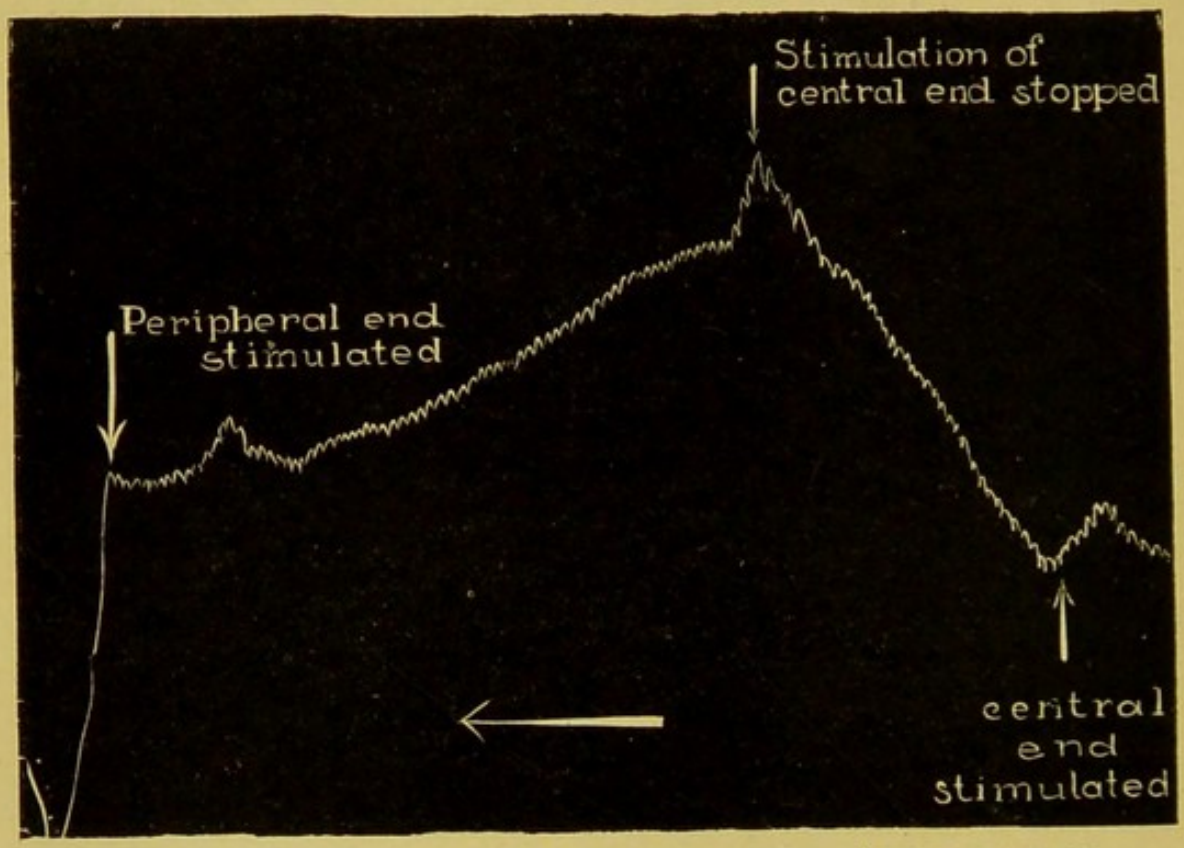


FIG. 73.—BLOOD-PRESSURE TRACING FROM A DOG. STIMULATION OF CENTRAL AND PERIPHERAL ENDS OF VAGUS.

The other vagus was intact. Stimulation of the peripheral end caused stoppage of the heart and a marked fall of pressure. Stimulation of the central end produced a great rise of pressure, with, perhaps, a slight acceleration of the heart.

Dilatation of the pupil may also be caused by stimulation of the upper end of the vago-sympathetic through the sympathetic fibres that supply the iris.

(*f*) Again stimulate the peripheral end of one vagus, or of both at the same time, while a tracing is being taken, and see how long it is possible to keep the heart from beating. Sometimes in the dog inhibition can be kept up so long that the animal dies.

(*g*) Close the tracheal cannula so that air can no longer enter the lungs. In a very short time the blood-pressure curve begins to rise (rise of asphyxia). After some minutes the pressure falls, and finally becomes zero; *i.e.*, the level of the mercury is the same in the two limbs of the manometer (or, rather, the mercury in the distal limb is

higher than that in the proximal limb by the amount needed to exactly balance the pressure of the column of sodium carbonate in the latter). Disconnect the arterial cannula from the manometer, and allow the writing-point to trace a horizontal straight line (line of zero pressure) on the drum (Figs. 56 and 57).

20. **The Influence of the Position of the Body on the Blood-pressure.**—Inject into the rectum of a dog 3 to 4 grammes of chloral hydrate dissolved in a little water. See that it does not run out again immediately after injection. In ten minutes anæsthetize the animal fully with the mixture of equal parts of alcohol, chloroform and ether, known as the ACE mixture, or with chloroform, and tie it very securely, back downward, on a board which can be rotated around a horizontal axis, corresponding in position to the point at which the cannula is to be inserted.* Set up a drum and manometer as in 19 (p. 185), but with a rubber connecting-tube of such length as will allow free rotation of the board. Insert a cannula into the central end of the carotid artery at a point immediately above the axis of rotation of the board, and connect it with the manometer. (*a*) Take a blood-pressure tracing with the board horizontal. (*b*) Whilst the tracing is being taken, rotate the board so that the position of the animal becomes vertical, with the feet down. Mark on the tracing the moment when the change of position takes place. The pressure falls. Replace the dog in the horizontal position. The manometer regains its former level. Now rotate the board, till the animal is again vertical, but with feet up and head down, and observe the effect on the blood-pressure. The respiratory variations are greater with feet down than with head down. Notice in both cases whether there is any change in the rate of the heart. (*c*) Take the board off the stands, lay it on a table, expose the femoral artery, and insert a cannula into it. Shift the axis so that it now lies below this cannula. Replace the board on the stands, and repeat (*a*) and (*b*). The fall of pressure will now take place in the head-down position.†

21. **Effects of Hæmorrhage and Transfusion on the Blood-pressure.**—Anæsthetize a dog with morphia and ether, and insert a cannula into the carotid artery, another into one femoral vein (p. 177), and a third into the femoral artery on the opposite side.

* A simple arrangement for this purpose is a board with a number of staples fastened in pairs into its lower surface, so that an iron rod can be pushed through any pair, and form a horizontal axis at right angles to the length of the board. The dog having been tied down, the rod is pushed through the pair of staples corresponding to the position of the cannula in the artery that is to be connected with the manometer. The projecting ends of the rod rest in two ordinary clamp-holders, fastened at a convenient height on two strong stands, whose bases are clamped to the end of a table. The other end of the board is supported by a piece of wood that rests on the floor, and can be removed when the board is to be rotated.

† In 16 dogs the fall of pressure in the carotid in the feet-down position varied from 12 to 100 mm. of mercury; average fall, 44.4 mm. In 12 out of the 16 animals the rise of pressure in the head-down position varied from 2 to 36 mm.; in 1 there was no change; in 3 there was a fall of 5 to 24 mm.

Connect the first cannula with a manometer, arranged to write on a drum as in experiment 19 (p. 185). Take the bulldog off the carotid, and measure the difference in the level of the mercury in the two limbs of the manometer with a millimetre scale.

(1) (*a*) While a tracing is being taken, draw off about 10 c.c. of blood from the femoral artery, and observe whether there is any effect on the tracing. Mark on the tracing the moment when the removal of the blood begins and ends.

(*b*) Repeat (*a*), but run off about 100 c.c.* of blood, and let this be immediately defibrinated. Then draw off portions of 100 c.c.* at short intervals until a distinct fall of blood-pressure has been produced. All the samples of blood should be defibrinated.

(2) (*a*) Now, while a tracing is being taken, inject the whole of the defibrinated blood slowly through the cannula in the femoral vein by means of a funnel supported by a stand at such a height that the blood runs in easily. A pinchcock should be put on the tube connecting the funnel and the cannula, and this should be closed before the funnel is quite empty, so as to obviate any risk of air getting into the vein. Of course, the cannula and connecting-tubes must all be freed from air before injection is begun. Again measure the difference in the level of the mercury and compare the pressure with that observed before the first hæmorrhage.

(*b*) Inject into the vein, while a tracing is being obtained, about 100 c.c. of normal saline*solution heated to 40° C., and go on injecting portions of 100 c.c. until a distinct rise of pressure has taken place, keeping a record of the total amount injected, and marking the time of each injection on the curve.

(*c*) After an interval of thirty minutes, again measure the height of the mercury in the manometer. Then bleed the dog to death while a tracing is being recorded.

22. **The Influence of Albumoses on the Blood-pressure—Albumose ('Peptone') Plasma.**—Set up the apparatus for taking a blood-pressure tracing as in experiment 19, but omit the induction coil. Weigh a dog. Weigh out a quantity of Witte's peptone equivalent to 0·5 gramme for every kilo of body-weight. Dissolve the peptone in about ten times its weight of normal saline solution. Anæsthetize the dog with morphia and ether or ACE mixture. Put cannulæ into the central end of one carotid, of one crural artery, and of the crural vein on the opposite side. Connect the carotid with the manometer, and the femoral vein with a burette or large syringe containing all the peptone solution except 15 drops, which are put into a test-tube labelled A. Take care that the connecting-tube and cannula are free from air. Label another test-tube B. Run into both test-tubes about 5 c.c. of blood from the femoral artery, and set them aside. Now commence to take a blood-pressure tracing, and while it is going on, quickly inject the peptone solution. Notice the effect on the tracing. The pressure falls owing largely to a dilatation of the small arteries through the direct action of the peptone on their muscular tissue or on the endings of the vaso-motor nerves. As

* 200 c.c. for a large dog.

soon as the injection is finished, draw off a sample of 5 c.c. of blood into a test-tube labelled C, and let it stand. In ten minutes collect three further samples of 5 c.c., D, E, and F, and a large one G; in half an hour another set of three small samples, and at as long an interval as possible thereafter three more. Add to E 15 drops of a 2 per cent. solution of calcium chloride, to F 5 c.c. of a solution of fibrin ferment containing some calcium chloride, and put D, E, and F into a water-bath at 40°. Treat the other sets of small samples in the same way, and also the plasma obtained by centrifugalising G. Note how long each specimen takes to clot, and report your results.*

23. **Effect of Suprarenal Extract on the Blood-Pressure.**—Make the arrangements for a blood-pressure tracing from a dog as in 19, p. 185. Put a cannula in the carotid and another in the femoral vein or one of its branches (p. 177). Expose both vagi in the neck, and pass threads loosely under them. Connect the carotid with the manometer and take a tracing. Then, while the tracing is continued, inject slowly into the femoral vein an amount of watery extract corresponding to about $\frac{1}{6}$th gramme of suprarenal. The blood-

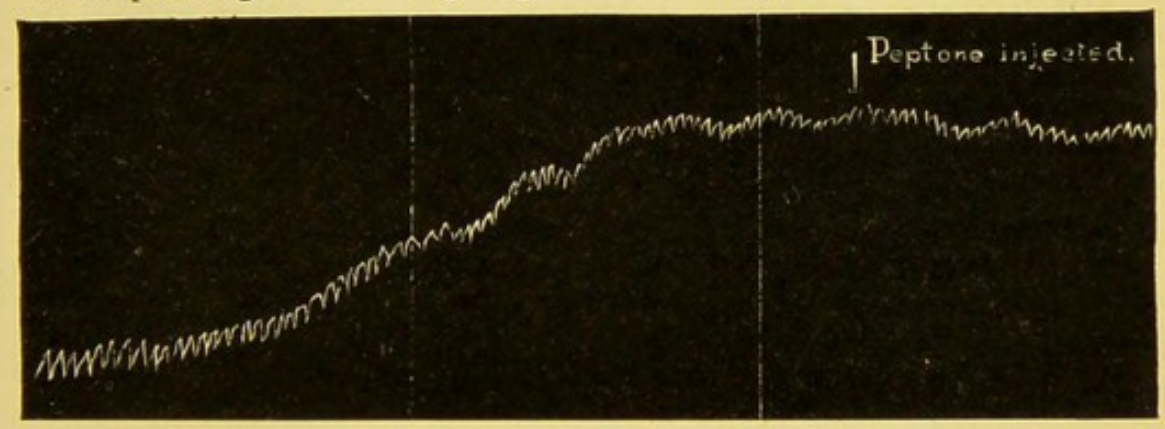


FIG. 74.—EFFECT OF INJECTION OF PEPTONE ON THE BLOOD-PRESSURE IN A DOG. (TO BE READ FROM RIGHT TO LEFT.)

pressure rises† owing to constriction of the arterioles by direct action of the extract on their muscular tissue. The heart is greatly slowed owing to stimulation of the cardio-inhibitory centre. At once cut

* Sometimes the injection of peptone hastens coagulation instead of hindering it. It has been asserted that this is only the case when small doses are used (less than 0·02 gramme per kilo of body-weight). But in 2 dogs out of 11 a dose of 0·5 gramme per kilo has been seen to hasten coagulation, and in 1 out of 12 to leave it unaffected; in the other 9 coagulation was markedly retarded. The blood-pressure always fell, the amount of the fall varying from 81 to 21 mm. of mercury (average, 60 mm.). It sometimes returned to normal in twenty to thirty minutes, but usually required a longer time.

† The amount of the initial rise of pressure is very variable, since the slowing of the heart tends to diminish the pressure, while the constriction of the arterioles tends to increase it. Thus, in one experiment the increase of pressure on injection of the extract was only 6 mm. of mercury, while in another it was 56 mm. On section of the vagi in this second experiment, there was an additional rise of 64 mm., and after a second injection a further rise of 70 mm., making an increase of 190 mm. in all above the original pressure.

both vagi while a tracing is being taken; the blood-pressure rises still more (p. 475). The rise is not long maintained, but a second injection causes a renewed increase of pressure.

24. **Section and Stimulation of the Cervical Sympathetic in the Rabbit.**—Weigh out ¾ gramme chloral hydrate. Dissolve in as small a quantity of water as possible, and inject into the rectum of a rabbit, preferably an albino. Half a gramme is sufficient for a small rabbit. Put a pair of bulldog forceps for a few minutes on the anus to prevent escape of the solution. Set up an induction coil arranged for an interrupted current (Fig. 65, p. 175), and connect it through a short-circuiting key with electrodes. The preparations necessary for an operation with antiseptic precautions are supposed to have been previously made—the instruments, sponges, and ligatures boiled in water; the instruments then immersed in a 5 per cent. solution of carbolic acid, the sponges and ligatures in corrosive sublimate solution (0·1 per cent.). The hands are to be thoroughly washed, with diligent use of the nail-brush, in soap and water before the cutting operation begins, and then soaked in the corrosive sublimate solution.

Fasten the rabbit on a holder, back downwards, as in Fig. 43. Keep the animal warm by covering it with a cloth, and do not handle or wet its ears. Clip off the hair on the anterior surface of the neck. Remove loose hairs with a wet sponge, shave the neck, and wash it thoroughly, first with soap and water, and then with corrosive sublimate. Give ether if necessary. Make a longitudinal incision in the middle line over the trachea, beginning a little below the thyroid cartilage and extending downwards for an inch and a half. Feel for the carotid artery, expose, and raise it up. Two nerves will now be seen coursing beside the artery. The larger is the vagus, the smaller the sympathetic. A third and much finer nerve (the depressor, or superior cardiac branch of the vagus) may also be seen in the same position, but the student should neglect this for the present. Get as little as possible of the antiseptic solutions in the wound till your observations have been completed, as the nerves may be injured by them. Pass a ligature under the sympathetic, and tie it, the ear being held up to the light while this is being done, so that its vessels may be clearly seen. A transient constriction of the arteries may be seen at the moment when the nerve is ligatured. This is due to stimulation of the vaso-constrictor fibres. Then follows a marked dilatation of the bloodvessels, due to paralysis of these fibres. The ear is flushed and hot. Note also that the pupil is probably narrower on the side on which the nerve has been tied. On stimulation of the upper (cephalic) end of the sympathetic with the electrodes, the vessels are markedly constricted, the ear becomes pale and cold, and the pupil dilates. Cut the nerve above and below the ligature, and take out the ligature. Wash the wound thoroughly with corrosive sublimate, and close it, the muscles being first brought together by a row of interrupted sutures, and then the skin by another row. Since it is difficult to thoroughly disinfect the hair-follicles, and a suture passed through a septic follicle is apt to give rise to suppuration, subcutaneous stitches—*i.e.*, stitches passed by a curved needle through

the deep layer of the skin without coming through to the surface—may be employed. The wound is to be protected by a coating of collodion. No other dressing is required. The animal is now removed from the holder and put back to its hutch. The student must examine it at least once a day for the next week, and study the differences between the two ears (p. 151) and the two pupils.

25.* **Stimulation of the Depressor Nerve in the Rabbit.**—Set up the apparatus for a blood-pressure tracing as described in 19 (p. 185).

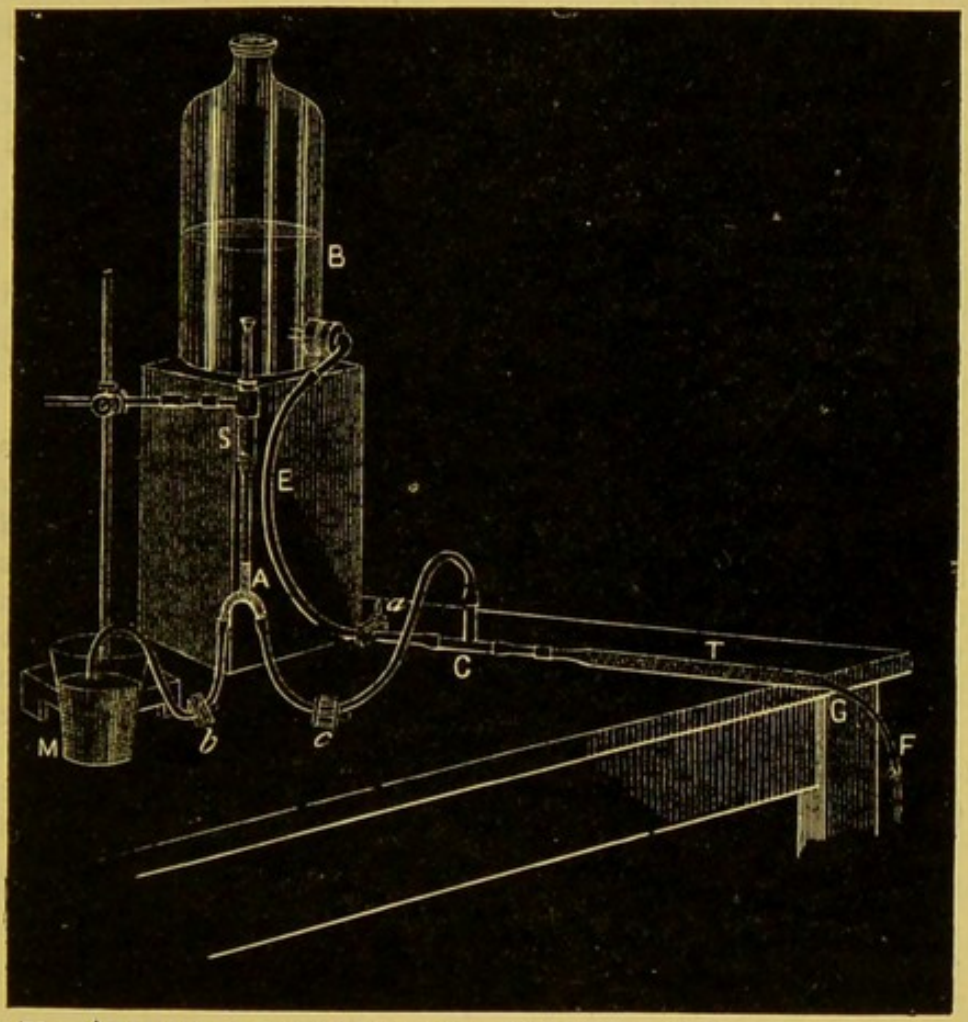


FIG. 75.—ARTIFICIAL SCHEME TO ILLUSTRATE A METHOD OF MEASURING THE CIRCULATION-TIME.

B, bottle containing water, the rate of outflow of which is regulated by screw clamp *a*; S, syringe filled with methylene-blue solution, connected with T-piece A; M, beaker containing methylene-blue solution; *b*, *c*, screw-clamps; C, T-piece, inserted in the course of the flexible tube E, and connected with the glass tube T, which is filled with beads; F, outflow tube. The clamp *c* having been closed and *b* opened, the syringe is filled with the methylene-blue solution. *b* is then closed, *c* opened, and a definite quantity of the solution injected into the system. The time from the beginning of injection till the appearance of the blue at G is measured with the stop-watch.

Arrange an induction coil and electrodes for an interrupted current. Anæsthetize a rabbit with ½ gramme chloral hydrate, and if necessary with ether. For blood-pressure experiments only small doses of chloral hydrate or chloroform can be given, as they affect the vaso-motor centre. Put the animal on the holder. Insert a cannula in

* This experiment is only suitable for advanced students.

the trachea and another cannula in the central end of the carotid artery. Isolate the depressor nerve. Put double silk ligatures on it, and divide between them. Connect the cannula in the carotid with the manometer and take a blood-pressure tracing. Stimulate the central (upper) end of the depressor. A marked fall of blood-pressure, accompanied with a slowing of the heart, will be obtained (Fig. 55). Stimulate the peripheral (lower) end; no effect. Divide both vagi, and again stimulate the central end of the nerve. The blood-pressure again falls, but there is no alteration in the rate of the heart (p. 160). Close the tracheal cannula, and obtain another tracing, showing the effect of asphyxia (Fig. 56, p. 163).

Autopsy.—Dissect the nerve that has been stimulated, up to the origin of the superior laryngeal branch of the vagus, to make sure that it is the depressor (Fig. 54, p. 161).

26. **Determination of the Circulation-time.**—(*a*) Begin with an artificial scheme (Fig. 75). Fill the syringe with a 0·2 per cent. solution of methylene blue. Allow the water to flow from the bottle by loosening the clamp. Inject a definite quantity of the methylene-blue solution, and with a stop-watch observe how long it takes to pass from the point of injection to the end of the glass tube filled with beads. Make ten readings of this kind and take the mean. Then raise the bottle so as to increase the rate of flow of the water, and repeat the observations. The 'circulation-time' will be found to be diminished. This corresponds to an increase of blood-pressure due to increased activity of the heart without change in the calibre of the bloodvessels. Next, leaving the bottle in its present position, diminish the outflow by tightening the clamp; the circulation-time will be increased. This corresponds to an increase of blood-pressure due to diminution in the calibre of the small arteries.

(*b*) Fill the syringe* with methylene-blue solution (0·2 per cent. in normal saline), as in (*a*). Keep the solution warmed to 40° C. by immersing the small beaker containing it in a water-bath, or heating it over a bunsen with a small flame. Weigh a rabbit, and inject ¾ gramme chloral into the rectum. Fasten it on a holder, back downwards (Fig. 43, p. 125). Cover it with a towel to keep it warm. Clip off the hair on the front of the neck, give ether if necessary, and make an incision 1½ inches long in the middle line, beginning a little way below the cricoid cartilage. Reflect the skin and isolate the external jugular vein, which is quite superficial. Carefully separate about ¾ inch of the vein from the surrounding tissue, and pass two ligatures under it, but do not tie them. Compress the vein with a pair of bulldog forceps between the heart and the ligatures. Now tie the uppermost of the two ligatures (that next the head), but only put a single loose loop on the other. The piece

* A burette, sloped so as to make a small angle with the horizontal, may be substituted for the syringe. The burette is supported on a stand at such a height that the methylene-blue solution runs without great force into the jugular (say 10-15 cm. above the level of the cannula). The danger of producing an abnormal result by suddenly raising the pressure in the right side of the heart is thus avoided.

of vein between the upper ligature and the bulldog is now distended with blood. With fine-pointed scissors make a small slit in the vein, taking great care not to divide it completely, insert the cannula, and tie the loose ligature firmly over its neck. Fill the cannula and the small piece of rubber tubing attached to it with normal saline by means of a pipette with a long point. Expose the carotid on the other side, isolate it for ¾ inch, clear it carefully from its sheath, slip under it a strip of thin sheet indiarubber, and between this and the artery a little piece of white glazed paper. Connect the cannula in the jugular with the T-piece attached to the syringe. Care must be taken that no air remains in the cannula or its connecting-tube, as an animal not unfrequently dies instantaneously when a bubble of air is injected into the right heart.

Now take off the bulldog from the vein, and make a series of observations on the pulmonary circulation-time. The animal must be so placed that a good light falls on the carotid. If necessary, the light of a gas-flame may be concentrated on it by a lens. The student holds the stop-watch in one hand, and injects a measured quantity of the methylene-blue solution with the other. Uniformity in the quantity injected is secured by fastening on the piston of the syringe a screw-clamp, which stops the piston at the desired point. The observation consists in setting off the watch at the moment when injection begins and stopping it when the blue appears in the carotid. After each injection the screw-clamp or pinchcock on the tube connected with the cannula must be tightened, the other opened, and the syringe refilled. Great care must be taken never to open the two clamps at the same time, as in that case blood may regurgitate through the jugular and fill the syringe, or methylene blue may be sucked into the circulation. As many observations as possible should be taken, and the mean determined. The circulation-time observed is approximately that of the lesser circulation, the time taken by the blood to pass from the left ventricle to the carotid being negligible. The specific gravity of the blood may also be tested at the beginning and end of the experiment by Hammerschlag's method (p. 57).

Autopsy.—Observe particularly the state of the lungs, whether the bladder is distended or not, and whether any of the serous cavities or the intestines contain much liquid ; so as to determine, if possible, by what channel the water injected into the blood may have been eliminated. Notice the distribution of the methylene blue in such organs as the kidneys and the muscles immediately after death, and notice that the blue colour becomes more pronounced after exposure for a time to the air. Make a longitudinal section through a kidney, and observe that the pigment is found especially in the cortex and around the pelvis at the apices of the pyramids, or it may be only in the cortex. The urine is greenish. If some methylene blue has been injected after the heart ceased to beat, the bloodvessels, particularly in the mesentery, may be beautifully mapped out by the pigment. This is not the case if the last injection took place before death, since the blue is rapidly reduced by living tissues.

CHAPTER III.

RESPIRATION.

RESPIRATION in its widest sense is the sum total of the processes by which the ultimate elements of the body gain the oxygen they require, and get rid of the carbon dioxide they produce.

Comparative.—In a unicellular organism no special mechanism of respiration is needed; the oxygen diffuses in, and the carbon dioxide diffuses out, through the general surface. The simple wants of such multicellular animals as the cœlenterates, the group to which the sea-anemone belongs, are also supplied by diffusion through the ectoderm from and into the surrounding water, and through the endoderm from and into the contents of the body-cavity and its ramifications.

But in animals of more complex structure special arrangements become necessary, and respiration is divided into two stages: (1) **External respiration**, an interchange between the air or water and a circulating medium or blood as it passes through richly vascular skin, gills, tracheæ, or lungs; and (2) **internal respiration**, an interchange between the blood, or lymph, and the cells.

In the lower kinds of worms respiration goes on solely through the skin, under which plexuses of bloodvessels often exist, but in some higher worms there are special vascular appendages that play the part of gills. The crustacea also possess gills, while in the other arthropoda respiration is carried on either by the general surface of the body (in some low forms), or more commonly by means of tracheæ, or branched tubes surrounded by blood spaces and communicating externally with the air and internally by their finest twigs with the individual cells. Most of the mollusca breathe by gills, but a few only by the skin.

Among vertebrates the fishes and larval amphibians breathe by gills, but most adult amphibians have lungs. The skin, too, in such animals as the frog has a very important respiratory function, more of the gaseous exchange taking place through it than through the lungs.

One small group of fishes, the dipnoi, has the peculiarity of

possessing both gills and a kind of lungs, the swim-bladder being surrounded with a plexus of bloodvessels and taking on a respiratory function.

In all the higher vertebrates the respiration is carried on by lungs; the trifling amount of gaseous interchange which can possibly take place through the skin is not worth taking into account. The lungs are to be regarded as developed from outgrowths of the alimentary canal, beginning near the mouth.

The object of all special respiratory arrangements being, in the first instance, to facilitate the gaseous exchange between the surrounding medium (air or water) and the blood, a prime necessity of a respiratory organ, be it skin, gill, trachea, or lung, is a free supply of blood, in vessels so fine and thin that diffusion readily takes place into them and out of them. But a free supply of blood would be of no avail if the medium to which the blood gave up its carbon dioxide and from which it drew its oxygen was not being constantly and sufficiently renewed.

Sometimes the natural currents of the water or the air are of themselves sufficient to secure this renewal; in other cases, artificial currents are set up by cilia, or special bailing organs, like the scaphognathites of the lobster. In all the higher animals active movements, by which air or water is brought into contact with the respiratory surfaces, are necessary; and it is possible that such movements take place even in the tracheæ of insects and other air-breathing arthropoda. Fishes, by rhythmical swallowing movements, take in water through the mouth and pass it over the gills and out by the gill-slits, while the frog distends its lungs by swallowing air.

Physiological Anatomy of the Respiratory Apparatus.—In man the respiratory apparatus consists of a tube (the trachea) widened at its upper part into the larynx, which contains the special mechanism of voice, and communicates through the nose or mouth with the external air. Below, the trachea divides dendritically into innumerable branches, the ultimate divisions of which are called bronchioles. Each bronchiole breaks up into several wider passages, or infundibula, the walls of which are everywhere pitted with recesses or alcoves, called alveoli. The trachea and larger bronchi are strengthened by hyaline cartilage in the form of incomplete rings, connected behind by non-striped muscular fibres, which also exist in the intervals between the rings. The middle-sized bronchi within the lungs have the cartilage in the form of detached pieces in the outer portion of the wall, while nearer the lumen lies a complete ring of non-striped muscle.

In the bronchioles, no cartilage is present, but the circularly-arranged muscular fibres still persist, and also form a thin layer in the infundibula. In the air-cells, or alveoli, however, there are no muscular fibres. Their walls consist essentially of a network of elastic fibres, continuous with a similar layer in the infundibula and bronchioles, and covered on the side next the lumen by a single layer of large, clear epithelial scales, with here and there a few smaller and more granular polyhedral cells.

From the larynx to the bronchioles the mucous membrane is ciliated on its free surface, the cilia lashing upwards so as to move the secretion towards the larynx and mouth. In the infundibula the ciliated epithelium begins to disappear, and is absent from the alveoli. Part of the nasal cavity and the upper part of the pharynx are also lined with ciliated epithelium. Mucous glands are present in abundance in the upper portions of the respiratory passages, but disappear in the smaller bronchi.

Blood-supply of the Lungs.—The quantity of blood traversing the lungs bears no proportion to the amount required for their actual nourishment. Small, however, as this latter quantity is, it cannot apparently be derived from the vitiated blood of the right ventricle, but is obtained directly from the aortic system by the bronchial arteries. These are distributed with the bronchi, which they supply as well as the connective-tissue of the interlobular septa running through the substance of the lung, the pleura lining it and the walls of the large bloodvessels. Most of the blood from the bronchial arteries is returned by the bronchial veins into the systemic venous system, but some of it finds its way by anastomoses into the pulmonary veins.

The branches of the pulmonary artery are also distributed with the bronchi, and break up into a dense capillary network around the alveoli. From the capillaries veins arise which, gradually uniting, form the large pulmonary veins that pour their blood into the left auricle.

The same quantity of blood must, on the whole, pass per unit of time through the lesser as through the greater circulation, otherwise equilibrium could not exist, and blood would accumulate either in the lungs or in the systemic vessels. But it does not follow that at each heart-beat the output of the two ventricles is exactly equal. If, indeed, the capacity of the lesser circulation were constant, the quantity driven out at one systole by the right ventricle would be the same as that ejected at the next by the left ventricle. But it is known that the capacity of the pulmonary vessels is altered by the movements of respiration and probably in other ways, so that it is only on the average of a number of beats that the output of the two ventricles can be supposed equal.

The time required by a given small portion of blood, *e.g.*, by a single corpuscle, to complete the round of the lesser circulation, is, as we have seen (p. 124), much less than the average time needed to complete the systemic circulation. In the rabbit the ratio is probably about 1 : 5. Since all the blood in a vascular tract must pass out of it in a period equal to the circulation time, the average quantity of blood in the lungs and right heart of a rabbit must be about one-fifth of that in the systemic vessels. On the assumption that the same proportion holds for a man, not less than 900 grm. out of the $5\frac{1}{2}$ kilos of blood in a seventy kilo man must be contained in the lesser circulation, and rather more than $4\frac{1}{2}$ kilos in the greater. This corresponds sufficiently well with calculations from other data.

For example, the average weight of the lungs in three persons,

executed by beheading, was 457 grm. (Gluge). The average weight of the lungs in a great number of persons who had died a natural death was 1024 grm. (Juncker). The weight of the pulmonary tissue alone in the first set of cases must be less than 457 grm., for the lungs of a person who has bled to death are never bloodless. In a dog killed by bleeding from the carotid, one-quarter of the weight of the lungs consisted of blood. Assuming the same proportion for the decapitated individuals, we get 343 grm. as the net weight of the blood-free lungs. Deducting this from 1024 grm., we arrive at 681 grm. as the average quantity of blood in the lungs. Adding to this the quantity in the right side of the heart (p. 127), we get, in round numbers, 750 grm. as the amount in the lesser circulation. It is true that in the living body the conditions are not the same as after death; but it is probable that in a large number of cases taken at random the differences would be approximately equalized.

It has been further calculated—but here the data are less certain—that the total area of the alveolar surface of the lungs of a man is about 100 square metres (sixty times greater than the area of skin), of which, perhaps, 75 square metres are occupied by capillaries. The average thickness of this immense sheet of blood has been reckoned to be equal to the diameter of a red blood-corpuscle, or, say, 8μ. This would give 600 c.c. (630 grm.) as the quantity of blood in the lungs, which is probably somewhat too low an estimate.

If we take the pulmonary circulation-time as 13 seconds (p. 124), and the quantity of blood in the lungs as 800 grm., then $\frac{0{\cdot}8 \times 60 \times 60}{13}$ = 221 kilos of blood will pass through the lungs in an hour, or 5,304 kilos (say, 5,000 litres) in twenty-four hours. This would fill a cubical tank in which the man could just stand upright with the lid closed.

Mechanical Phenomena of Respiration.

The lungs are enclosed in an air-tight box, the thorax; or it may be said with equal truth that they form part of the wall of the thoracic cavity, and the part which has by far the greatest capacity of adjustment. The alveolar surface of the lungs is in contact with the air. The pleura, which covers their internal surface, is reflected over the chest-walls and diaphragm, so as to form two lateral sacs, the pleural cavities. In health these are almost obliterated, and the visceral and parietal pleuræ, separated and lubricated by a few drops of lymph, glide on each other with every movement of respiration. But in disease the pleural cavities may be filled and their walls widely separated by exudation as in pleurisy, or by blood as in rupture of an

aneurism, or by air in the condition known as pneumothorax. Between the two pleural sacs lies a mesial space, the mediastinum, commonly divided into an anterior mediastinum in front of the heart, and a posterior mediastinum behind it. The pleural and pericardial sacs and the mediastinum constitute together the thoracic cavity. The external surface of the chest-wall and the alveolar surface of the lungs are subjected to the pressure of the atmosphere, to which the pressure in the thoracic cavity (intra-thoracic pressure) would be exactly equal if its boundaries were perfectly yielding. But in reality the intra-thoracic pressure is always normally something less than this. For even the lungs, the least rigid part of the boundary, oppose a certain resistance to distension, and so hold off, as it were, from the thoracic cavity a portion of the alveolar pressure; and in any given position of the chest the intra-thoracic pressure is equal to the atmospheric pressure *minus* this elastic tension of the lungs.

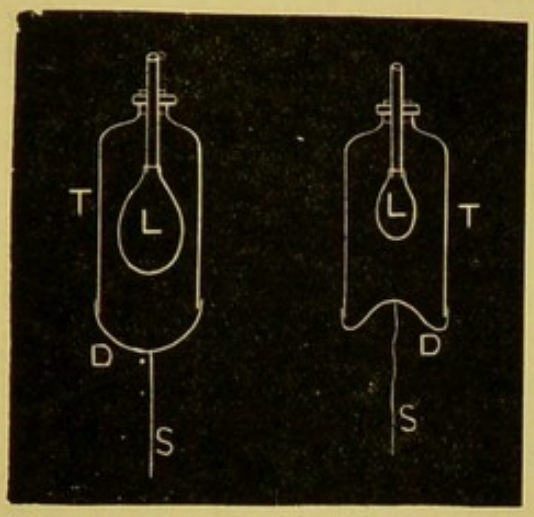


FIG. 76.—SCHEME TO ILLUSTRATE THE MOVEMENTS OF THE LUNGS IN THE CHEST.

T is a bottle from which the bottom has been removed; D a flexible and elastic membrane tied on the bottle, and capable of being pulled out by the string S so as to increase the capacity of the bottle. L is a thin elastic bag representing the lungs. It communicates with the external air by a glass-tube fitted airtight through a cork in the neck of the bottle. When D is drawn down, the pressure of the external air causes L to expand. When the string is let go, L contracts again, in virtue of its elasticity.

The object of the respiratory movements is the renewal of the air in contact with the alveolar membrane—in other words, the ventilation of the lungs. Two main methods are followed by sanitary engineers in the ventilation of buildings: they force air in, or they draw it in. In both cases the movement of the air depends on the establishment of a slope of pressure from the inlet to the interior. In the first method, this is done by increasing the pressure at the inlet; in the second, by diminishing the pressure at the outlet. In certain animals Nature, in solving its problem of ventilation,

has made use of the first principle. Thus, the frog forces air into its lungs by a swallowing movement. In artificial respiration, as practised in physiological experiments, the same method is usually employed: air is driven into the lungs under pressure. But in the vast majority of air-breathing animals, including man, the opposite principle has been adopted; and the 'indraught' of air from nose and pharynx to alveoli is not set up by increasing the pressure in the former, but by diminishing it in the latter. This 'indraught,' or **inspiration**, is brought about by certain movements of the chest-wall, which increase the capacity of the thoracic cage and lower the pressure in the thoracic cavity. The expansion of the highly-distensible lungs keeps pace with the diminution of pressure in the pleural sacs, and they follow at every point the retreating chest-wall and diaphragm. The pressure of the air in the alveoli during the rapid expansion of the lungs necessarily sinks below that of the atmosphere, and air rushes in through the trachea and bronchi till the difference is equalized. Then commences the movement of **expiration**. The expanded chest falls back to its original limits; the pressure in the thoracic cavity increases; the distended lungs, in virtue of their elasticity, shrink to their former volume; the pressure of the air in the alveoli rises above that of the atmosphere, and with this reversal of the slope of pressure air streams out of the bronchi and trachea.

In **inspiration** the chest dilates in all its diameters. Its vertical diameter is increased by the contraction of the *diaphragm*, which, composed of a central tendon and a peripheral ring of muscular tissue, bulges up into the thorax in the form of a flattened dome, and closes its lower aperture. When the diaphragm contracts, the central tendon descends; the acute angle which the muscular ring makes during relaxation with the thoracic wall opens out around its whole circumference, so as to form a deep groove of triangular section. The lungs follow the descending diaphragm, their lower borders keeping accurately in contact with it, while their apices move very slightly or not at all. Since the diaphragm is attached to the lower ribs, there is a

tendency during its contraction for these to be drawn inwards and upwards; but this is opposed by the pressure of the abdominal viscera, and by the action of the *quadratus lumborum*, which fixes the twelfth rib, and of the *serratus posticus inferior*, which draws the lower four ribs backward. When these and the other inspiratory muscles that act especially upon the ribs are paralyzed by injury to the spinal cord, and respiration is carried on by the diaphragm alone, the line of its attachment to the ribs is distinctly marked during inspiration by a shallow circular groove.

The antero-posterior and transverse diameters of the thorax are enlarged by the action of certain muscles that elevate the ribs. Of these, the most important are the *levatores costarum*—twelve in number on each side. They arise from the transverse processes of the last cervical and first eleven dorsal vertebræ, and, passing obliquely downwards and outwards, are inserted between the tubercle and the angle into the first or second rib below their origin. The *scalene muscles*, which may in a lean person be felt to be tense during inspiration, fix the first and second ribs (scalenus anticus and medius, the first; scalenus posticus, the second rib), and so afford a fixed line for the *intercostal muscles* to work from on the lower ribs.

The action of the *intercostals* has been much debated; but it seems to be certain that the external intercostals do aid to a slight extent in raising the ribs when the upper two have been fixed by the contraction of the scaleni. The intercartilaginous portion of the internal intercostals also contracts simultaneously with the diaphragm, and may therefore be reckoned in the list of inspiratory muscles; but the function of the interosseous portion is still in doubt. It is probable that the chief importance of the intercostal muscles (both external and internal) is not so much to act upon the ribs, as to increase by their contraction the rigidity of the intercostal spaces, and so prevent them from being drawn in when the chest is expanded by the action of the diaphragm, the levatores, and the scaleni. Since the ribs slant downwards and forwards to their sternal attachments, the sternum is raised when they are elevated; or, rather, since the upper

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end of that bone is practically immovable in ordinary breathing, its lower extremity is tilted forwards. This causes an increase in the antero-posterior diameter of the thorax. Further, since the arches formed by the ribs widen in regular progression from above downwards, at least in the upper portion of the thoracic cage, so that the second rib is a segment of a larger circle than the first, and the third than the second, it is clear that a general elevation of the chest will tend also to increase the transverse diameter at any given level. Such an increase is also favoured by the opening out of the angles between the bony ribs and the costal cartilages under the influence of the couple (or pair of oppositely directed forces) that acts on them—viz., the upward pull of the levatores costarum and the other elevators exerted on the ribs, and the resistance of the sternum to further displacement exerted on the cartilages. The widening of the thorax from side to side may also be in a slight degree ascribed to a twisting movement of the ribs, which tends to evert their lower borders.

Expiration in perfectly tranquil breathing is brought about with very little aid from active muscular contraction. The sense of effort disappears as soon as the chest ceases to expand. The diaphragm and the elevators of the ribs relax. The structures that have been stretched or twisted recoil into their original positions; the structures that have been raised against the force of gravity fall back by their weight, and in the measure in which the pressure increases in the thoracic cavity the elasticity of the lungs causes them to shrink. The pressure in the alveoli, which at the end of inspiration was just equal to that of the atmosphere, is thus increased, and the air expelled. It is possible that, even in man and in quiet respiration, a slight contraction of the *abdominal muscles* hastens the return of the diaphragm to its position of rest, and that the *triangularis sterni* helps in depressing the costal cartilages. In reptiles and birds, expiration is normally effected by an active muscular contraction. This is also true in some mammals—the rabbit, for instance, in which the external oblique muscle of the abdominal wall takes an important share in the expiratory act.

Types of Respiration. — Differences exist also, not only between different groups of animals, but even between women and men, in the relative importance in inspiration of the diaphragm on the one hand, and the muscles that elevate the ribs on the other. When the movements of the diaphragm predominate, the respiration is said to be of the *abdominal or diaphragmatic type;* when the movements of the ribs and sternum are most conspicuous, of the *costal or thoracic type.* In abdominal respiration, the inspiratory movement commences at the diaphragm, and then involves the lower ribs and the tip of the sternum. In costal respiration, the upper ribs initiate the movement, and are followed by the abdomen. In the rabbit, during quiet breathing, the respiration is purely diaphragmatic, the ribs remain motionless; and herbivorous animals in general conform more or less closely to this type. In the carnivora, on the contrary, the costal type prevails. Man allies himself as regards his respiration with the rabbit and the sheep; he uses his diaphragm more than his ribs. Civilized woman falls into the class of the wolf and the tiger; she uses her ribs more than her diaphragm. The cause of the difference between men and women has been much discussed. It is not a primitive sexual difference, for it is far from being universal; in the uncivilized and semi-civilized races that have been investigated, the women breathe like the men. It is therefore probable that the predominance of the costal type among women of European race is a peculiarity developed by a mode of dressing which hampers the movements of the diaphragm while permitting the elevation of the ribs. This conclusion is strengthened by the fact that in children no difference exists; both boys and girls show the abdominal type of respiration.

All this refers to ordinary breathing. In forced respiration, when the need for air becomes urgent, costal breathing always becomes prominent alike in men, in women, and in animals, for by elevation of the ribs the capacity of the chest can be increased to a greater degree than by any contraction of the diaphragm.

In forced inspiration, indeed, all the muscles that can

elevate the ribs may be thrown into contraction, as well as other muscles which give these fixed points to act from. During a paroxysm of asthma, for example, the patient may grasp the back of a chair with his hands, so as to fix the arms and shoulders and allow the pectoral and serratus magnus to raise the ribs. Similarly in **forced expiration** all the muscles are used which can depress the ribs, or increase the intra-abdominal pressure and push up the diaphragm.

Certain **accessory phenomena (movements and sounds)** are associated with the proper movements of respiration. The larynx rises in expiration, and sinks in inspiration. The glottis (and particularly its posterior portion, the glottis respiratoria) is widened during deep inspiration and narrowed during deep expiration. The same is the case with the nostrils, and, indeed, in some persons the alæ nasi move even in ordinary breathing.

As regards the **respiratory sounds**, all that is necessary to be said here is that when we listen over the greater portion of the lungs with the ear, or, much better, with a stethoscope, a soft breezy murmur, that has been compared to the rustling of the wind through distant trees, is heard. This has been called the *vesicular murmur*. It is only heard in health during inspiration and the very beginning of expiration, and is louder in children than in adults. It is not definitely settled whether this sound arises at the glottis and is modified by transmission through the pulmonary tissue, or whether it arises somewhere in the terminal bronchi, the infundibula or the alveoli. Both views may be supported by certain arguments, and to both some objections may be raised. But it is generally admitted, and this is of great importance in practical medicine, that when the normal sound is heard over any portion of the lung tissue, it may be inferred that this portion is being properly distended, and that air is freely entering its alveoli. Around the larger bronchi and the trachea a blowing sound is heard. In health this is not recognised over the greater portion of the lung, but in certain diseases in which the alveoli are filled up with exudation, this *bronchial* or *tubular breathing*

may be heard over a large area, the vesicular sound being now suppressed, and the bronchial sound being better conducted by the consolidated tissue than by the portions of the lung that still contain air.

Up to this point we have contented ourselves with a purely qualitative description of the mechanical phenomena of respiration. We have now to consider their quantitative relations, and the methods by which these have been studied.

The expansion of the lungs in inspiration may be easily demonstrated in man, and even a rough estimate of its amount obtained, by the clinical method of **percussion**. For example, the resonant note that is elicited when a finger laid on the chest at a part where it overlies the right lung is smartly struck can be followed down until it is lost in the 'liver dulness.' If the lower limit of the resonant area be marked on the chest-wall first in full inspiration and then in full expiration, the mark will be lower in the former than in the latter, and the difference will represent the difference in the vertical length of the shrunken and distended lung. A similar enlargement in the transverse direction may be demonstrated in the same way, the inner borders of the lungs coming nearer to the middle line in inspiration, and receding from it in expiration.

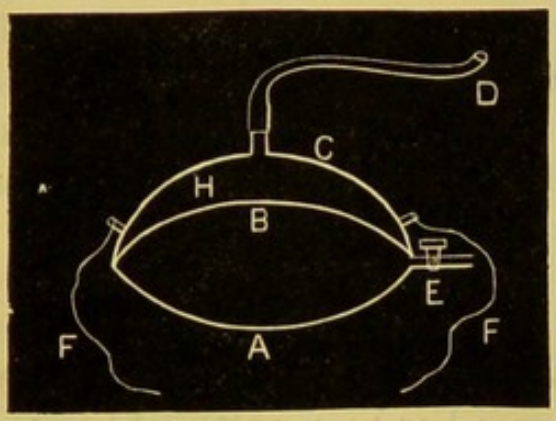

FIG. 77. — SCHEME OF TAMBOUR (BRONDGEEST'S) FOR RECORDING RESPIRATORY MOVEMENTS.

C, a metal capsule connected airtight with B, A, two caoutchouc membranes, the chamber formed by which can be inflated by means of the tube and stopcock E. The tube D connects the space H with a registering tambour provided with a lever. The membrane A is applied to the chest, round which the inextensible strings F are tied. At every expansion of the chest the pressure in H is increased, and the increase of pressure is transmitted to the registering tambour.

For most physiological purposes, however, we require methods more delicate and more exact, and in many investigations a faithful graphic record of the respiratory movements is indispensable. This may be obtained:

(1) By registering the movements of a single point, or the variations in a single circumference, of the boundary of the thoracic cavity. In animals the end of a lever, or a small compressible bag containing air and connected with a recording tambour, may be placed between the lower surface of the diaphragm and the liver, through an incision in the abdominal wall. In man changes in the circumference of the chest at any level can be recorded by means of a tambour so adjusted that in inspiration the pressure of the air in

it is increased and in expiration diminished. This tambour is in communication with another, which is provided with a writing lever (Marey's pneumograph, Sanderson's stethometer, Brondgeest's pan-sphygmograph). (Fig. 77.) Or an elastic tube, with a spiral spring in its lumen, may be fastened around the thorax or abdomen and connected with a piston-recorder (a small cylinder in which works a piston carrying a writing-point) (Fitz).

(2) By recording the changes of pressure produced in the air-passages by the respiratory movements. This can be done by connecting a cannula in the trachea of an animal with a recording tambour in the manner described in the Practical Exercises, p. 272. The changes of pressure may be measured by connecting a manometer with the trachea, or in man with the nostril.

(3) By writing off the changes of pressure which occur in the thoracic cavity during respiration. For this purpose a trocar is

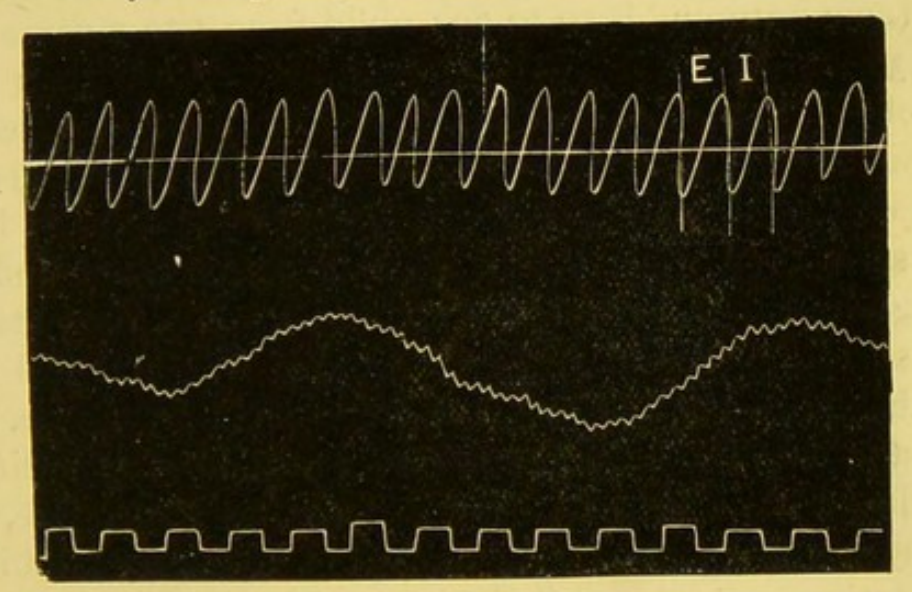

FIG. 78.

The upper tracing is a record of the respiratory movements in a rabbit, taken with Kronecker's lever between the diaphragm and liver. The lower curve is a blood-pressure tracing showing large oscillations (like Traube-Hering waves). E, expiration; I, inspiration. Time trace, seconds. The animal was under the influence of gelsemin.

introduced through an intercostal space into one of the pleural sacs, without the admission of air, or into the pericardium, and then connected with a manometer or other recording apparatus. Or a tube, similar in construction to a cardiac sound (p. 86), and, like it, terminating in an elastic bag, may be pushed down the œsophagus. The variations in the intra-thoracic pressure are transmitted to the air in the bag, and thence to a tambour connected with the sound.

When the respiratory movements are studied in any of these ways, it is found that there is practically no pause between the end of inspiration and the beginning of expiration. Nor, although the chest collapses more gradually than it expands, is there any distinct interval in ordinary

breathing between the end of expiration and the beginning of the succeeding inspiration. When, however, the respiration is unusually slow, an actual pause (expiratory pause) may occur at this point. Expiration takes somewhat longer time than inspiration, the ratio varying from 7 : 6 to 3 : 2, according to age, sex, and other circumstances.

The **frequency of respiration** is by no means constant even in health. All kinds of influences affect it. It is difficult even to direct the attention to the respiratory act without bringing about a modification in its rhythm. In the adult 15 to 20 respirations per minute may be taken as about the normal. In young children the frequency may be twice as great (new-born child, 50 to 70; child from 1 to 5 years old, 20 to 30 per minute). It is greater in a female than in a male of the same age. A rise of temperature increases it, and this is probably one of the causes of the increased rate of respiration in fever; 150 respirations per minute have been seen in a dog with a high temperature. Sudden cooling of the skin, exercise, and various emotional states, increase the rate, and sleep diminishes it. The will can alter the frequency and depth of respiration for a time, and even stop it altogether, but in about a minute, in ordinary individuals, the desire to breathe becomes imperative, nor can any training extend this interval of voluntary inhibition beyond three minutes. Cato's assertion that he could kill himself at any time 'merely by holding his breath' is only a proof that he was a better philosopher than physiologist. In animals the rate can be greatly affected by drugs and by the section and stimulation of certain nerves; but to this we shall return when we come to consider the nervous mechanism of respiration.

It cannot fail to be observed that to a great extent the rate of respiration is affected by the same circumstances as the frequency of the heart (p. 95), and in the same direction. And, indeed, in health, these two physiological quantities, amid all their absolute variations, maintain to each other a fairly constant ratio (1 to 4 or 1 to 5 in man). Even in many diseases this proportion remains tolerably stable, although in others it is disturbed.

The **total quantity of air expired**, or, what comes to the same thing, the alteration in the capacity of the chest during expiration, can be measured by means of a spirometer, which consists of an inverted graduated glass bell dipping by its open mouth into water and balanced by weights. The vessel is sunk till it is full of water, the air being allowed to escape by a cock. The expired air is now permitted to enter it through a tube, and displaces some of the water. The spirometer is adjusted so that the level of the water inside and outside is the same, and then the volume of air contained in it is read off. This gives the volume of the expired air at atmospheric pressure. Similarly, by breathing air from the spirometer the amount inspired can be measured.

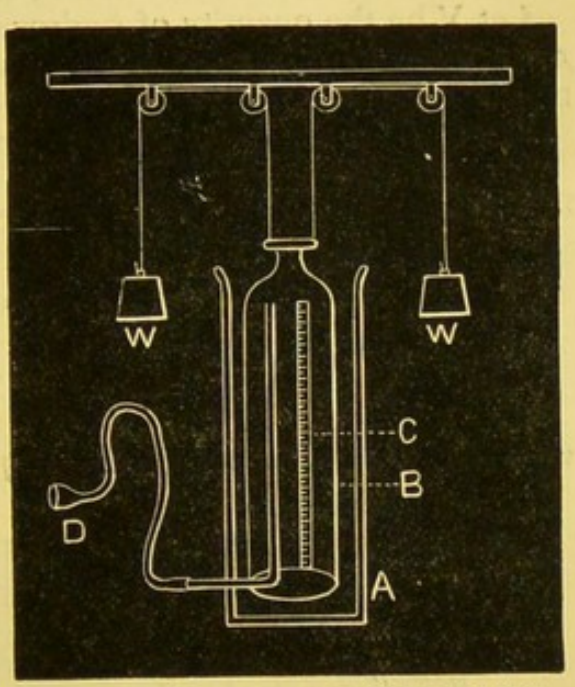

FIG. 79.—DIAGRAM OF SPIROMETER.

A, vessel filled with water. B, glass cylinder with scale C, swung on pulleys and counterpoised by weights W. D, tube for breathing through.

From 400 to 500 c.c. of air* are taken in and given out at each respiration in quiet breathing. This is called **tidal air**. It amounts to 35 pounds by weight in twenty-four hours, or enough to fill, at atmospheric pressure, a cubical box with a side of 8 feet. With the deepest possible inspiration room can be made for 2,000 c.c. more; this is called **complemental air**. By a forced expiration 1,500 c.c. can be expelled besides the tidal air; and to this quantity the name of **supplemental** or **reserve air** has been given. After the deepest expiration there always remain about 700 or 800 c.c. of air in the lungs, and this is called

* The average for 81 healthy students, with an average body-weight of 66 kilos, was 460 c.c., or 7 c.c. per kilo. In 4 newborn children the tidal air varied from 20 to 30 c.c., and from 7·6 to 7·3 c.c. per kilo, which is not very different from the amount in the adult. The pulmonary ventilation must therefore be far more rapid in the child, since its respiratory frequency is so much greater.

the **residual air.** After a normal expiration following a normal inspiration the lungs still contain *stationary* air to the amount of about 2,500 c.c.

The *residual air* may be measured by causing a person, starting immediately after the deepest possible expiration, to breathe out and in several times into a vessel (a spirometer) filled with hydrogen, till it can be assumed that the hydrogen and the residue of air in the lungs have been completely mixed. Knowing the quantity of hydrogen originally contained in the vessel, we can calculate from the percentage at the end of the experiment the quantity of air with which it has been mixed—that is, the residual air (Davy).

Let V be the quantity of hydrogen in the spirometer at first, and p the percentage amount in it at the end of the experiment. Let x be the volume of residual air in the lungs at the beginning.

Then, since the quantity of hydrogen remains unchanged after the mixture,

$$\frac{p}{100}(x+V)=V,$$

$$\therefore\ x=\frac{V\,(100-p)}{p}.$$

Suppose $V=4{,}000$ c.c.,
and $p=85$ per cent.,

we get $x=\frac{12{,}000}{17}=$ about 705 c.c.

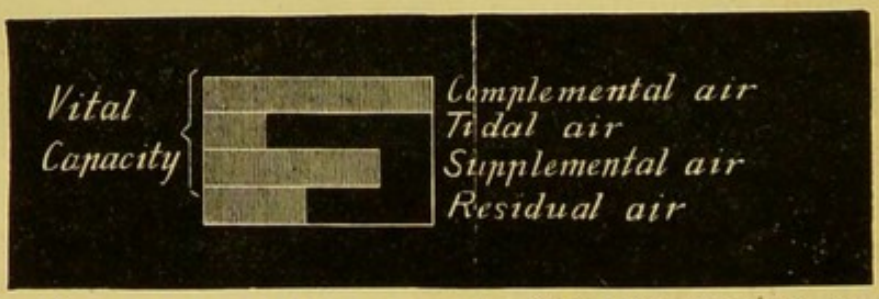

FIG. 80.—DIAGRAM TO ILLUSTRATE THE RELATIVE AMOUNT OF COMPLEMENTAL, TIDAL, SUPPLEMENTAL, AND RESIDUAL AIR.

But some carbon dioxide would be given off by the lungs, and some oxygen, and perhaps hydrogen, absorbed, during the experiment, and therefore slight corrections might have to be made. Sir Humphry Davy actually calculated the residual air in his own lungs, as determined by this method, at 672 c.c.

The *coefficient of ventilation*, that is, the ratio of the quantity of air taken in at each inspiration to the quantity already in the lungs, has been estimated at about $\frac{1}{5}$ or $\frac{1}{6}$.

The term **vital or respiratory capacity** is applied to the quantity of air which can be expelled by the deepest expiration following the deepest inspiration, and amounts in an adult of average height to 3,500 or 4,000 c.c. The maximum

quantity of air which the lungs can contain is evidently equal to vital capacity plus residual air. At one time the vital capacity was thought to be capable of affording valuable information in the diagnosis of chest diseases; but little stress is now laid upon it, as it varies from so many causes. For instance, it can be increased by practice with the spirometer. It is greater in mountaineers than in the inhabitants of lowland plains.

It is clear from the figures we have given that in ordinary breathing only a small proportion of the air in the lungs comes in direct at each inspiration from the atmosphere, and only a small proportion escapes into the atmosphere at each expiration. The greater part of the air in the lungs is simply moved a little farther from the upper respiratory passages, or a little nearer them; and fresh oxygen reaches the alveoli, as carbon dioxide leaves them, mainly by diffusion, aided by convection currents due to inequalities of temperature, and to the churning which the alternate expansion and shrinking of the lungs, and the pulsations of their arteries, must produce. But that some of the tidal air strikes right down to the alveoli is evident enough. For the respiratory 'dead space'—that is, the capacity of the upper air passages and the bronchial tree down to the infundibula—is only 140 c.c., or one-third of the amount of the tidal air (*Zuntz*, Loewy). The immense extent of the pulmonary surface, and the extreme thinness of the layer of blood in the capillaries of the lungs, facilitate the interchange between the gases of the blood and the gases of the alveoli.

The Amount and Variations of the Intra-thoracic Pressure.—In the deepest expiration the lungs are never completely collapsed; their elastic fibres are still stretched; and the tension of these acts in the opposite direction to the external atmospheric pressure, and diminishes by its amount the pressure inside the thoracic cavity. In the dead body Donders measured the value of this tension, and therefore of the negative pressure of the thorax, by tying a manometer into the trachea, and then causing the lungs to collapse by opening the chest. It varied from 7·5 mm. of

mercury in the expiratory position to 9 mm. in the inspiratory. So far as can be judged from observations made on persons suffering from various diseases of the respiratory organs, the alterations during ordinary breathing do not amount to more than 3 or 4 mm. of mercury. But when an attempt is made in the dead body to imitate a deep inspiration by making traction on the chest-walls so as to expand the lungs, the intra-thoracic pressure may fall to −30 mm. of mercury; and in a living rabbit during a deep natural inspiration, a pressure of −20 mm. has been seen.

The reason why the lungs collapse when the chest is opened is that the pressure is now equal on the pleural and alveolar surfaces, being in both cases that of the atmosphere. There is therefore nothing to oppose the elasticity of the lungs, which tends to contract them. So long as the chest is unopened, the pressure on the pleural surface of the lungs is less than that on the alveolar surface, and the elastic tension can only cause them to shrink until it just balances this difference.

In intra-uterine life, and in stillborn children who have never breathed, the lungs are completely collapsed (atelectatic), and there is no negative intra-thoracic pressure. They are kept in this condition by adhesion of the walls of the bronchioles and alveoli. If the lungs have been once inflated, this adhesion ceases to act, and they never completely collapse again.

Amount and Variations of the Respiratory or Intra-pulmonary Pressure.—As we have already remarked, the pressure in the alveoli and air-passages is less than that of the atmosphere while the inspiratory movement is going on, greater than that of the atmosphere during the expiratory movement, and equal to that of the atmosphere when the chest-walls are at rest. When the external air-passages are closed, *e.g.*, by connecting a manometer with the mouth and pinching the nostrils, the greatest possible variations of pressure are produced. In the deepest inspiration under these conditions a negative pressure of about 75 mm. of mercury (*i.e.*, a pressure less than that of the atmosphere by this amount)

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has been found, and in deep expiration a somewhat greater positive pressure* (Practical Exercises, p. 274).

But with ordinary breathing, the variations of pressure as measured by this method do not exceed 5 to 10 mm. of mercury above or below the pressure of the atmosphere.

When the external openings are not obstructed, as, for example, when the lateral pressure is taken in the trachea of an animal by means of a cannula with a side-tube connected with a manometer, still smaller, and doubtless truer, values have been found (2-3 mm. of mercury as the positive expiratory pressure, and 1 mm. as the negative inspiratory pressure in dogs). But since the respiratory passages are abruptly narrowed at the glottis, the variations of pressure must be greater below than above it, and in general they must increase with the distance from that orifice, being greater, for instance, in the alveoli than in the bronchi.

Relation of Respiration to the Nervous System.—Unlike the beat of the heart, the respiratory movements are entirely dependent on the nervous system; and the 'centre' which presides over them is situated in the spinal bulb. It is a bilateral centre—that is, it has two functionally symmetrical halves, one on each side of the middle line; and each of these halves seems to have to do more particularly with the respiratory muscles of its own side, for destruction of one-half of the spinal bulb causes paralysis of respiration only on that side. Anatomically the respiratory centre has not been sharply localized; but it lies lower than the vaso-motor centre, not far from the point of the calamus scriptorius. It is brought into relation with the muscles of respiration by efferent nerves. The phrenic nerves to the diaphragm, and the intercostal nerves to the muscles which elevate the ribs, are the most important of those concerned in ordinary breathing. The circular muscles of the bronchi are also supplied with motor fibres that run in the pneumogastric. The bronchial tubes are narrowed by their artificial excitation, but their function in respiration is unknown. The respiratory

* The maximum negative pressure in deepest inspiration averaged for 49 students, −73 mm. (highest observation −137 mm.) of mercury; the maximum positive pressure in deepest expiration, +80 mm. (highest observation +140 mm.).

centre is further related to afferent nerves, of which the most influential is the vagus, particularly its pulmonary fibres, and its superior laryngeal branch. But almost any afferent nerve may powerfully affect the centre; and it is also influenced by fibres passing to it from the higher parts of the central nervous system.

Section of the spinal cord in animals above the origin of the phrenic nerves causes complete paralysis of respiration, and consequent death. The phrenics arise from the third and fourth cervical nerves, and are joined by a branch from the fifth; and in man fracture of any of the four upper cervical vertebræ is, as a rule, instantly fatal. But in one case respiration was carried on, and life maintained for thirty minutes, merely by the contraction of the muscles of the neck and shoulders in a man entirely paralyzed below this level (Bell). Section of the cord just below the origin of the phrenics leaves the diaphragm working, although the other respiratory muscles are paralyzed. A case has been recorded of a man in whom, from disease of the spine in the lower cervical region, all the ribs became completely immovable. He was able to lead an active life, and to carry on his business, although he breathed entirely by his diaphragm and abdominal muscles (Hilton).

Section of one phrenic is followed by paralysis of the corresponding half of the diaphragm, section of both phrenics by complete paralysis of that muscle, and although respiration still goes on by means of the muscles which act upon the ribs, it is usually inadequate to the prolonged maintenance of life. In the horse, however, not only has survival been seen after this severe operation, but the animal, after the first temporary increase in the frequency of the breathing had disappeared, could be driven in a light vehicle without any marked dyspnœa. The phrenic nuclei in the two halves of the cord are connected across the middle line. For when a hemisection of the cord is made between this level and the respiratory centre in the medulla, respiratory impulses are still able to reach both phrenic nerves. In some animals both halves of the diaphragm go on contracting. But when, as usually happens, this is not

the case, and the diaphragm on the side of the hemisection has ceased to act, it at once begins to contract again when the opposite phrenic nerve is cut, and the respiratory impulse, descending from the bulb, is blocked out from the direct, and forced to follow the crossed path. It has been shown that the crossing takes place at the level of the phrenic nuclei, and nowhere else (Porter).

When one vagus is divided, there is little or no change in the respiratory movements. Half an inch of one vagus nerve has been excised in removing a tumour, and the patient showed no symptoms whatever (Billroth). But section of both vagi generally (though not always) causes respiration to become for a time much deeper and slower, the one change just compensating the other, so that the total amount of air taken in and given out, and the amount of carbon dioxide eliminated, are not altered. Gad has shown that the effect is really due to the loss of impulses that normally ascend the vagi, not to any irritation of the cut ends. For a nerve can be frozen without exciting it; and when a portion of each vagus is frozen, the respiration is affected in precisely the same way as when the nerves are divided.

A similar change follows the blocking of the paths connecting the respiratory centre with the brain above, by injection of paraffin wax into the common or internal carotid. The bloodvessels supplying the nerve-fibres which connect the respiratory centre with the brain may in this way be closed by artificial emboli. The nerves lose their function, as if they had been cut; no impulses now reach the respiratory centre from above; and the respiration becomes markedly slowed and deepened, just as happens when the vagi are divided. Where only the vagus *or* these 'higher paths,' but not both, are cut off, the respiration remains regular, although deep, and perhaps in course of time tends to resume its original type. But when both paths are cut, the character of the respiration is entirely changed; periods of rapid and spasmodic breathing alternate with periods of complete cessation, till the animal dies (Marckwald).

From these facts it appears that the periodic automatic

discharges of the respiratory centre are being continually controlled and modified by impulses passing up the vagus or down from the brain, but especially up the vagus. When the vagus is severed, the control of the higher paths becomes more complete, and is sufficient still to keep the breathing regular. When the higher paths are cut off, the vagus of itself is able to regulate the discharge. But when both are gone, the respiratory centre, freed from control, passes into a condition of alternate spasm and exhaustion.*

The rhythmical excitation of the regulating vagus fibres must be brought about either by mechanical stimulation of the nerve-endings in the lungs, due to the alternate stretching and shrinking, or by chemical stimulation depending on the

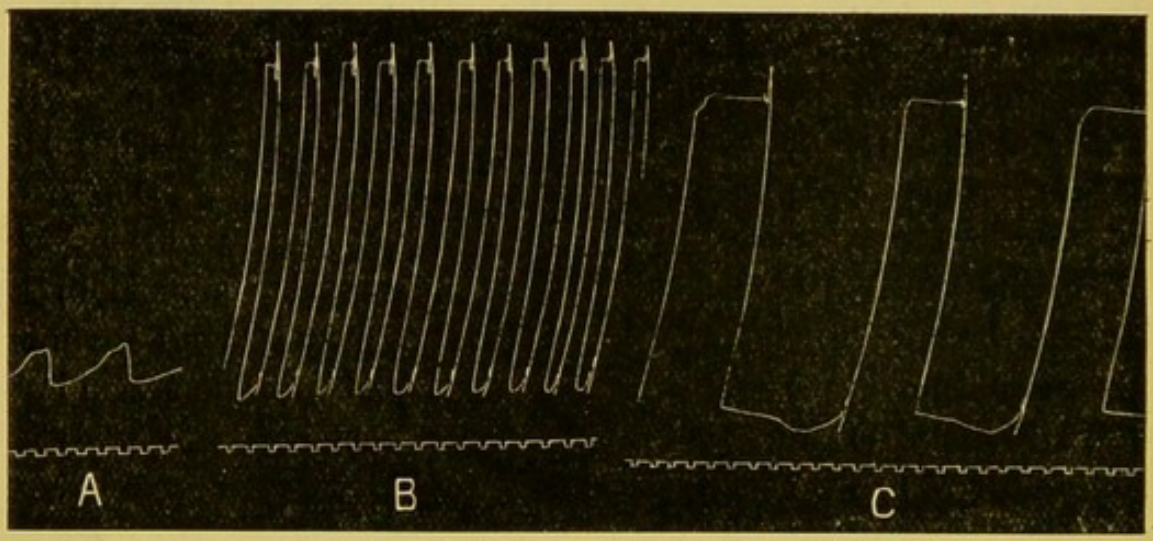


FIG. 81.—RESPIRATORY TRACINGS (DOG).

A, normal; B, effect of stimulation of the central end of the vagus; C, effect of section of both vagi. (Tracing taken as in Fig. 100, p. 273.) Time-tracing, seconds.

state of the blood.† Both views have found advocates, but neither has been definitely proved. Nor are the results of experimental stimulation of the nerve-trunk so clear or so constant that we can confidently appeal to them in making a decision. Excitation, with induction shocks, of the central end of the cut vagus below the origin of its superior laryngeal branch certainly causes quickening of respiration, or, if the excitation be strong, arrest in the inspiratory phase. A brief mechanical stimulus, or a series of such, has a

* We may, perhaps, think of the respiratory centre as being 'wound up' like a clock, the periodic arrival of regulating impulses acting like an escapement movement, and allowing a certain amount of discharge.

† That the vagus is really excited is shown by the recent observations of Lewandowsky, who finds that a negative variation (see p. 607) is set up in the nerve when the lungs are inflated, though not when they collapse.

similar effect. But chemical stimulation (*e.g.*, with a strong solution of potassium chloride) or long-continued mechanical excitation like that produced by stretching or compression of the nerve, or certain kinds of electrical stimulation—for instance, the closure of an ascending voltaic current*—cause slowing of the respiratory movements or expiratory standstill. This is also the usual, though not the invariable, result of stimulating the superior laryngeal, even when induction shocks are employed. These facts undoubtedly suggest the existence in the vagus of two kinds of afferent nerve-fibres that affect the respiratory centre in opposite ways—inspiratory fibres, which stimulate it to greater activity of discharge, and expiratory fibres, which inhibit its action. The latter variety we may suppose to be more numerous in the superior laryngeal, the former in the pulmonary branches of the vagus. And there is nothing forced in the hypothesis that certain kinds of stimuli act particularly on the one set of fibres, and certain kinds on the other, for we have already seen an instance of this in studying the differences between the vaso-constrictor and the vaso-dilator nerves (p. 150). It is possible, however (although this view has less inherent probability, in spite of the fact that it has been maintained by some of the most recent writers on the subject), that, at any rate in the vagus trunk, only one set of fibres exists, and that these are affected differently by different kinds of stimulation—momentary stimuli, for example, setting up in them impulses which we may call inspiratory, and long-lasting stimuli impulses which we may call expiratory.

However this may be, the facts we have been discussing have an importance of their own, apart from any hypothetical explanations of them; and they may be readily demonstrated by means of such a graphic method as is described in the Practical Exercises (p. 273), or by merely opening the abdomen in a rabbit, and observing the lungs through the thin diaphragm (Gad). Some of them have been more than once unintentionally illustrated on man. In one case the left vagus trunk was included in a ligature

* *I.e.*, a current passing towards the head in the nerve.

with the common carotid. The respiratory movements immediately stopped, the pulse was slowed, and death occurred in thirty minutes (Rouse). The superior laryngeal fibres, unlike those of the vagus proper, do not appear to be constantly in action, as section of both nerves has no effect on respiration. Any source of irritation in the larynx may stimulate these fibres and produce a cough, which may also be caused by irritation of the pulmonary fibres of the vagus.

The cutaneous nerves, and especially those of the face (fifth nerve), abdomen and chest, have a marked influence on respiration. They can be easily excited in the intact body by thermal and mechanical stimulation. A cold bath, for instance, usually causes acceleration and deepening of the respiratory movements; and the efficacy of mechanical stimulation of sensory nerves in stirring up a sluggish respiratory centre is well known to midwives, who sometimes slap the buttocks of a newborn child to start its breathing.

Another set of afferent nerves that seem to have an important relation to the respiratory centre are those which supply the muscles. We have already noticed that the frequency of respiration is greatly augmented by muscular exercise. This seems to be brought about in part through the stimulation of those afferent muscular nerves either by mechanical compression of their terminal 'spindles,' or by the chemical action on them of certain waste products produced in contraction. But this cannot be the only way in which the respiratory centre is affected by muscular activity. For everybody is agreed that an increase in the respiratory movements is caused by tetanizing the muscles of a limb whose nerves have been completely severed, and which is indeed connected with the rest of the body by no other structures than its bloodvessels. This can only be due to two things: a direct action on the respiratory centre by the blood that has passed through, and been altered in, the contracting muscles, or an action exerted by the blood indirectly on the centre through the excitation of afferent respiratory nerves whose connection with it is still intact—

for example, the other muscular nerves or the pulmonary branches of the vagus.

That the respiratory centre is greatly affected by the quality of the blood which circulates through it is well known. And it is generally acknowledged that it may be excited both by blood that is rich in carbon dioxide and by blood that is poor in oxygen, the actual stimulating substance in the latter case being, perhaps, an easily oxidizable body which rapidly disappears from properly oxygenated blood (Pflüger).

But it has been the subject of long-continued discussion whether excess of carbon dioxide or deficiency of oxygen is the more potent stimulus. The truth appears to be that much depends upon the conditions of the experiment, upon the size of the chamber, for instance, in which an animal or a man is made to breathe. The best evidence points to the conclusion that comparatively small alterations in the amount of carbon dioxide in the inspired air cause a relatively great increase in the respiration, while in the case of the oxygen the departure from the normal proportion must be much more decided to bring about any notable effect (Zuntz and Loewy). Nor is it at all out of harmony with this that, when very large quantities of carbon dioxide (30 per cent. and upwards in rabbits) are inhaled, a condition of narcosis comes on without any previous respiratory distress (Benedicenti). For many substances act differently in large and in small doses.

Be this as it may, when the gaseous interchange from any cause becomes insufficient, the respiratory movements are exaggerated, and ultimately every muscle which can directly or indirectly act upon the chest-walls is called into play in the struggle to pass more air into and out of the lungs. To a lesser and greater degree of this exaggeration of breathing the terms *Hyperpnœa* and *Dyspnœa* have been respectively applied. If the gaseous interchange remains insufficient, or is altogether prevented, *asphyxia* or suffocation sets in. Sometimes in man impending asphyxia from loss of function by a part of the lungs, as in pneumonia, may be warded off by inhalations of oxygen. Increase in the temperature of

the blood circulating through the spinal bulb, as when the carotid arteries of a dog are laid on metal boxes through which hot water is kept flowing, also causes dyspnœa (*heat-dyspnœa*), (p. 272). But if the temperature be too high, the respiratory movements may be slowed, perhaps by a partial paralysis or inhibition of the respiratory centre. When the blood is cooled the respiration becomes deeper and slower, but if the temperature is greatly and suddenly lowered, the centre may be stimulated and the breathing quickened. In man the increased temperature of the blood in fever is probably connected with the increase in the rate of respiration.

The physiological opposite of dyspnœa is *apnœa*. This condition may be produced in an animal by rapid artificial respiration. For some seconds, in a successful experiment, after the artificial respiration is stopped, the animal remains without breathing. The apnœic state seems to be due partly to an excess of oxygen in the arterial blood or in the lungs, partly to some nervous effect produced through the vagi on the respiratory centre. Possibly the pulmonary nerve-endings of the vagi are affected mechanically by the inflation; for rapid and repeated inflation of the lungs with hydrogen may cause apnœa (Traube). The venous blood in apnœa is, if anything, poorer in oxygen than normal venous blood.

That poorly oxygenated blood produces dyspnœa by acting on some portion of the brain may be shown in an interesting manner by establishing what is called a cross-circulation in two rabbits or dogs. The vertebral arteries and one carotid are tied in both animals; the remaining carotids are divided and connected crosswise by glass tubes, so that the brain of each is supplied by blood from the other (Bienfait and Hogge). When the respiration is artificially hindered or stopped in one of the animals, it shows no dyspnœa; it is in the other, whose brain is being fed with improperly oxygenated blood, that the respiratory movements become exaggerated. The point of attack of the 'venous' blood has been further localized in the spinal bulb by the observation that when the brain has been cut away above it, the cord severed below the origin of the phrenics, and all other

nerves connected with the region between the two planes of section divided, any interference with the gaseous exchange in the lungs is at once followed by dyspnœa.*

The question has been raised whether, in the absence of this 'natural' stimulation by the blood, and of the impulses that constantly reach the centre along its afferent nerves, it would continue to discharge itself, or whether it would sink into inaction. We have already discussed a similar question in regard to the cardiac and vaso-motor centres, and the subject must again present itself when we come to examine the functions of the central nervous system. In the meantime it is only necessary to say that the apparent automatism of the respiratory centre, although modified by the quality of the blood which circulates in it, is not essentially dependent on it; for in animals whose blood has been replaced by normal saline, or serum, and in frogs after excision of the heart, quiet, regular breathing has been seen.

Action of Drugs on the Respiratory Centre.—The respiratory centre is directly affected by numerous drugs. Pituri and nicotin, for instance, cause in various animals a quickening and deepening of the respiration, followed, if the dose has been large, by slowing and ultimate cessation. The action of the great majority of such substances, however, possesses only a pharmacological interest, and it would be out of place even to enumerate them in a text-book of physiology. But there are one or two points in the action on the respiratory centre of chloroform and alcohol—substances so greatly employed in practical medicine and in physiological research—which may properly be touched on here:

Chloroform.—The cause of the deaths from chloroform which, at rare intervals, startle the operating theatre of every great hospital where this anæsthetic is used, has been, on account of its extreme practical interest, the subject of prolonged discussion and experiment. Is it the heart that fails? Or is it the respiration? The answer of what is known as the 'Edinburgh School' is that the respiration (in physiological terms, the respiratory centre) is always first paralyzed. Their golden rule of doctrine in chloroform administration is, 'Watch the respiration; the heart will take care of itself'—a rule which, however, in 'Edinburgh' practice does not exclude careful observation of the pulse. This view, having the merit of simplicity, has been widely adopted. It has been lately upheld by a scientific commission appointed by the Nizam of Hyderabad to investigate the question with the aid of modern physiological methods. But the conclusions of the Hyderabad Commission seem to have been too

* The conclusion is doubtless correct, but this experiment is not decisive. For the phrenic nerves themselves contain afferent fibres, through which the respiratory centre *might* have been affected.

absolutely drawn. For it has been shown by a number of observers (MacWilliam, Gaskell and Shore, etc.) that chloroform may paralyze the heart without primarily affecting the respiration; and, further, that paralysis of the vaso-motor centre, and the consequent withdrawal of blood from the heart and brain to the dilated splanchnic area, may be an important factor in bringing about a fatal result (p. 164). In normal chloroform anæsthesia in man it is easy to demonstrate by the sphygmometer a fall of blood-pressure in the brachial artery of 20 to 40 mm. of mercury (Hill). It would seem that death from chloroform may take place either from primary failure of the respiratory centre followed by failure of the heart, or from primary paralysis of the heart or of the whole vascular mechanism (including the muscular tissue of the heart and bloodvessels and the vaso-motor centre), followed by paralysis of the respiratory centre. Sometimes the respiratory failure and the vascular paralysis may be simultaneous; often one may follow so hard on the heels of the other that it is difficult to decide which is primary and which secondary. The practical lesson is that both the respiration and the pulse must be watched, and with equal care. At a certain stage in chloroform anæsthesia, before it has become very deep, comparatively trifling causes may bring about great and sudden changes in the pulse-rate, owing to the abnormal mobility of the vagus centre (MacWilliam).

Alcohol in small doses, when given by the stomach or (in animals) injected into the blood, causes stimulation of the respiratory centre and increase in the pulmonary ventilation. In man, this increase usually amounts to 8-15 per cent., but is occasionally much greater. But the limit which separates the favourable action of the small dose from the hurtful action of the large, is easily overstepped. When this is done, and the dose is continually increased, the activity of the respiratory centre is first diminished and finally abolished. In dogs, for instance, after the injection of considerable quantities of alcohol into the stomach, death takes place from respiratory failure, and the breathing stops while the heart is still unweakened (Fig. 57, p. 165). This is the final outcome of a progressive impairment in the activity of the centre, of which the slow and heavy breathing of the drunken man represents an earlier stage.

Spinal respiratory centres.—Although the chief respiratory centre lies in the medulla oblongata, under certain conditions impulses to the respiratory muscles may originate in the spinal cord. Thus, in young mammals (kittens, puppies), especially when the excitability of the cord has been increased by strychnia, in birds and in alligators, movements, apparently respiratory, have been seen after destruction of the brain and spinal bulb. But no proof has ever been given that in the intact organism the spinal cord below the level of the bulb takes any other part in respiration than that of a mere conductor of nerve impulses; and it is not justifiable to assume the existence of spinal respiratory centres on the strength of such experiments as these.

Death after Double Vagotomy.—Alterations in the rhythm of respiration are not the only effects that follow division of both vagi. In certain animals, at least, this operation is

incompatible with life. In the rabbit, as a rule, death takes place in twenty-four hours. A sheep may live three days, and a horse five or six. Dogs often live a week, occasionally a month or even two, and in rare instances they may survive indefinitely. The most prominent symptoms (in the dog), in addition to the marked and permanent slowing of respiration, quickening of the pulse and contraction of the pupils, are the frequent vomiting and progressive emaciation. The appetite is sometimes ravenous, but no sooner is the food swallowed than it is rejected; and this is particularly true of water or liquid food. The fatal result is usually caused, or at least preceded, by changes of a pneumonic nature in the lungs. The precise significance of the pulmonary lesion is obscure. But it would seem that paralysis of the laryngeal and œsophageal muscles, with the consequent entrance of food, foreign bodies, and perhaps bacteria, into the lungs, is responsible to a great extent. And when only a partial palsy of the glottis is produced, by dividing the right vagus below the origin of the recurrent laryngeal, and the left, as usual in the neck, pneumonia either does not occur or is long delayed. It may be that the tissue of the lungs is rendered particularly susceptible to such insults in consequence of a hyperæmic condition induced by the section of pulmonary vaso-motor fibres in the vagi. The vomiting is certainly connected with the paralysis and consequent dilatation of the œsophagus; and by previously making an artificial opening into the stomach, or by a surgical prophylaxis still more heroic, the establishment of a double gastric and œsophageal fistula, certain observers have been able to prevent death for many months.

Special Modifications of the Respiratory Movements.—*Cheyne-Stokes' Respiration* is the name given to a peculiar type of breathing, marked by pauses of many seconds alternating with groups of respirations. In each group the movements gradually increase to a maximum amplitude, and then become gradually shallower again, till they cease for the next pause. The cause is unknown. The phenomenon is not peculiar to pathological conditions, although it often occurs in certain diseases of the brain, and although pressure

on the spinal bulb may produce it. But it is also seen, more or less perfectly, in normal sleep, especially in children, and in morphia and chloral poisoning. A periodic change in the activity of the respiratory centre, corresponding to the change in the vaso-motor centre which is credited with the production of Traube-Hering oscillations in the blood-pressure (p. 250), has been suggested as the cause, but there is no certainty as to this.

In frogs, Cheyne-Stokes' breathing has been observed as the result of interference with the circulation in the spinal bulb, 'drowning,' or ligature of the aorta, and also as a consequence of removal of the brain, or parts of it (hemispheres and optic thalami) (Langendorff, Sherrington, etc.).

Peculiarly modified, but more or less normal respiratory acts are coughing, sneezing, yawning, sighing and hiccup.

A *cough* is an abrupt expiration with open mouth, which forces open the previously closed glottis. It may be excited reflexly from the mucous membrane of the respiratory tract or stomach through the afferent fibres of the vagus, from the back of the tongue or mouth, and (by cold) from the skin.

Sneezing is a violent expiration in which the air is chiefly expelled through the nose. It is usually excited reflexly from the nasal mucous membrane through the branch of the fifth nerve which supplies it. Pressure on the course of the nasal nerve will often stop a sneeze. A bright light sometimes causes a sneeze, and so in some individuals does pressure on the supra-orbital nerve, when the skin over it is slightly inflamed.

Yawning is a prolonged and very deep inspiration, sometimes accompanied with stretching of the arms and the whole body. It is a sign of mental or physical weariness.

A *sigh* is a long-drawn inspiration, followed by a deep expiration.

Hiccup is due to a spasmodic contraction of the diaphragm, which causes a sudden inspiration. The abrupt closure of the glottis cuts this short and gives rise to the characteristic sound. The following readings of the intervals between successive spasms were obtained in one attack: 13 secs., 12 secs., 15 secs., 9 secs., 14 secs., etc.—*i.e.*, one-fourth or

one-fifth of the frequency of the ordinary respiratory movements. The mere fixing of the attention on the observations soon stopped the hiccup.

Chemistry of Respiration.

Our knowledge of this subject has been entirely acquired in the last 200 years, and chiefly in the last century.

Boyle showed by means of the air-pump that animals die in a vacuum, and Bernouilli that fish cannot live in water from which the air has been driven out by boiling.

Mayow, of Oxford, seems to a considerable extent to have anticipated Black, who in 1757 demonstrated the presence of carbonic acid (carbon dioxide) in expired air by the turbidity which it causes in lime-water.

A most fundamental step was the discovery of oxygen by Priestley in 1771, and his proof that the venous blood could be made crimson, like arterial, by being shaken up with oxygen.

Lavoisier discovered the composition of carbonic acid, and applied his discovery to the explanation of the respiratory processes in animals, the heat of which he showed to be generated like that of a candle by the union of carbon and oxygen. He made many further important experiments on respiration, publishing some of his results in 1789, when the French Revolution, in which he was to be one of the most distinguished victims, was breaking out. He made the mistake, however, of supposing that the oxidation of the carbon takes place in the blood as it passes through the lesser circulation.

That some carbon dioxide is formed in the lungs there is no reason to doubt, and the quantity may even be considerable (Bohr and Henriques). But that they are not the chief seat of oxidation was sufficiently proved as soon as it was known that the blood which comes to them from the right heart is rich in carbon dioxide, while the blood which leaves them through the pulmonary veins is comparatively poor.

There are two main lines on which research has gone in trying to solve the chemical problems of respiration: (1) The analysis and comparison of the inspired and expired

air, or, in general, the investigation of the gaseous interchange between the blood and the air in the lungs. (2) The analysis and comparison of the gases of arterial and venous blood, of the other liquids, and of the solid tissues of the body, with a view to the determination of the gaseous interchange between the tissues and the blood. We shall take these up as far as possible in their order.

The methods which have been used for comparing the **composition of inspired and expired air** are very various.

(1) Breathing into one spirometer and out of another, the inspired and expired air being directed by valves. The contents of the spirometers are analyzed at the end of the experiment (Speck).

(2) A small apparatus, much on the same principle, was used for rabbits by Pflüger and his pupils. A cannula in the trachea was connected with a balanced and self-adjusting spirometer containing oxygen, and the inspired and expired air separated by caustic potash valves, which absorbed the carbon dioxide. The amount of oxygen used could be read off on the spirometer, and the amount of carbon dioxide produced estimated in the liquid of the valves.

(3) Larger and more elaborate arrangements, such as Pettenkofer's great respiration apparatus, in which a man can remain for an indefinite period, working, resting, or sleeping. Smaller chambers of the same kind have also been used for animals. In Pettenkofer's apparatus air is drawn through by an engine, its volume being measured by a gasometer. But as it would be far too troublesome to analyze the whole of the air coming from the chamber, a sample stream of it is constantly drawn off, which also passes through a gasometer, through drying tubes containing sulphuric acid, and through tubes filled with baryta-water. The baryta solution is titrated to determine the quantity of carbon dioxide; the increase in weight of the drying tubes gives the quantity of aqueous vapour. A similar sample stream of the air before it passes into the chamber is treated exactly in the same way, and from the data thus got the quantity of carbon dioxide and aqueous vapour given off can readily be ascertained. But the oxygen has to be calculated by difference, and all the errors fall upon it.

(4) Haldane and Pembrey have elaborated a gravimetric method, which is the most suitable of any—at least, for small animals. It depends upon the absorption of carbon dioxide by soda lime. See Practical Exercises, p. 276.

The **expired air** is at or near the body temperature, is saturated with watery vapour, and contains about 4 per cent. more carbon dioxide and 4 to 5 per cent. less oxygen than the inspired. There may be in addition in expired air small quantities of hydrogen or ammonia, but these are probably

derived from the alimentary canal, either directly or after absorption into the blood. It is entirely free from floating matter (dust), which is always present in the inspired air. The volume of the expired air, owing to its higher temperature and excess of watery vapour, is somewhat greater than that of the inspired air, but if it be measured at the temperature and degree of saturation of the latter, the volume is somewhat less. Since the oxygen of a given quantity of carbon dioxide would have exactly the same volume as the carbon dioxide itself at a given temperature and pressure, it is clear that the deficiency is due to the fact that all the oxygen which is taken up in the lungs is not given off as carbon dioxide; some of it, going to oxidize hydrogen, reappears as water—a small amount of it unites with the sulphur of the proteids (p. 392). The quotient of the volume of oxygen given out as carbon dioxide by the volume of oxygen taken in is the **respiratory quotient.** It shows what proportion of the oxygen is used to oxidize carbon. It may approach unity on a carbo-hydrate diet, which contains enough oxygen to oxidize all its own hydrogen to water. With a diet rich in fat it is least of all; with a diet of lean meat it is intermediate in amount. For ordinary fat contains no more than one-sixth, and proteids not one-half, of the oxygen needed to oxidize their hydrogen. In man on a mixed diet the respiratory quotient may be taken as ·8 or ·9. So long as the type of respiration is not changed, the respiratory quotient may remain constant for a wide range of metabolism. In hibernating animals, however, the respiratory quotient becomes very small during winter sleep (as low as ·4), the output of carbon dioxide falling far more than the consumption of oxygen. On the other hand, in excised mammalian muscles at a low temperature the consumption of oxygen is lessened to a greater extent than the production of carbon dioxide, and the respiratory quotient may be as high as 3·2 (Rubner). Muscular work increases the respiratory quotient, because carbo-hydrates are chiefly used up. In starvation the respiratory quotient diminishes, the production of carbon dioxide falling off at a greater rate than the consumption of oxygen, for the

starving organism lives on its own fat and proteids, and has only a trifling carbo-hydrate stock to draw upon. In a diabetic patient, fed on a diet of fat and proteid alone, the respiratory quotient was only ·6 to ·7, just as in a starving man.

In an average man weighing 70 kilos the mean production of carbon dioxide is about 800 grammes (400 litres) in twenty-four hours, and the mean consumption of oxygen about 700 grammes (490 litres) (Pettenkofer and Voit). But there are very great variations depending upon the state of the body as regards rest or muscular activity, and on other circumstances. In hard work the production of carbon dioxide was found to rise to nearly 1,300 grammes, and in rest to sink to less than 700 grammes, the consumption of oxygen in the same circumstances increasing to nearly 1,100 grammes and diminishing to 600 grammes. In rest, in moderate exertion, and in hard work, the production of carbon dioxide was found to be nearly proportionate to the numbers 2, 3 and 6, respectively. In a case of diabetes the consumption of oxygen was 50 per cent. greater than in a healthy man, corresponding to the higher heat-equivalent of the food of the diabetic patient (Weintraud and Laves).

Taking 400 litres per twenty-four hours, or 17 litres per hour, as the mean production of carbon dioxide by an average male adult at rest or doing only light work, we can calculate **the quantity of fresh air which must be supplied to a room in order to keep it properly ventilated.**

It has been found that when the carbon dioxide given off in respiration amounts to no more than 2 parts in 10,000 in the air of an ordinary room, the air remains sweet. When the carbon dioxide given off reaches 4 parts in 10,000, the room feels distinctly, and at 6 in 10,000 disagreeably, close, while at 9 parts in 10,000 it is oppressive and almost intolerable. This has been supposed by some to be due to a volatile poison exhaled from the lungs, for pure carbon dioxide added alone in similar proportions to the air of a room has not the same bad effect. Certain observers, indeed, alleged that the condensed vapour of the breath, when injected into rabbits, produced fatal symptoms. But this has been shown to be erroneous; and the most careful experiments have failed to detect in the air expired by healthy persons any trace of such a poison. It has therefore been suggested that the odour and other ill effects of a close room are due to substances given off in the sweat and the sebum, and allowed by persons of uncleanly habits to accumulate on the skin, and also to

the products of slow putrefactive processes constantly going on, under favourable conditions, on the walls, floors or furniture, but only becoming perceptible to the sense of smell when ventilation is insufficient. In a small, newly-painted chamber, presumably free from such impurities, it was not until the carbon dioxide reached 3 to 4 per cent. that discomfort began to be felt and the respiration to be quickened.* No close odour could be detected (Haldane and Lorrain Smith).

Nevertheless, experience has shown that it is a good working rule for **ventilation** to take the limit of permissible respiratory impurity at 2 parts of carbon dioxide per 10,000; and the 17 litres of carbon dioxide given off in the hour will require 85,000 litres (or 3,000 cubic feet) of air to dilute it to this extent. This is the average quantity required for the male adult per hour. For men engaged in active labour, as in factories or mines, twice this amount may not be too much. For women and children less is required than for men. If a room smells close, it needs ventilation, whatever be the proportion of carbon dioxide in the air.

It must be remembered that in permanently-occupied rooms mere increase in the size will not compensate for incomplete renewal of the air, although it may be easier to ventilate a large room than a small one without causing draughts and other inconveniences. But as few apartments are occupied during the whole twenty-four hours, a large room which can be thoroughly ventilated in the absence of its inmates has a distinct advantage over a small one in its great initial stock of fresh air.

The cubic space per head in an ordinary dwelling-house should be not less than 28 cubic metres or 1,000 cubic feet.

The quantity of carbon dioxide given off (and of oxygen consumed) is not only affected by muscular work, but also by everything which influences the general metabolism. In males it is greater than in females (in the latter there is a temporary increase during pregnancy), and greater in proportion to the body-weight in the young than the old. This depends, partly at least, on the fact that the metabolism is relatively more active in a small than in a large organism. The taking of food increases it, chiefly in consequence of the increased mechanical and chemical work performed by the alimentary canal and the digestive glands. Sleep diminishes the production of carbon dioxide partly

* Hyperpnœa from defect of oxygen also appears when the amount of it in the air has fallen to a point which varies in different individuals (in one case 12 per cent.). Warm-blooded animals confined in a small air-space die from want of oxygen, and not from the accumulation of carbon dioxide; but the opposite appears to be the case with cold-blooded animals.

because the muscles are at rest, but also to some extent because the external stimuli that in waking life excite the nerves of special sense are absent or ineffective. Even a bright light is said to cause an increase in the amount of carbon dioxide produced and of oxygen consumed; but recent experiments have cast doubt on the statement (C. Ewald). The external temperature also has an influence. In *poikilothermal* animals (such as the frog), the temperature of which varies with that of the surrounding medium, the production of carbon dioxide, on the whole, diminishes as the external temperature falls, and increases as it rises. In *homoiothermal* animals, that is, animals with constant blood temperature, external cold increases the production of carbon dioxide and the consumption of oxygen. But if the connection of the nervous system with the striated muscles has been cut out by curara, the warm-blooded animal behaves like the cold-blooded (Pflüger and his pupils in guinea-pig and rabbit). These interesting facts will be returned to under Animal Heat.

Cold-blooded animals produce far less carbon dioxide, and consume far less oxygen, per kilo of body-weight than warm-blooded.

The following table shows the relation between the body-weight and the excretion of carbon dioxide in man:

Age.	Weight in kilos.	CO_2 excreted per kilo per hour.
Male 35	65	·51 gramme
Male 28	82	·49 „
Male 16	57·7	·59 „
Male 9·6	22	·92 „
Female 19	55·7	·45 „
Female 10	23	·83 „

The next table illustrates the difference in the intensity of metabolism in different kinds of animals, a difference, however, largely dependent upon relative size:

Animal.	Oxygen absorbed per kilo per hour		Carbon dioxide given off per kilo per hour		Respiratory quotient $\frac{CO_2}{O_2}$ or $\frac{O_2 \text{ (in } CO_2)}{O_2}$.
	in grms.	in c.c.	in grms.	in c.c.	
Greenfinch	13·000	9091	13·590	6909	·76
Hen - -	1·058	740	1·327	675	·91
Dog - -	1·303	911	1·325	674	·74
Rabbit - -	0·987	690	1·244	632	·91
Sheep - -	0·490	343	0·671	341	·99
Boar - -	0·391	273	0·443	225	·82
Frog - -	0·105	73·4	0·113	57·7	·78
Crayfish -	0·054	38	0·064	32·7	·86

Forced respiration, although it will temporarily increase the quantity of carbon dioxide given off by the lungs, does not sensibly affect the production; it is only the store of already formed carbon dioxide in the body which is drawn upon. The amount of oxygen taken up is little altered by changes in the movements of respiration except for a very short time.

How it is that the depth of the respiration may affect the rate at which carbon dioxide is eliminated, we can only understand when we have examined the process by which the gaseous interchange between the blood and the air of the alveoli is accomplished; and before doing this it is necessary to consider the condition of the oxygen and carbon dioxide in the blood.

The Gases of the Blood.

Physical Introduction.—Matter may be assumed to be made up of molecules beyond which it cannot be divided without altering its essential character. A molecule may consist of two or more particles of matter (atoms) bound to each other by chemical links. The kinetic theory of matter supposes the molecules of a substance to be in constant motion, frequently colliding with each other, and thus having the direction of their motion changed.

In a gas the mean free path, that is, the average distance which a molecule travels without striking another, is comparatively long, and far more time is passed by any molecule without an encounter than is taken up with collisions. Although the average velocity of the molecules is very great, these collisions will produce all sorts of differences in the actual velocity of different molecules at any given time. Some will be moving at a greater, some at a slower rate, than the average; while some may be for a moment at rest. If the

gas is in a closed vessel, the molecules will be constantly striking its sides and rebounding from them. If a very small opening is made in the vessel, some molecules will occasionally hit on the opening and escape altogether. If the opening is made larger, or the experiment continued for a longer time with the small opening, all the molecules will in course of time have passed out of the vessel into the air, while molecules of the oxygen, nitrogen, and argon of the air will have passed in. In a gas, then, not enclosed by impenetrable boundaries, there is no restriction on the path which a molecule may take, no tendency for it to keep within any limits.

When two chemically indifferent gases are placed in contact with each other, *diffusion* will go on till they are uniformly mixed. The diffusion of gases may be illustrated thus. Suppose we have a perfectly level and in every way uniform field divided into two equal parts by a visible but intangible line, the well-known whitewash line, for instance. On one side of the line place 500 blind men in green, and on the other 500 blind men in red. At a given signal let them begin to move about in the field. Some of the men in green will pass over the line to the 'red' side; some of the men in red will wander to the 'green' side. Some of the men may pass over the line and again come back to the side they started from. But, upon the whole, after a given interval has elapsed, as many green coats will be seen on the red side as red coats on the green. And if the interval is long enough there will be at length about 250 men in red and 250 in green on each side of the boundary-line. When this state of equilibrium has once been reached, it will henceforth be maintained, for, upon the whole, as many red uniforms will pass across the line in one direction, as will recross it in the other.

In a liquid it is very different; the molecule has no free path. In the depth of the liquid no molecule ever gets out of the reach of other molecules, although after an encounter there is no tendency to return on the old path rather than to choose any other; so that any molecule may wander through the whole liquid. Although the average velocity of the molecules is much less in the liquid state than it would be for the same substance in the state of gas or vapour (gas in presence of its liquid), some of them may have velocities much above the average. If any of these happen to be moving near the surface and towards it, they may overcome the attraction of the neighbouring molecules and escape as vapour. But if in their further wanderings they strike the liquid again, they may again become bound down as liquid molecules. And so a constant interchange may take place between a liquid and its vapour, or between a liquid and any other gas, until the state of equilibrium is reached, in which on the average as many molecules leave the liquid to become vapour as are restored by the vapour to the liquid, or as many molecules of the dissolved gas escape from solution as enter into it.

For the sake of a simple illustration, let us take the case of a shallow vessel of water originally gas-free, standing exposed to the air. It will be found after a time that the water contains the atmo-

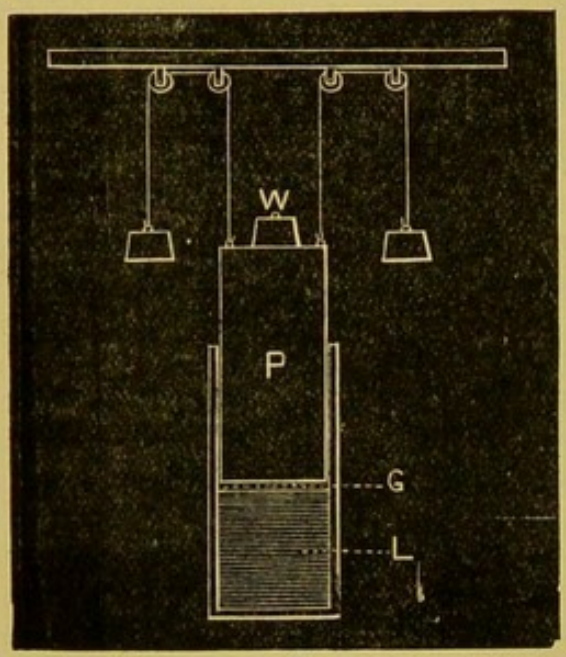
spheric gases in certain proportions—in round numbers, about $\frac{1}{100}$ of its volume of oxygen and $\frac{1}{50}$ of its volume of nitrogen (measured at 760 mm. mercury and 0° C.).

Now, let a similar vessel of gas-free water be placed in a large air-tight box filled with air at atmospheric pressure, and let the oxygen be all absorbed before the water is exposed to the atmosphere of the box. The latter now consists practically only of the nitrogen of the air, and its pressure will be only about four-fifths that of the external atmosphere. Nevertheless, the quantity of nitrogen absorbed by the water will be exactly the same as was absorbed from the air. If the box was completely exhausted, and then a quantity of oxygen, equal to that in it at first, introduced before the water was exposed to it, the pressure would be found to be only about one-fifth that of the external atmosphere; but the quantity of oxygen taken up by the water would be exactly equal to that taken up in the first experiment.

Two well-known physical laws are illustrated by our supposed experiments: (1) *In a mixture of gases which do not act chemically on each other the pressure exerted by each gas (called the partial pressure of the gas) is the same as it would exert if the others were absent.* (2) *The quantity (mass) of a gas absorbed by a liquid which does not act chemically upon it is proportional to the partial pressure of the gas.* It also depends upon the nature of the gas and of the liquid, and on the temperature, increase of temperature in general diminishing the quantity of gas absorbed. It is to be noted that when the volume of the absorbed gas is measured at a pressure equal to the partial pressure under which it was absorbed, the same *volume* of gas is taken up at every pressure.

Suppose, now, that a vessel of water, saturated with oxygen and nitrogen for the partial pressures under which these gases exist in the air, is placed in a box filled with pure nitrogen at full atmospheric pressure. As we have seen, there is a constant interchange going on between a liquid which contains gas in solution and the atmosphere to which it is exposed. Oxygen and nitrogen molecules will therefore continue to leave the water; but if the box is large, few oxygen molecules will find their way back to the water, and ultimately little oxygen will remain in it. In other words, the quantity of oxygen absorbed by the water will become again proportional to the partial pressure of oxygen, which is now not much above zero. On the other hand, molecules of nitrogen will at first enter the water in larger number than they escape from it, for the pressure of the nitrogen is now that of the external atmosphere, of which its partial pressure was formerly only four-fifths. In unit volume of the gas above the water there will be 5 molecules of nitrogen for every 4 molecules in the same volume of atmospheric air. Therefore, on the average 5 nitrogen molecules will in a given time get entangled by liquid molecules for every 4 which came within their sphere of attraction before. On the whole, then, the water will lose oxygen and gain nitrogen, while the atmosphere of the air-tight box will gain oxygen and lose nitrogen.

If, now, the partial pressures of oxygen and nitrogen under which the water had been originally saturated were unknown, it is evident that by exposing it to an atmosphere of known composition, and afterwards determining the changes produced in the composition of that atmosphere by loss to, or gain from, the gases of the water, we could find out something about the original partial pressures. If, for example, the quantity of oxygen in the atmosphere of the chamber was increased, we could conclude that the partial pressure of oxygen under which the water had been saturated was greater than that in the chamber at the beginning of the experiment. And if we found that with a certain partial pressure of oxygen in the atmosphere of the chamber there was neither gain nor loss of this gas, we might be sure that the partial pressure (the temperature being supposed not to vary) was the same when the water was saturated. We shall see



P, frictionless piston ; L, liquid in cylinder; G, gas beginning to escape from liquid. P is exactly counterpoised. In addition to the manner described in the text, the experiment may be supposed to be performed thus. Let the weight, W, be determined which, when the receiver is completely exhausted, suffices just to keep the piston in contact with the liquid. The pressure of the gas is then just counterbalanced by W; and if S is the area of the cross-section of the piston the pressure of the gas per unit of area is $\frac{W}{S}$. Or if the piston is hollow, and mercury is poured into it so as just to keep it in contact with the liquid, the height of the column of mercury required is also equal to the pressure or tension of the gas.

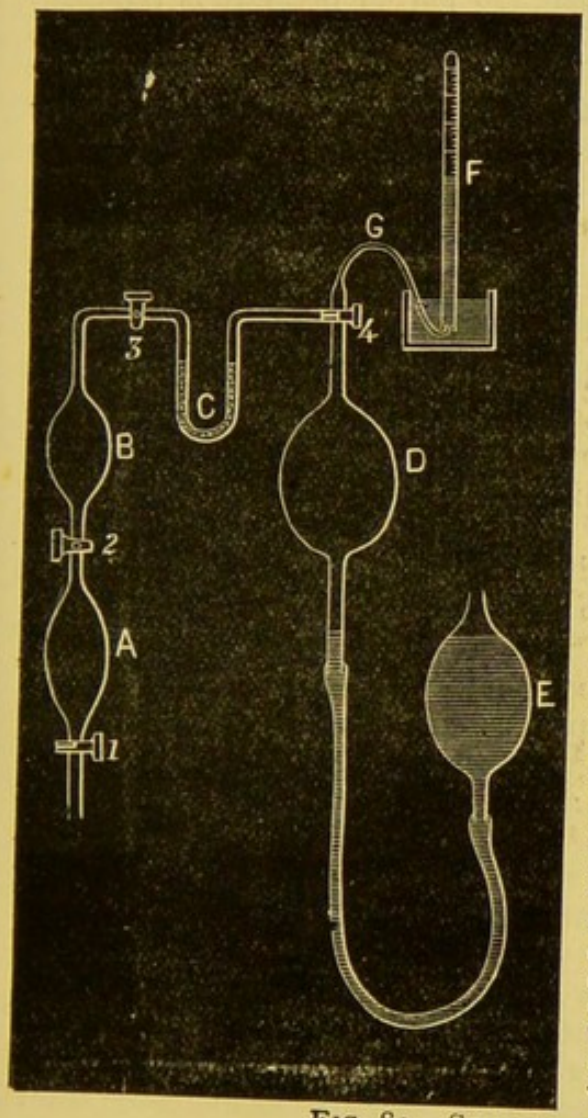
FIG. 82.—IMAGINARY EXPERIMENT TO ILLUSTRATE 'TENSION' OF A GAS IN A LIQUID.

later on how this principle has been applied to determine the partial pressure of oxygen or carbon dioxide which just suffices to prevent blood, or any other of the liquids of the body, from losing or gaining these gases. This pressure is evidently equal to that exerted by the gases of the liquid at its surface, which is sometimes called their 'tension'; for if it were greater, gas would, upon the whole, pass into the blood ; and if it were less, gas would escape from the blood. Thus, *the tension of a gas in solution in a liquid is equal to the partial pressure of that gas in an atmosphere to which the liquid is exposed, which is just sufficient to prevent gain or loss of the gas by the liquid* (p. 240).

The following imaginary experiment may further illustrate the meaning of the term 'tension' of a gas in a liquid in this connection:

Suppose a cylinder filled with a liquid containing a gas in solution, and closed above by a piston moving air-tight and without friction, in contact with the surface of the liquid (Fig. 82). Let the weight

of the piston be balanced by a counterpoise. The pressure at the surface of the liquid is evidently that of the atmosphere. Now, let the whole be put into the receiver of an air-pump, and the air gradually exhausted. Let exhaustion proceed until gas begins to escape from the liquid and lies in a thin layer between its surface and the piston, the quantity of gas which has become free being very small in proportion to that still in solution. At this point the piston is



A, the blood bulb; B, the froth chamber; C, the drying tube; D, fixed mercury tube; E, movable mercury bulb connected by a flexible tube with D; F, eudiometer; G, a narrow delivery tube; 1, 2, 3, 4, taps, 4 being a three-way tap. A is filled with blood by connecting the tap 1 by means of a tube with a blood-vessel. Taps 1 and 2 are then closed. The rest of the apparatus from B to D is now exhausted by raising E, with tap 4 turned so as to place E only in communication with G, till the mercury fills D. Tap 4 is now turned so as to connect C with D, and cut off G from D, and E is lowered. The mercury passes out of D, and air passes into it from B and C. Tap 4 is again turned so as to cut off C from D and connect G and D. E is raised, and the mercury passes into D and forces the air out through G, the end of which has not hitherto been placed under F. This alternate raising and lowering of E is continued till a manometer connected between C and 4 indicates that the pressure has been sufficiently reduced. The tap 2 is now opened; the gases of the blood bubble up into the froth chamber, pass through the drying-tube C, which is filled with pumice-stone and sulphuric acid, and enter D. The end of G is placed under the eudiometer F, and by raising E, with tap 4 turned so as to cut off C, the gases are forced out through G and collected in F. The movements required for exhaustion can be repeated several times till no more gas comes off. The escape of gas from the blood is facilitated by immersing the bulb A in water at 40°-50° C.

FIG. 83.—SCHEME OF GAS-PUMP.

acted upon by two forces which balance each other, the pressure of the air in the receiver acting downwards, and the pressure of the gas escaping from the liquid acting upwards. If the pressure in the receiver is now slightly increased, the gas is again absorbed. The pressure at which this just happens, and against which the piston is still supported by the impacts of gaseous molecules flying out of the liquid, while no pressure is as yet exerted directly between the liquid and the piston, is obviously equal to the pressure or tension of the gas in the liquid.

From the above principles it follows that a gas held in solution

may be extracted by exposure to an atmosphere in which the partial pressure of the gas is made as small as possible. Thus, oxygen can be obtained from liquids in which it is simply dissolved by putting them in an atmosphere of hydrogen or nitrogen, in which the partial pressure of oxygen is zero, or in the vacuum of an air-pump, in which it is extremely small. Heat also aids the expulsion of dissolved gases. Some gases held in weak chemical union, like the loosely-combined oxygen of oxyhæmoglobin, can be obtained by dissociation of their compounds when the partial pressure is reduced. More stable combinations may require to be broken up by chemical agents—carbonates, for instance, by acids.

Extraction of the Blood-gases.—This is best accomplished by exposing blood to a nearly perfect vacuum. The gas-pumps which have been most largely used in blood analysis are constructed on the principle of the Torricellian vacuum. A diagram of a simple form of Pflüger's gas-pump is given in Fig. 83. The gases obtained are ultimately dried and collected in a eudiometer, which is a graduated glass tube with its mouth dipping into mercury. The carbon dioxide is estimated by introducing a little caustic potash to absorb it. The diminution in the volume of the gas contained in the eudiometer gives the volume of the carbon dioxide. The oxygen may be estimated by putting into the eudiometer more than enough hydrogen to unite with all the oxygen so as to form water, and then, after reading off the volume, exploding the mixture by means of an electric spark passed through two platinum wires fused into the glass. One-third of the diminution of volume represents the quantity of oxygen present. It can also be estimated by absorption with a solution of pyrogallic acid and potassium hydrate. The remainder of the original mixture of blood-gases, after deduction of the carbon dioxide and oxygen, is put down as nitrogen (with, no doubt, a small proportion of argon). For the sake of easy comparison, the observed volume of gas is always stated in terms of its equivalent at a standard pressure and temperature (760 mm., or sometimes on the Continent 1 metre of mercury, and 0° C.).

It is also possible in various ways to estimate the amount of oxygen in blood without the use of the pump. Thus, since a definite volume of oxygen (1·338 c.c. at 0° C. and 760 mm. pressure) combines with a gramme of hæmoglobin, we can calculate the total volume of oxygen present if we know how much of the blood-pigment is in the form of oxyhæmoglobin; and this can be determined by means of the spectrophotometer (Hüfner). Or the blood may be shaken with carbon monoxide (carbonic oxide), which expels the oxygen from its combination with the hæmoglobin. The oxygen can then be estimated in the gas collected (Bernard).

In dog's blood, which has been up to this time chiefly investigated, there are considerable variations in the quantity of oxygen and carbon dioxide which can be extracted; and this is particularly true of the venous blood, as might

naturally be expected, since even to the eye it varies greatly according to the vein it is obtained from, the rapidity of the circulation, and the activity of the tissues which it has just left. On the average,

	Volumes of		
	O_2	CO_2	N_2
100 volumes of arterial blood yield - - -	20	40	1·2
„ mixed venous blood (from right heart) yield - - - - - - - -	10·12	45-50	1·2

(reduced to 0° C. and 760 mm. of mercury).

Average venous blood contains 7 or 8 per cent. by volume less oxygen, and 7 or 8 per cent. more carbon dioxide, than arterial blood. Thus, in the lungs the blood gains about twice as many volumes of oxygen per cent. as the air loses, and the air gains about half as many volumes of carbon dioxide per cent. as the blood loses. And it is easy to see that this must be so, for the volume of the air inspired in a given time is about twice as great as that of the blood which passes through the pulmonary circulation (pp. 197, 207, 224). Even arterial blood is not quite saturated with oxygen; it can generally still take up one-tenth to one-fifteenth of the quantity contained in it. Nor is venous blood nearly saturated with carbon dioxide; when shaken with the gas it can take up about 150 volumes per cent.

When the gases are not removed from blood immediately after it is drawn, its colour becomes darker, and it yields more carbon dioxide and less oxygen than if it is evacuated at once (Pflüger). From this it is concluded that oxidation goes on in the blood for some time after it is shed. The oxidizable substances appear, however, to be confined to the corpuscles, which suggests that ordinary metabolism simply continues for some time in the formed elements of the shed blood, and that the disappearance of oxygen is not due to the oxidation of substances which have reached the blood from the tissues.

The Distribution of the Gases in the Blood.—The oxygen is nearly all contained in the corpuscles. A little oxygen can be pumped out of serum (·1 to ·2 per cent. by volume), but this follows the Henry-Dalton law of pressures; that is, it

comes off in proportion to the reduction of the partial pressure of the oxygen in the pump, and is simply in solution.

When blood is being pumped out, very little oxygen comes off till the pressure has been reduced to about half an atmosphere. At about a third of an atmosphere, if the blood is nearly at body temperature, the oxygen begins to escape a little more freely; and when the pressure has fallen

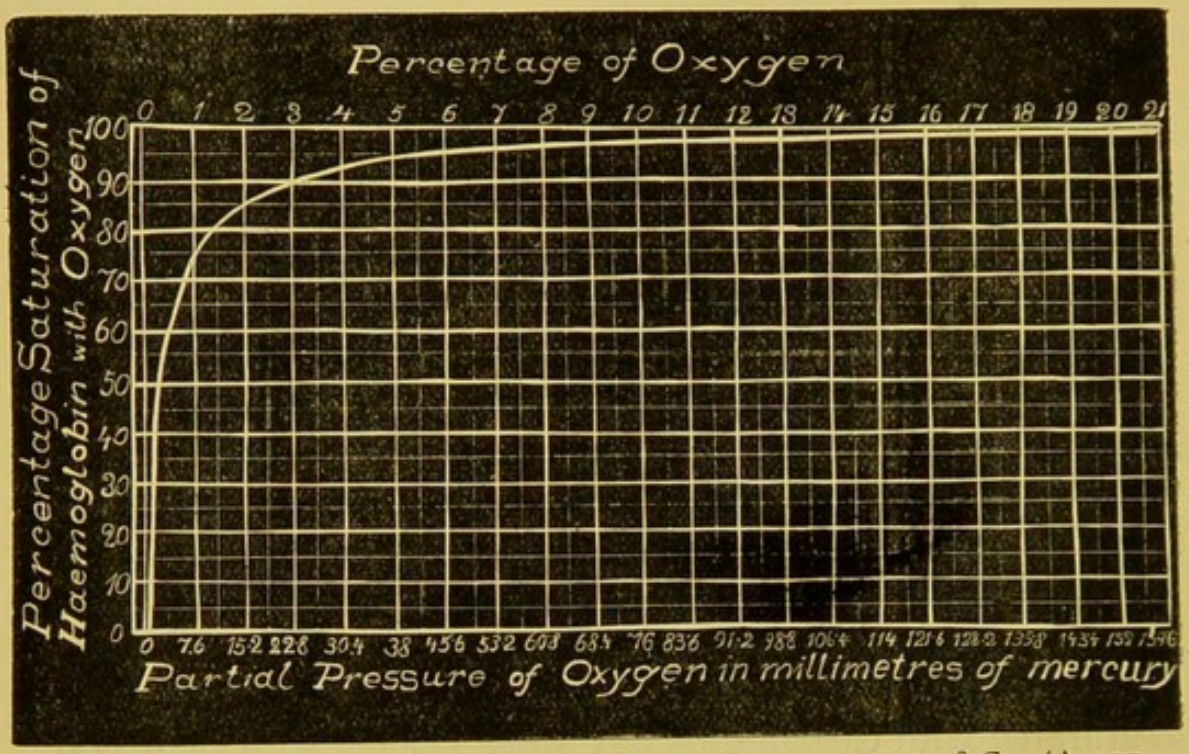


FIG. 84.—CURVE OF DISSOCIATION OF OXYHÆMOGLOBIN AT 35° C. (AFTER HÜFNER'S RESULTS.)

Along the horizontal axis are plotted the partial pressures (numbers below the curve) of oxygen in air, to which a solution of hæmoglobin was exposed. The corresponding percentages of oxygen are given above the curve. Along the vertical axis is plotted the percentage saturation of the hæmoglobin with oxygen. Thus, on exposure to an atmosphere in which oxygen existed to the extent of 1 per cent., corresponding to a partial pressure of 7·6 millimetres of mercury, the hæmoglobin took up about 75 per cent. of the amount of oxygen required to saturate it. When the oxygen was present in the atmosphere to the amount of about 10 per cent., corresponding to a partial pressure of 76 millimetres of mercury, the quantity taken up by the hæmoglobin was about 96 per cent. of that required for saturation.

to about one-sixth of an atmosphere (corresponding to a partial pressure of oxygen of 25-30 mm. of mercury), it is disengaged with a burst. This shows that it is not simply absorbed, but is united by chemical bonds to some constituent of the blood. The same thing is seen when defibrinated blood is saturated at body temperature with oxygen at different pressures. The quantity taken up

lessens but slowly as the pressure is reduced, till at about 25 to 30 mm. of mercury an abrupt diminution takes place. It is found that a solution of pure hæmoglobin crystals behaves towards oxygen just like blood; and there is no doubt that the body in blood with which the oxygen is loosely united is hæmoglobin.

We may suppose that at the ordinary temperature and pressure* some oxygen is continually escaping from the bonds by which it is tied to the hæmoglobin; but, on the whole, an equal number of free molecules of oxygen, coming within the range of the hæmoglobin molecules, are entangled by them, and thus equilibrium is kept up. If now the atmospheric pressure, and therefore the partial pressure of oxygen, is reduced, the tendency of the oxygen molecules to break off from the hæmoglobin will be unchanged, and as many molecules on the whole will escape as before; but even after a considerable reduction of pressure the hæmoglobin, such is its avidity for oxygen, will still be able to seize as many atoms as it loses. The more, however, the partial pressure of the oxygen is diminished—that is to say, the fewer oxygen molecules there are in a given space above the hæmoglobin—the smaller will be the chance of the loss being made up by accidental captures. At a certain pressure the escapes will become conspicuously more numerous than the captures; and the gas-pump will give evidence of this, although it could give us no information as to mere molecular interchange, so long as equilibrium was maintained.

The higher the temperature of the hæmoglobin is, the greater will be the average velocity of the molecules, and the greater the chance of escape of molecules of oxygen. The 'dissociation tension' of oxyhæmoglobin, or the partial pressure of oxygen at which the oxyhæmoglobin begins to lose more oxygen than it gains, is increased by raising the temperature. The curve of dissociation of oxyhæmoglobin at a temperature of 35° C. is shown in Fig. 84.

The Carbon Dioxide of the Blood.—Blood freed from gas absorbs carbon dioxide partly in proportion to the pressure, and in part independently of it. Some of the carbon dioxide must therefore be simply dissolved; some, and this the greater portion, is chemically combined. The serum contains a larger percentage of carbon dioxide than the clot, but this percentage is not great enough to allow us to assume that the whole of the carbon dioxide is confined to the serum. Some of it must belong to the corpuscles.

* The partial pressure of oxygen in air at 760 mm. atmospheric pressure is $\frac{21}{100} \times 760$, or 159·6 mm.

In the serum the combined carbon dioxide exists chiefly as carbonate and bicarbonate of sodium, the relative amount of each depending on the quantity of carbon dioxide and of other acids, such as phosphoric acid, which dispute with it the possession of the bases. That its relations are peculiar, however, is shown by the fact that from defibrinated blood the whole of the carbon dioxide can in time be pumped out without the addition of an acid to displace it from the bases with which it is combined. It is hardly necessary to say that this could not be done with a solution of sodium carbonate. Yet when sodium carbonate is added to blood, even in considerable amount, all the carbon dioxide in it can be obtained by the pump. From serum a great deal, but not the whole, of the carbon dioxide can be likewise pumped out. The residue is set free on the addition of an acid.

The most satisfactory explanation seems to be that in the serum there exist substances which can act as weak acids in gradually driving out the carbon dioxide, when its escape is rendered easier by the vacuum, but which, nevertheless, do not affect litmus paper (since the reaction of serum is alkaline). The quantity of these, however, is so small that a portion of the carbon dioxide remains in the serum. The proteids of the serum, such as serum-globulin, behave in certain respects like weak acids, and may contribute to the driving out of the carbon dioxide.

When defibrinated blood is pumped out, the whole of the carbon dioxide can be removed, apparently because substances of an acid nature pass from the corpuscles into the serum and help to break up the carbonates.

In the red corpuscles a portion of the carbon dioxide may be in combination with alkalies. We know that the corpuscles contain alkalies, for the alkalinity of 'laked' blood (pp. 34, 35), in which the red corpuscles have been broken up, is found to be greater than that of unlaked blood, unless a long time is allowed in the case of the latter for the alkalies of the corpuscles to reach the acid used in titration (Loewy). Some observers believe that a weak compound of carbon dioxide can be formed with hæmoglobin; for

a solution of hæmoglobin absorbs more of this gas than water, and the quantity absorbed is not proportional to the pressure. The hæmoglobin of the corpuscles may therefore hold a portion of the carbon dioxide in combination (Bohr). This cannot, however, be considered as settled.

When blood is saturated with carbon dioxide and then separated into serum and clot, the serum is found to yield more gas than the clot; but if the serum and clot are separately saturated, the latter takes up more carbon dioxide than the former. From this it is argued that a substance combined with carbon dioxide must in blood saturated with the gas pass out of the corpuscles into the serum. This cannot be hæmoglobin, for it remains in the corpuscles, but it may very well be an alkali, combined with the carbon dioxide and thus set free from its connection with the hæmoglobin. And, as a matter of fact, under the circumstances described, it has been found that alkalies do pass from the clot into the serum (Zuntz), and chlorine from the serum into the corpuscles (Lehmann), which at the same time gain water and become larger. The molecular concentration (p. 360) of the serum of defibrinated blood, as measured by the lowering of the freezing-point, increases when it is saturated with carbon dioxide. On the other hand, when blood is saturated with oxygen, alkalies pass out of the serum into the corpuscles, which at the same time lose water and shrink in volume, while the molecular concentration of the serum is diminished. Hamburger has extended these observations to the circulating blood, and has shown that the plasma of venous blood has a higher percentage of alkali, proteid, sugar and fat than the plasma of arterial blood, and that the corpuscles have a greater volume, though not a greater diameter. We may, therefore, suppose that in the pulmonary capillaries, under the influence of oxygen, water passes into the plasma from the corpuscles. In the systemic capillaries the blood becomes loaded with carbon dioxide, and therefore the corpuscles take up water from the plasma, which accordingly has a more concentrated supply of food-substances to offer to the tissues than the plasma of arterial blood itself. Some writers see in this interchange an

automatic arrangement by which oxidation is favoured. Whatever may be thought of this view—and objections to it are not wanting—the current theory, that the corpuscles are simply passive carriers of oxygen, and exercise no further influence on the plasma, breaks down in face of the facts. We must admit that an active and many-sided commerce exists between them and the liquid in which they float.

The nitrogen of the blood is simply absorbed.

The Tension of the Blood-gases.—If the gases of the blood existed in simple solution, their tension or partial pressure could be deduced from the amount dissolved and the co-efficient of absorption. Since they are chemically combined, it is necessary to determine it directly. This has been done by means of an apparatus called the aerotonometer (Pflüger, Strassburg). The blood is made to pass directly from the vessel to two tubes, which it traverses at the same time, the stream being divided between them; it then passes out again. The tubes are warmed by means of a water-jacket to the body-temperature. One of them is filled with a gaseous mixture having a greater, and the other with a mixture having a smaller, partial pressure, say of carbon dioxide, than is expected to be found in the blood. As the latter runs in a thin sheet over the walls of the tubes, it loses carbon dioxide to the one and takes up carbon dioxide from the other. From the alteration in the proportion of the carbon dioxide in the two tubes, it is easy to calculate the partial pressure of that gas in the blood; that is, the partial pressure which it would be necessary to have in the tubes in order that the blood might pass through them without losing or gaining carbon dioxide (p. 232).

The pressure of oxygen in arterial blood was given by Strassburg as about 30 mm. of mercury in the dog, and in venous blood as something like 20 mm. If we were to accept the recent experiments of Bohr, made by means of a special form of aerotonometer constructed and worked much in the same way as Ludwig's stromuhr (p. 110), and inserted into the course of a bloodvessel, it would be necessary to treble or quadruple these numbers.

The pressure of carbon dioxide in arterial blood we may take at 10 to 40 mm., in venous blood at 30 to 50 mm., according to the results of different observers.

Whenever the venous blood has to pass through a region in which the pressure of carbon dioxide is kept lower than in itself, it will begin to lose carbon dioxide by diffusion. If the pressure of oxygen in this region is at the same time

higher than in the venous blood, some of it will be taken up. And to bring about these results no peculiar 'vital' force need be invoked; ordinary physical processes will, under the assumed conditions, be alone required.

Now, we know that in the lungs carbon dioxide is given off from the blood, and oxygen taken up by it. We have, therefore, to inquire what the partial pressures of these gases are in the alveoli, and whether they are so related to the corresponding partial pressures in the blood that a simple process of dissociation and diffusion will be sufficient to explain pulmonary respiration.

The percentage of carbon dioxide in expired air cannot tell us the pressure of that gas in the alveoli, for the air in the upper part of the respiratory tract is necessarily expelled along with the alveolar air. But it gives us a minimum value, below which it is not conceivable that the alveolar partial pressure can lie, for we cannot imagine that any air in the respiratory tract can be richer in carbon dioxide than that of the alveoli. Now, Vierordt found with the deepest possible expiration a little over 5 per cent. of carbon dioxide in the expired air. From this it seems justifiable to conclude that in man the partial pressure of carbon dioxide in the alveoli may be at least one-twentieth of an atmosphere, or 38 mm. of mercury.

In animals, samples of the alveolar air have been drawn off directly (Wolffberg) by means of Pflüger's *pulmonary catheter*. This consists of two tubes, one within the other. The inner tube, which is a fine elastic catheter, projects free from the other for a little distance at its lower end. The outer tube terminates in an indiarubber ball, which can be inflated so as to block the bronchus into which it is passed, and cut off the corresponding portion of the lung from communication with the outer air. A sample of the air below the block can be drawn off through the inner tube. In this way the proportion of carbon dioxide in the alveoli of the dog was found to be only about 3·8 per cent., corresponding to a partial pressure of about 29 mm. of mercury. But this would be undoubtedly too high, owing to the impossibility of interchange with the external atmosphere, and

would represent the partial pressure of the carbon dioxide in the blood rather than in the alveolar air under normal conditions. For gaseous equilibrium is soon established between blood and air separated only by a thin membrane like the alveolar wall.

In Bohr's experiments, in some of which the animals were made to breathe air containing carbon dioxide in various proportions, the tension of that gas in the air of the lungs varied from 5·8 to 34·6 mm. of mercury, while in arterial blood, taken at the same time, it usually ranged from 10 to 38 mm., and was often less than in the alveolar air.

If we accept these results, we seem shut up to the conclusion that carbon dioxide does not pass through the walls of the alveoli solely by diffusion. And although Bohr's experiments have been severely criticised, it does not seem improbable in itself that the physical process of diffusion is aided by some other process, which may provisionally be termed secretion. It is possible, too, that when the conditions are especially unfavourable to diffusion—when, for instance, the partial pressure of carbon dioxide is artificially increased in the alveoli—the cells which line them are stimulated to increased activity.

As to the oxygen, we are in the same position. Its partial pressure does not appear to be always higher, even under normal conditions, in the alveoli than in the arterial blood as it leaves the lungs. Indeed, Bohr found that, in the majority of his observations on dogs, the oxygen tension was distinctly greater in the blood than in the pulmonary air. And Haldane and Smith, using a new method, have obtained a value for the oxygen tension in human blood (26·2 per cent., equal to 200 mm. of mercury) that even exceeds the partial pressure of oxygen in the external air, and is about twice as great as that of the air of the alveoli. This remarkable result cannot be reconciled with any purely physical explanation of the absorption of oxygen. The relative excess of the oxygen-tension in arterial blood over the alveolar oxygen-tension increases as the proportion of oxygen in the alveolar air is diminished.

Additional evidence in favour of the view that there is, besides diffusion, an element of selective secretion in the

interchange of gases through the pulmonary membrane is afforded by a study of the gases of the swim-bladder in fishes. These consist of oxygen, nitrogen, and usually a small quantity of carbon dioxide, but in very different proportions from those in which they exist in the air or the water. Thus, Biot found as much as 87 per cent. of oxygen in the bladder of fishes taken at a considerable depth, but a smaller amount in those captured near the surface. Moreau observed that when the gas is withdrawn by puncturing the bladder with a trocar, the organ rapidly refills, and the percentage of oxygen increases. Further, this process of gaseous secretion is under the influence of nerves, for gas ceases to accumulate in the organ when the branches of the vagi that supply it are cut (Bohr).

We have now completed the description of the phenomena of external respiration, with the discussion of its central fact, the exchange of gases between the blood and the air at the surface of the lungs. It remains to trace the fate of the absorbed oxygen, and to determine how and where the carbon dioxide arises.

Internal Respiration—Seats of Oxidation.—The suggestion which lies nearest at hand, and which, as a matter of fact, was first put forward, is that the oxygen does not leave the blood at all, but that it meets with oxidizable substances in it, and unites with their carbon to form carbon dioxide. While there is a certain amount of truth in this view, oxygen, as already mentioned, being to some extent taken up by freshly-shed blood, and also by blood under other conditions, to oxidize bodies, other than hæmoglobin, either naturally contained in it or artificially added, there is no doubt that the cells of the body are the busiest seats of oxidation. This is shown by the presence of carbon dioxide in large amount in lymph and other liquids which are, or have been, in intimate relation with tissue elements; by its presence, also in considerable amount, in the tissues themselves—in muscle, for instance; by its continued and scarcely lessened production not only in a frog whose blood has been replaced by normal saline solution, and which continues to live in an atmosphere of pure oxygen, but in

excised muscles; and by the remarkable connection between the amount of this production and the functional state of those tissues. In insects the finest twigs of the tracheæ, through which oxygen passes to the tissues, actually end in the cells; and in luminous insects, like the glowworm, it has been noticed that the phosphorescence, which is certainly dependent on oxidation, begins and is most brilliant in those parts of the cells of the light-producing organ that surround the ends of the tracheæ.

Lymph, bile, urine, and the serous fluids contain very little oxygen, but so much carbon dioxide that the pressure of that gas in all of them is greater than in arterial blood, while in lymph alone (taken from the large thoracic duct) has it been found less than that of venous blood. And it is extremely probable that lymph gathered nearer the primary seats of its production (the spaces of areolar tissue) would show a higher proportion of carbon dioxide.

Strassburg found that with a pressure of carbon dioxide in the arterial blood of 21 mm. of mercury, the pressure in bile was 50 mm., in peritoneal fluid 58 mm., in urine 68 mm., in the surface of the empty intestine 58 mm. Saliva, pancreatic juice, and milk, also contain much carbon dioxide, and only a little, if any, oxygen.

From muscle (to facilitate pumping, the muscle is minced, and often warmed) no free oxygen at all can be pumped out, but as much as 15 volumes per 100 of carbon dioxide, some of which is free, that is, is given up to the vacuum alone, while some of it is fixed, and only comes off after the addition of an acid, such as phosphoric acid. If the muscle be left long in the pump, putrefaction begins to appear, and this causes a discharge of carbon dioxide, which may last indefinitely.

Muscle may be safely taken as a type of the other tissues in regard to the problems of internal respiration. It is instructive, therefore, to observe that the great scarcity of oxygen in the parenchymatous liquids which bathe the tissues, here in the tissues themselves deepens into actual famine. The inference is plain. The active tissues are greedy of oxygen; as soon as it enters the muscle it is seized and

'fixed' in some way or other. The traces of oxygen in the lymph cannot therefore be journeying away from the tissue elements; they must have come from another source, and this can only be the blood. Could we gather lymph for analysis directly from the thin sheets that lie between the blood capillaries and the tissues, we might find more oxygen present as well as more carbon dioxide. But if we did find more oxygen, it would still be oxygen in transit from the capillaries towards places where the partial pressure of oxygen is less. In the lymph, the pressure is kept low by the avidity of the tissues with which it is in contact, and possibly by the existence in it of oxidizable substances which have come from the tissues. In the tissues there is no partial pressure at all, because the oxygen that reaches them is at once stowed away in some compound, in which it has lost the properties of free oxygen.

Assuming, then, that at least a great part of the oxidation and consequent production of carbon dioxide goes on in the tissues, let us follow the steps of the process, as far as we can, in the light of our knowledge of the respiration of muscle.

Respiration of Muscle.—Three methods have been used to determine the respiratory changes going on in resting muscle, or to compare them with those in the excited state:

(1) The excised muscles of cold-blooded animals are exposed for a considerable time to an atmosphere of known composition in a small chamber; and the changes in this atmosphere are then determined. Or, what is better, especially for short periods of observation, a stream of air or nitrogen is drawn through the chamber and the carbon dioxide absorbed by baryta water, which is then titrated with standard acid.

(2) Samples of the blood coming to and leaving a muscle of a warm-blooded animal may be taken in its natural position, and the gases analyzed and compared.

(3) Artificial circulation may be kept up through a muscle or group of muscles; for example, through one or both hind-limbs of a dog. The blood may be oxygenated in a special chamber from a graduated cylinder containing oxygen, and the carbon dioxide collected in baryta or caustic potash valves. The oxygen consumption can be read off from the cylinder, and the production of carbon dioxide estimated by titrating the baryta water or potash (Fig. 85).

By the first of these methods a very remarkable fact, among others, has been brought to light. It has been

found that a frog's muscle is capable of going on producing carbon dioxide for a long time, in the entire absence of

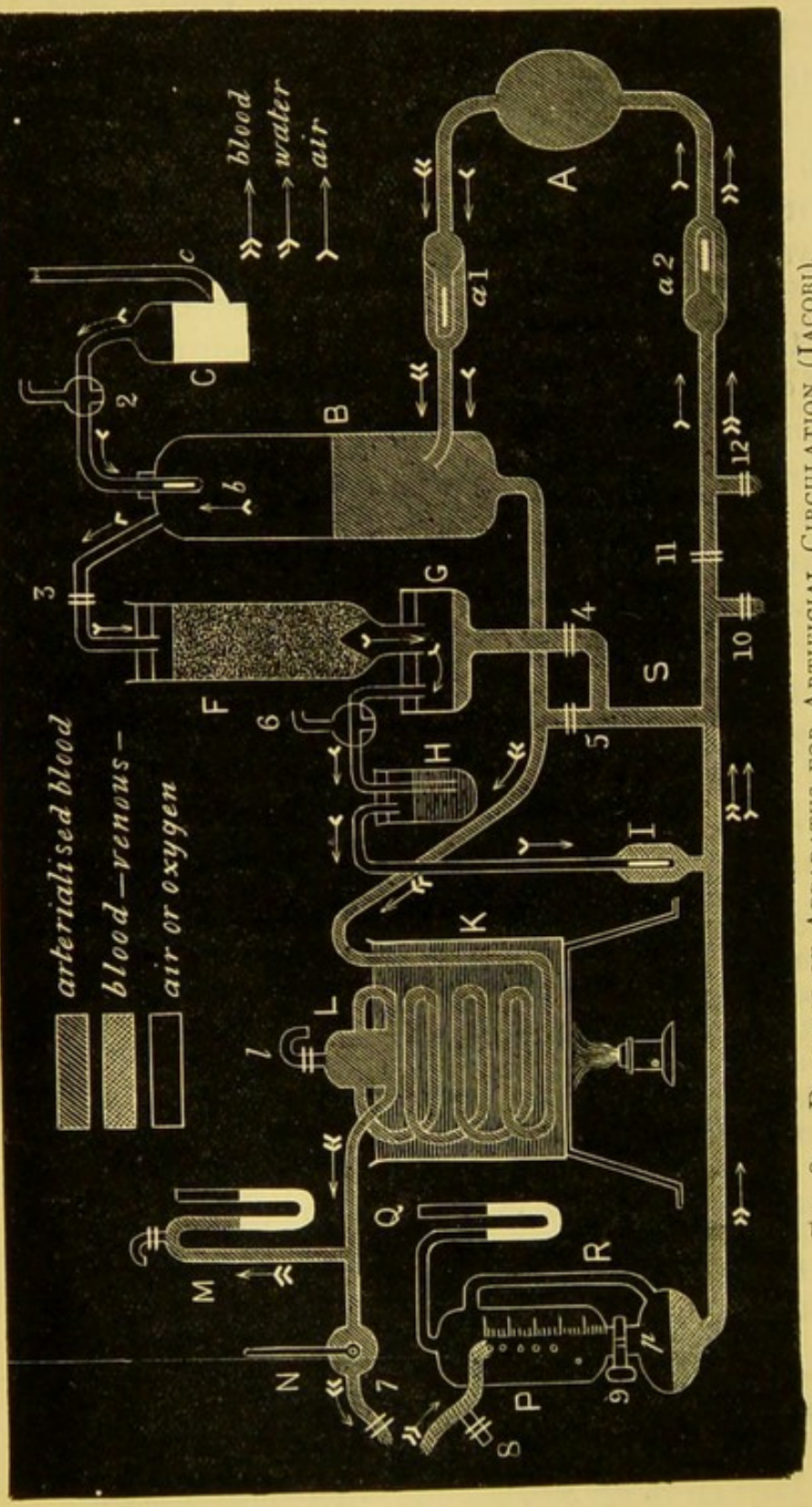


FIG. 85.—DIAGRAM OF APPARATUS FOR ARTIFICIAL CIRCULATION (JACOBI).

A, artificial heart (indiarubber injection syringe). B, artificial lungs (a reservoir into which the blood is driven, and where it meets with oxygen passing along the tube *c* through the mercury valve C from a graduated reservoir not shown in figure. H, a caustic potash valve for absorbing carbon dioxide. K, a glass spiral immersed in a water-bath, L, warmed by a Bunsen burner. The blood is heated in passing through the spiral. N, a thermometer which measures the temperature of the blood just before it passes into the organ. P, a measuring cylinder in which the blood coming from the organ can be collected by turning the cock 9, and the rate of flow thus determined. M and Q, mercury manometers. R, a tube which serves to connect P and *p* when the cock 9 is closed, and so to prevent a rise of pressure in Q. F, a froth chamber in which any bubbles passing out of B are retained. *a*1, *a*2, *b*, I, membrane valves. 2, 3, 4, 5, 6, 7, 11, clamps by which the passing of blood or gas may be regulated. 10, 12, clamped tubes by which blood can be respectively introduced into the apparatus and withdrawn from it. S, short-circuiting tube by which some of the blood passes back from B to A without passing through the organ. By means of the clamp 5 the quantity of blood passing through S, and therefore the quantity passing through the organ, can be regulated. 4 is only opened when blood has collected in G, which it is desirable to return to the circulation.

oxygen, when the chamber, for instance, is filled with nitrogen or other indifferent gas. Not only so, but it can

be made to contract many times in this oxygen-free atmosphere, and to produce a correspondingly large quantity of carbon dioxide. In mammals the muscles can also be made to contract repeatedly when the dissociable oxygen has, as far as possible, been got rid of from the blood by asphyxiating the animal, although they lose their contractility much more rapidly than the muscles of the frog. This leads us to the very important conclusion that the carbon dioxide does not arise, so to speak, on the spot, from the immediate union of carbon and oxygen. Oxygen is essential to muscular life and action. But a stock of it is apparently taken up by the muscle, and stored in some compound or compounds which are broken down during muscular contraction, and more slowly during rest, carbon dioxide in both cases being one of the end products. It is possible that there is an ascending series of bodies through which oxygen passes up, and a descending series through which it passes down, before the final stage is reached.

When muscle goes into rigor (p. 565)—and this is most strikingly seen when the rigor is caused by raising the temperature of frog's muscle to about 40° or 41° C.—there is a sudden increase in the quantity of carbon dioxide given off. Moreover, in an isolated muscle the total quantity of carbon dioxide obtainable during rigor is markedly less if the muscle has been previously tetanized. From this it has been argued that the hypothetical substance (inogen), the decomposition of which yields carbon dioxide in contraction, is also the substance which decomposes so rapidly in rigor; that a given amount of it exists in the muscle at the time it is removed from the influence of the blood; and that this can all explode either in contraction or in rigor, or partly in the one and partly in the other.*

* Fletcher states that during tetanus there is no increase in the amount of carbon dioxide given off by an excised muscle unless the stimulation is so severe and prolonged as to hasten the onset of rigor. He therefore supposes that in the contraction the decomposition does not proceed quite to the formation of carbon dioxide, which in the intact body is afterwards liberated from some more complex carbon-containing waste-product.

Many of the older experiments made by method (2) are too inexact to yield more than qualitative results, and the same is true of some of the researches with the more primitive and imperfect methods of artificial circulation. The mere difference of colour between the venous and arterial blood of a muscle, or other active organ, is sufficient to show that oxygen is taken up and carbon dioxide given out by it to the blood. This is the case in muscles at rest, and even in muscles with artificial circulation after they have become inexcitable.

In active muscles more oxygen is used up and more carbon dioxide produced than in the resting state. Chauveau and Kaufmann, in their experiments on one of the muscles used by the horse in feeding, found that the consumption of oxygen and the production of carbon dioxide might be three times as great in activity as in rest.

In the submaxillary salivary gland there was also an increase of carbon dioxide during activity, but not proportionally so great as in muscle. In the active brain it is not easy to demonstrate any increase at all (Hill).

For excised mammalian muscles (hind-limbs of dog), as has been said, the respiratory quotient increases when the temperature is reduced. As the temperature is raised, the opposite effect is observed. Stimulation of the muscle causes a rise in both oxygen consumption and carbon dioxide production, but proportionally more in the former, and the respiratory quotient diminishes. When the excised muscle begins to deteriorate in the course of some hours, the consumption of oxygen falls off more quickly than the production of carbon dioxide.

All this goes to show that the two processes are to a great extent independent of each other. At the higher temperatures, during muscular contraction, and when the vitality of the muscle is still but little impaired, the conditions are relatively favourable to the chemical changes in which oxygen is combined. Low temperature, rest, and diminished vitality, are relatively favourable to the splitting up of substances that yield carbon dioxide. But it must be remem-

bered that in the intact organism the conditions are different (p. 225).

The Influence of Respiration on the Blood-pressure.—We have already stated, in treating of arterial blood-pressure (p. 103), that a normal tracing shows a series of waves corresponding with the respiratory movements.

When the respiratory movements are recorded simultaneously with, and immediately below the pressure curve, it is seen that although the mean blood-pressure is falling for a short time at the beginning of inspiration, it soon reaches its minimum, then begins to rise, and continues rising during the rest of this period. At the commencement of expiration it is still mounting, but soon reaches its maximum, begins to fall, and continues falling through the remainder of the expiratory phase.

The explanations given of this phenomenon are many, but they may all be grouped into two divisions, in which *nervous* and *mechanical* influences are respectively invoked as the chief cause.

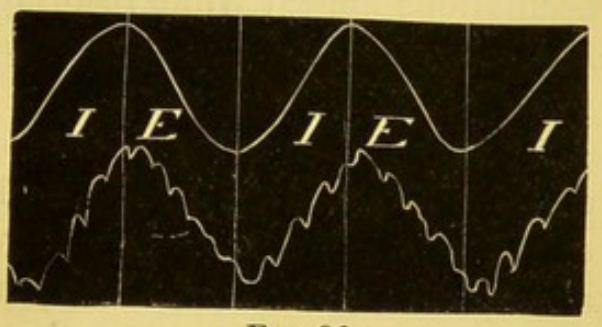


FIG. 86.

The upper tracing shows the respiratory movements in a rabbit; the lower tracing is the blood-pressure curve; I, inspiration; E, expiration, including the pause.

Theory of Nervous Influences.—Everybody admits that in certain animals (the dog, for instance), and very often, if not constantly, in man, the rate of the heart is greater during inspiration, especially towards its end, than in expiration. This is due to nervous influence, to a rhythmical rise and fall in the activity of the cardio-inhibitory centre, synchronous with the respiratory movements, for the difference disappears after division of both vagi. Now, it might be said that the rise of blood-pressure during the latter part of inspiration is simply caused by the increased rate of the heart, which, as we know, can raise the blood-pressure. Nevertheless, this is not the explanation, for the respiratory oscillations persist after section of the vagi, and they are seen in animals like the rabbit, in which little or no variation in the rate of the heart is connected with the phases of respiration.

Quite a number of observers have supposed that rhythmical discharges from the vaso-motor centre, either automatic or due to stimulation of the centre by the venous blood, and causing a periodic increase and diminution in the peripheral resistance, are responsible for the respiratory oscillations. Such rhythmical variations in the blood-pressure (Traube-Hering curves) may, under certain conditions, appear in the absence of respiratory movements, *e.g.*, when in a curarized animal the artificial respiration is stopped. But this is hardly an argument in favour of the central origin of the normal respiratory waves, since the Traube-Hering curves have a much longer period. This is well seen when, as sometimes happens, Traube-Hering oscillations appear while respiration is still going on. Their long sweeping curves then show the ordinary respiratory waves superposed on them.

Mechanical Theory.—A more satisfactory explanation is afforded by a consideration of the mechanical changes produced in the thorax by the respiratory movements. Of these two are of special importance: (1) the changes of intra-thoracic pressure, (2) the changes of vascular resistance in the lungs.

The intra-thoracic pressure, which, as we have seen, is always less than that of the atmosphere, unless during a forced expiration when the free escape of air from the lungs is obstructed, diminishes in inspiration and increases in expiration. The great veins outside the chest, the jugular veins in the neck, for example, are under the atmospheric pressure, which is readily transmitted through their thin walls, while the heart and thoracic veins are under a smaller pressure. The venous blood both in inspiration and expiration will, therefore, tend to be drawn into the right auricle. In inspiration the venous flow will be increased, since the pressure in the thorax is diminished; and upon the whole more venous blood will pass into the right heart during inspiration than during expiration. But all the blood which reaches the right heart during an inspiration is at once sent into the lungs, although not even the first of it can have passed through to the left side of the heart at the

end of the inspiration, since the pulmonary circulation-time (four to five seconds in a small dog, two to three seconds in a rabbit) is longer than the time of a complete inspiration at any ordinary rate. The increase in the quantity of blood pumped into the pulmonary artery will, if not counteracted by other circumstances, tend to raise the blood-pressure in the artery and its branches, and therefore at once to accelerate the outflow through the pulmonary vein. This will be greatly aided if at the same time the vascular resistance in the lungs is reduced, as there seems good reason for believing is the case.

The increased blood-flow into the left ventricle will of course correspond to better filling of the systemic arteries; that is, to a rise of arterial blood-pressure.

In expiration the contrary will happen. The return of blood to the thorax will be checked. This is well shown by the swelling of the veins at the root of the neck in expiration, their shrinking in inspiration, the so-called *pulsus venosus*. Less blood being drawn into the right heart, less will be pumped into the pulmonary artery, in which the pressure will, of course, fall. The outflow into the left auricle will thus be diminished—all the more as in the expiratory phase the vascular resistance in the lungs is increased—and the systemic arterial pressure will be lowered. Now, this is just what is seen on the blood-pressure curve, except that in both cases the change is somewhat belated, and does not coincide exactly with the commencement of the inspiration or the expiration. But this delay may be explained on several grounds. First, we cannot expect the curve of pressure to alter its course quite suddenly, at the very moment when the respiration changes its phase; for the change in the blood-flow through the lungs must require time to establish itself, in the face of the opposite tendency to which it succeeds. The same is true of the systemic arteries, in which at the end of expiration the movements of the blood associated with the falling pressure are going on. It is impossible that these movements can be checked at once; inertia must carry them on into inspiration.

The negative pressure of the thorax acts also on the

aorta, although, on account of the greater thickness of its walls, to a much smaller extent than on the thoracic veins. The diminution of pressure in inspiration tends to expand the thoracic aorta, and to draw blood back out of the systemic arteries, while expiration has the opposite effect. And although the hindrance caused in this way to the flow of blood into the arteries during inspiration, and the acceleration of the flow during expiration, cannot be great, the tendency will be to diminish the pressure in the one phase and increase it in the other. As soon as the changes of pressure produced by alterations in the flow of venous blood into the chest and through the lungs are thoroughly established, the slight arterial effect will be overborne; but before this happens, that is, at the beginning of inspiration and expiration, it will be in evidence, and will help to delay the main change.

Another factor in this delay may be found in the changes of vascular resistance and capacity which take place in the lungs when they pass from the expanded to the collapsed condition.

According to the most careful of recent observations, the expansion of the lungs in natural respiration causes a widening of the pulmonary capillaries, with a consequent increase of their capacity and diminution of their resistance (De Jager). This is supported by experiments on the rabbit, in which the vessels at the base of the heart were ligatured either at the height of inspiration or the end of expiration, so as to obtain the whole of the blood in the lungs. It was found that the lungs invariably contained more blood in inspiration than in expiration (Heger and Spehl).

During inspiration, as we have seen, the right ventricle is sending an increased supply of blood into the pulmonary artery; but before any increase in the outflow through the pulmonary veins can take place, the vessels of the lung must be filled to their new capacity. The first effect, then, of the lessened vascular resistance of the lungs in inspiration is a temporary falling off in the outflow through the aorta, and therefore a temporary fall of arterial pressure. As soon as

a more copious stream begins to flow through the lungs, this is succeeded by a rise.

In like manner the first effect of expiration, which increases the resistance and diminishes the capacity of the pulmonary vessels, is to force out of the lungs into the left auricle the blood for which there is no room. This causes a temporary rise of arterial blood-pressure, succeeded by a fall as soon as the lessened blood-flow through the lungs is established.

In artificial respiration oscillations of blood-pressure, synchronous with the movements of the lungs, are also seen, even when the thorax is opened. In the latter case

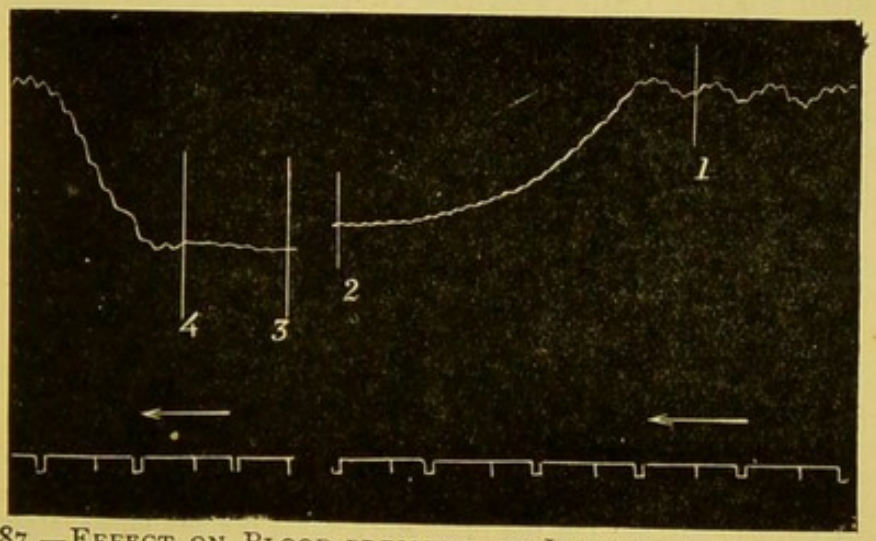


FIG. 87.—EFFECT ON BLOOD-PRESSURE OF INFLATION OF THE LUNGS (RABBIT).

Artificial respiration stopped in inflation at 1. Interval between 2 and 3 (not reproduced) 51 seconds, during which the curve was almost a straight line. Time-tracing shows seconds.

there are, of course, no variations of intra-thoracic pressure, and the oscillations must be connected with the changes in the pulmonary circulation. The respiratory waves differ in certain respects from those in natural breathing, as might be expected from the very different mechanical conditions. During inspiration (inflation) there is first a small rise and then a large fall of pressure. In expiration (collapse) there is first a slight fall and then a great rise.

The meaning of this is clearly seen when artificial respiration is stopped at the height of inflation (Fig. 87). The arterial blood-pressure then falls rapidly, and continues low until the stock of oxygen is exhausted and the rise of

asphyxia begins. When the respiration is stopped in collapse, instead of a fall a steady rise of pressure occurs (as in Fig. 56, p. 163). This ultimately merges in the elevation due to asphyxia, which shows itself sooner than in inflation, since the lungs contain less air. The difference in the course of the blood-pressure curve in the two cases immediately after stoppage of respiration cannot, however, depend on this latter circumstance. It is undoubtedly due to the fact that in artificial inflation the vascular capacity of the lungs is less and the resistance greater than in collapse. When the tracheal cannula is closed in natural respiration, no initial fall of pressure takes place (Fig. 88).

To sum up the causes of the respiratory oscillations in the

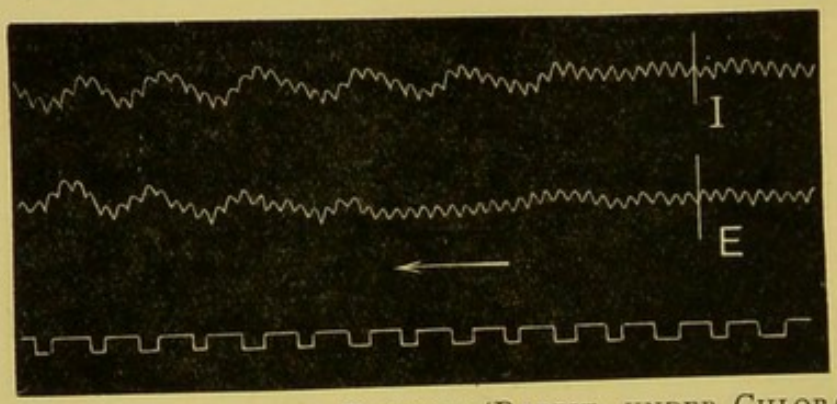


FIG. 88.—BLOOD-PRESSURE TRACING (RABBIT, UNDER CHLORAL).

Natural respiration stopped at I in inspiration, at E in expiration. The mean blood-pressure is scarcely altered; but the respiratory waves become much larger owing to the abortive efforts at breathing. Time-tracing shows seconds.

arterial blood-pressure: *The changes of intra-thoracic pressure and of the vascular resistance in the lungs seem the most important factors, but nervous influences may also play a subordinate part.*

The respiratory oscillations in the veins, as might be expected, run precisely in the opposite direction to those in the arteries, and so do the Traube-Hering curves. The increased flow from the veins to the thorax during inspiration lowers the pressure in the jugular vein, while it increases the pressure in the carotid. The constriction of the small bloodvessels to which the Traube-Hering curves are due increases the blood-pressure in the arteries, because it increases the peripheral resistance to the blood-flow; in the veins it lowers the pressure, because less blood gets through to them. Accordingly, when the Traube-Hering

curve is ascending in the carotid, it is descending in the jugular.

The respiratory variations in the volume of the brain, which are so striking a phenomenon when a trephine hole is made in the skull, have by some been attributed to interference with the venous outflow from the cranial cavity during expiration, and by others to those changes in the arterial pressure whose causes we have just been discussing. The question turns largely upon the time-relations of the movements. The swelling of the brain is usually synchronous with expiration, and the shrinking with inspiration; and this is in favour of the first view. But sometimes the dura mater bulges into the trephine hole in inspiration and sinks down in expiration. This is in favour of the second. The truth appears to be that both factors may be involved.

The effects of breathing condensed and rarefied air are—(1) mechanical, shown chiefly by changes in the circulation, in the blood-pressure, for instance; (2) chemical.

The mechanical effects differ according to whether the whole body, or only the respiratory tract, is exposed to the altered pressure. When the trachea of an animal is connected with a chamber in which the pressure can be raised or lowered, it is found that at first the arterial blood-pressure rises as the pressure of the air of respiration is increased above that of the atmosphere. But a maximum is soon reached; and when respiration begins to be impeded, the pressure falls in the arteries and increases in the veins.

When the pressure of the air in the chamber is diminished a little below that of the atmosphere, there is a slight sinking of the arterial blood-pressure, which rises if the air-pressure is further diminished (Einbrodt).

It is clear that any change of the air-pressure which tends to diminish the intra-thoracic pressure will favour the venous return to the heart, and therefore, if the exit of blood from the thorax is not proportionally impeded, the filling of the arteries. An increase in the intra-alveolar pressure must tend on the whole to increase, and a diminution in it to lessen, the pressure inside the thorax, which always remains equal to the intra-alveolar pressure, *minus*

the elastic tension of the lungs. Breathing compressed air should, therefore, under the conditions described, be upon the whole unfavourable to the venous return to the heart and to the filling of the arteries, and the arterial pressure should fall; while breathing rarefied air should have the opposite effect. But a very great diminution of the intra-thoracic pressure is not necessarily favourable to the circulation, since the auricles are then unable to contract perfectly.

Certain chest diseases have been treated by the use of apparatus by which the patient is made to breathe either compressed or rarefied air; or to inspire air at one pressure and to expire into air at another pressure. And it has, upon the whole, been found, in agreement with theory, that condensed air cannot help the circulation however it is applied, but always hinders it; while rarefied air aids the circulation both in inspiration and in expiration. But the increased work of the inspiratory muscles may counterbalance the advantage.

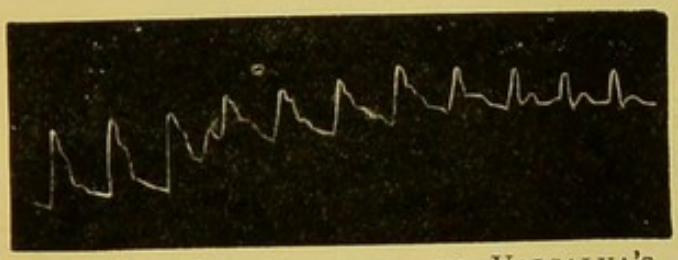


FIG. 89.—PULSE-TRACING IN VALSALVA'S EXPERIMENT (ROLLETT).

Valsalva's experiment, which is performed by closing the mouth and nostrils after a previous inspiration, and then forcibly trying to expire, is an imitation of breathing into compressed air. The intra-thoracic pressure is raised, it may be, to considerably more than that of the atmosphere; the venous return to the heart is impeded, and may be stopped; and the pulse curve is altered in such a way as to indicate first an increase and then a decrease of the arterial blood-pressure (Fig. 89).

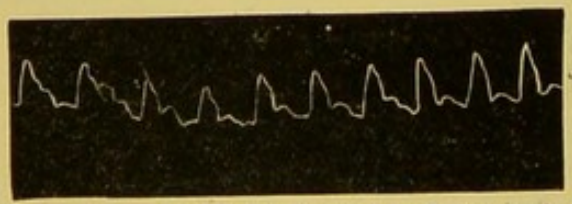


FIG. 90.—PULSE-TRACING IN MÜLLER'S EXPERIMENT (ROLLETT).

Müller's experiment, which should be bracketed with Valsalva's, consists in making, after a previous expiration, a strong inspiratory effort with mouth and nostrils closed. Here the intra-thoracic pressure is greatly diminished, more blood is drawn into the chest, and upon the whole effects opposite to those of Valsalva's experiment are produced (Fig. 90). Neither experiment is quite free from danger. In both the dicrotism of the pulse becomes more marked.

When the whole body is subjected to the changed pressure, as in a balloon or on a mountain, in a diving-bell or a caisson used in building the piers of a bridge, the

conditions are very different. For the blood-pressure, the intra-thoracic pressure, and the intra-alveolar pressure, all fall together when the pressure of the atmosphere is diminished, and all rise together when it is increased. It is possible not only to live, but to do hard manual labour, at very different atmospheric pressures. Loewy found that the quantity of oxygen absorbed by a man breathing air in the pneumatic cabinet remained constant at all pressures between about two atmospheres and half an atmosphere. At 440 mm. of mercury dyspnœa became evident; but if the person was now made to work, the dyspnœa passed away, and did not again manifest itself till the pressure was reduced to 410 mm. There are towns on the high table-lands of the Andes, and in the Himalayas, where the barometric pressure is not more than 16 to 20 inches, yet the inhabitants feel no ill effects. And in the caissons of the Forth Bridge the workmen were engaged in severe toil under a maximum pressure of over three atmospheres, while in the caissons of the St. Louis Bridge in America a maximum pressure of about four atmospheres was reached.

Inside the caissons the men sometimes suffer from pain and noise in the ears, due to excessive pressure on the external surface of the tympanic membrane. If the pressure in the tympanum is raised by a swallowing movement, which opens the Eustachian tube and permits air to enter it, the symptoms generally disappear. The suddenness of the change of pressure has much to do with its effects, and it is found that the men are most liable to dangerous symptoms while passing through the air-lock from the caissons to the external air. It may be concluded from experiments on animals, that some of the most serious of these—the localized paralysis usually affecting the legs (paraplegia) and the circulatory disturbances—are due to the formation of gaseous emboli, by the liberation of nitrogen in the blood when the pressure is abruptly reduced. And, indeed, it is found that the symptoms can often be caused to disappear, both in animals and men, by promptly subjecting them again to compressed air.

But that the action of oxygen under a high pressure is not merely mechanical seems to follow from the experiments of Bert. He discovered the singular fact that in pure oxygen at a pressure of 3 to 5 atmospheres, which corresponds to air at 15 to 25 atmospheres, animals die in a short time in convulsions like those produced by strychnine. Even seeds and vegetable organisms in general are killed in a short time; and an atmosphere of pure oxygen, equal to five atmospheres of air, hinders the development of eggs. Lorrain Smith has recently shown that in small birds and mice exposure for

many hours to a pressure of between 1 and 2 atmospheres of pure oxygen causes pneumonia. He confirms Bert's observations on the acute toxic effects produced by higher pressures, and supposes that in the production of caisson disease the special action of the oxygen at high pressure may play a part as well as the rapid decompression.

When the air-pressure is diminished below a certain limit, death takes place from asphyxia, more or less gradual according to the rate at which the pressure is reduced. The hæmoglobin cannot get or retain enough oxygen to enable it to perform its respiratory function; its dissociation tension is no longer balanced by an equal or greater partial pressure of oxygen in the air. The quantity of carbon dioxide in the blood is also lessened. These belong to the *chemical* effects of changes of pressure in the air of respiration.

To such changes, as well as to the cold, some of the deaths in high balloon ascents must be attributed. Messrs. Glaisher and Coxwell supposed that they reached the height of 37,000 feet; the former became unconscious at 29,000 feet (8,800 metres), at which height the amount of oxygen in the arterial blood would probably not exceed 10 volumes per cent., but recovered during the descent. The symptoms of the 'mountain sickness' so familiar to Alpine climbers are also mainly due to deficiency of oxygen in the blood. But evidence has been brought forward that changes in the mechanics as well as in the chemistry of respiration are concerned, and that there is something not connected with the want of oxygen which diminishes the capacity for muscular work. This 'something' is perhaps a peculiar excitation of the nervous system in the fierce light of those high levels, which acts not only on the retina, but on the skin, and may even affect the distribution of the blood (Zuntz and Schumburg).

Cutaneous Respiration.—It has already been remarked that a frog survives the loss of its lungs for some time, respiration going on through the skin. Indeed, it has been calculated that in the intact frog as much as three-quarters of the total gaseous exchange is cutaneous. In mammals the structure of the skin is different, and respiration can only go on through it to a very slight extent. The amount of carbon dioxide excreted in man, although only about 4 grm. or 2 litres in twenty-four hours, is much greater than corresponds to the quantity of oxygen absorbed through the skin. It has been asserted, and no doubt with justice, that some at least of the carbon dioxide given off is due to putrefactive processes taking place on the surface of the body. Such processes, as has already been pointed out, seem also responsible in part for the heavy odour of a 'close' room. For no harmful products appear to be exhaled from the skin when it is properly cleansed. In spite of the romantic

statements to the contrary in ancient and modern books (for instance, the story of the child that was gilded to play the part of an angel at the coronation of a mediæval pope, but died before the ceremony began), the whole of the human skin may be coated with an impermeable varnish without any ill effects. The entire surface of the body of a patient with cutaneous disease was covered with tar, and kept covered for ten days. There was not the least disturbance of any normal function (Senator). The serious effects of varnishing the skin in animals are due, not to retention of poisonous substances, but to increased heat loss. Varnishing is not so rapidly harmful in large animals like dogs, as in rabbits, which have a relatively great surface and a delicate skin. The danger of widespread superficial burns is well known. But it is not due to diminished excretion by the skin, for death occurs when large cutaneous areas remain uninjured. The patient nearly always dies when a quarter of the whole skin is burnt; yet the remaining three-quarters may surely be considered capable, from all analogy, of making up the loss by increased activity. One kidney is enough to eliminate the products of the nitrogenous metabolism of the whole body. It is difficult to see why the excretion of the trifling amount of solid matter in the perspiration should be interfered with by the loss of 25 per cent. of the sweat-glands. The real explanation of the serious effects of extensive superficial burns is perhaps the excessive irritation of the sensory nerves, which may lead to changes in the nervous centres, or reflexly in other organs. Some observers have supposed that the chemical changes in the damaged tissue, for example, in the blood-corpuscles, may be the cause of death (Hunter), and others that it may be due to the transudation of lymph at the injured part, and the consequent increase in the concentration of the blood.

Voice and Speech.

Voice.—Sounds of various kinds are frequently produced by the movements of animals as a whole, or of individual organs. The muscular sound, the sounds of the heart and of respiration, we have already had to speak of. Such sounds may be considered as purely accidental as the foot-fall of a man or the buzzing of a fly. The wings of an insect beat the air, not to cause sound, but to produce motion; the respiratory murmur is a mere indication that air is finding its way into the lungs, it is in no way related to the oxidation of the blood in the pulmonary capillaries. But in many of the higher animals mechanisms exist which are specially devoted to the utterance of sounds as their prime and proper end. In man the voice-producing mechanism consists of a triple series of tubes and chambers: (1) The

trachea, through which a blast of air is blown; (2) the larynx, with the vocal cords, by the vibrations of which sound waves are set up; and (3) the upper resonance chambers, the pharynx, mouth, and nasal cavities, in which the sounds produced in the larynx are modified and intensified, and in which independent notes and noises arise.

The **larynx** is a cartilaginous box, across which are stretched, from front to back, two thin and sharp-edged membranes, the (true) vocal cords. In front the cords are attached to the thyroid cartilage, one a little to each side of the middle line; behind they are connected to the vocal or anterior processes of the pyramidal arytenoid cartilages. The thyroid and the two arytenoids are mounted upon a cartilaginous ring, the cricoid, on which the former can rotate about a transverse horizontal axis, the latter around a vertical axis. The thyroid can thus be depressed by the contraction of the crico-thyroid muscle, and the vocal cords stretched. By the pull of the posterior crico-arytenoid muscles, attached to the external or muscular processes of the arytenoid cartilages, the vocal processes are rotated outwards, the cords separated from each other or *abducted*, and the chink between them, the rima glottidis, widened. When the vocal processes are approximated by contraction of the lateral crico-arytenoid muscles and the consequent forward movement of the muscular processes, the vocal cords are brought closer together, or *adducted*, and the rima is narrowed. The transverse or posterior arytenoid muscle, which connects the two arytenoid cartilages behind, also helps by its contraction to narrow the glottis by shifting the cartilages on their articular surfaces somewhat nearer the middle line. Running in each vocal cord, and, in fact, incorporated with its elastic tissue, is a muscle, the thyro-arytenoid, the external portion of which may to some extent cause inward rotation of the vocal processes and adduction of the cords; but the main function, at least of its inner part, is to alter the tension of the cords. The diagrams in Figs. 91 and 92 illustrate the action of the abductors and adductors of the vocal cords.

The crico-thyroid muscle and the deflectors of the epi-

glottis are supplied by the superior laryngeal branch of the vagus, which also contains the sensory fibres for the mucous membrane of the larynx above the vocal cords. All the other intrinsic muscles are supplied by the recurrent laryngeal branch of the vagus. It receives these motor fibres from the spinal accessory, and supplies sensory fibres to the mucous membrane of the larynx below the vocal cords and to the trachea.

The voice is produced, like the sounds of a reed instrument, by the rhythmical interruption of an expiratory blast of air by the vibrating vocal cords. When a bell is struck,

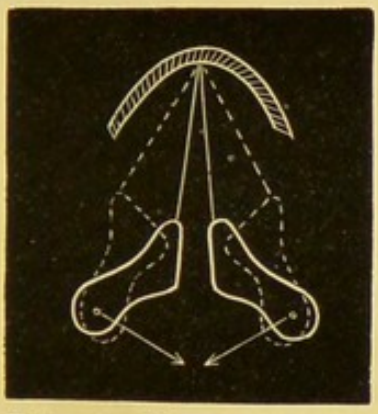


FIG. 91.—DIAGRAMMATIC HORIZONTAL SECTION OF LARYNX TO SHOW THE DIRECTION OF PULL OF THE POSTERIOR CRICO-ARYTENOID MUSCLES, WHICH ABDUCT THE VOCAL CORDS.

Dotted lines show position in abduction.

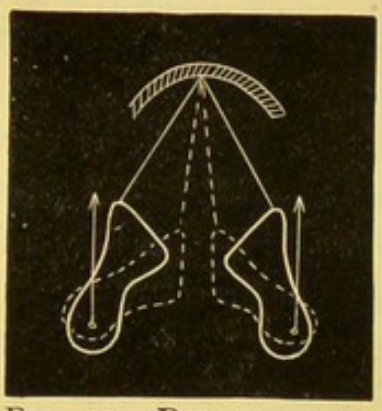


FIG. 92.—DIRECTION OF PULL OF THE LATERAL CRICO-ARYTENOIDS, WHICH ADDUCT THE VOCAL CORDS.

Dotted lines show position in adduction.

vibrations are set up in the metal, which are communicated to the air. It is not the same with the vibrations of the vocal cords; if they were plucked or struck, they would only produce a feeble note. The air in the mouth, pharynx, larynx, trachea, and lungs is the real sounding body; a pulse of alternate rarefaction and condensation is set up in it by the interference, at regular intervals, of the vocal cords with the expiratory blast. Forced abruptly from their position of equilibrium as the blast begins, they almost immediately regain and pass below it, in virtue of their elasticity, and continue to vibrate as long as the stream of air continues to issue in sufficient strength. The sound-waves thus set up

spread out on every side, impinge on the tympanic membrane, set it quivering in response, and give rise to the sensation of sound.

We may say, in a word, that the whole exquisite mechanism of cartilages, ligaments, and muscles, has for its object the production of a sufficient pressure in the blast of air driven through the windpipe by an expiratory act, and of a suitable tension in the vibrating cords. An approximation of the cords, a narrowing of the glottis, is essential to the production of voice; with a widely-opened glottis the air escapes too easily, and the necessary pressure cannot be attained. The pressure in the windpipe was found in a woman with a tracheal fistula to be about 12 mm. of mercury for a note of medium height, about 15 mm. for a high note, and about 72 mm. for the highest possible note. The period of vibration of structures like the vocal cords depends on their length, thickness, and tension; the shorter, thinner, more tense and less dense a stretched string is, the greater is the vibration frequency, the higher the note. In the child the cords are short (6 to 8 mm.), in woman longer (10 to 12 mm. when slack, 13 to 15 mm. when stretched), in man longest of all (14 to 18 mm. in the relaxed, and 18 to 22 mm. in the stretched position); and the lower limit of the voice is fixed by the maximum length of the relaxed cords. A boy or a woman cannot utter a deep bass note, because their vocal cords are relatively short, and do not vibrate with sufficient slowness. It is true that by the action of the crico-thyroid muscle the cords can be lengthened, and that the maximum length in a woman approaches or exceeds the minimum length in a man. But the lengthening of the vocal cords in one and the same individual is always accompanied by other changes—increase of tension, decrease of breadth and thickness—which tell upon the vibration frequency in the opposite way, and more than compensate the effect of the increase of length. It is probable that when the highest notes are uttered, only the anterior portions of the cords are free to vibrate, their posterior portions being damped by the approximation of the vocal processes of the arytenoid cartilages by the contraction of the lateral crico-

arytenoid and transverse arytenoid muscles. The range of an ordinary voice is 2 octaves; by training $2\frac{1}{2}$ octaves can be reached; but in exceptional cases a range of 3, and even $3\frac{1}{2}$, octaves has been known.

The development of the voice in children is of great interest. At the age of six years the boy's voice has a rather narrower range than the girl's in both directions. The boy's voice reaches its full height in the twelfth and its full depth in the thirteenth year, when the range is almost 3 octaves, its upper limit being a semitone higher than the girl's, but its lower limit a whole tone deeper. When the voice 'breaks' in boys at the age of puberty, the control of the vocal organs becomes so incomplete that only in one-fourth of the cases can notes of sufficient steadiness to be used in music be produced. The vocal cords, as may be seen with the laryngoscope, are frequently, though not always, congested (Paulsen).

The *pitch* of a note, while it depends chiefly, as has been said, on the tension of the vocal cords, rises and falls somewhat with the strength of the expiratory blast; the highest notes are only reached with a strong expiratory effort. The *intensity* of all sounds is determined by the strength of the blast, for the amplitude of vibration of the vocal cords is proportional to this. Besides pitch and intensity, the ear can still distinguish the *quality* or *timbre* of sounds; and the explanation is as follows: Two simple tones of the same pitch and intensity, that is, the sounds caused by two series of air-waves of the same period and amplitude—of the same frequency and height, if these terms seem simpler—would appear absolutely identical to the sense of hearing; just as the aerial disturbances on which they depend would be absolutely alike to any physical test that could be applied. But no musical instrument ever produces sound-waves of one definite period, and one only; and the same is true of the voice. When a stretched string is displaced in any way from its position of rest, it is set into vibration; and not only does the string vibrate as a whole, but portions of it vibrate independently and give out separate tones. The tone corresponding to the vibration period of the whole string is the lowest of all. It is also the loudest, for it is more difficult to set up quick than slow vibrations. The ear therefore picks it out from all the rest; and the pitch of the compound note is taken to be the pitch of this, its funda-

mental tone. The others are called partial or over-tones, or harmonics of the fundamental tone, their vibration frequency being twice, three times, four times, etc., that of the latter. Now, the fundamental tone of a compound note or *clang* produced by two musical instruments may be the same, while the number, period, and intensity of the harmonics are different; and this difference the ear recognises as a difference of timbre or quality. The timbre of the voice depends for the most part on partial tones produced or intensified in the upper resonance chambers.

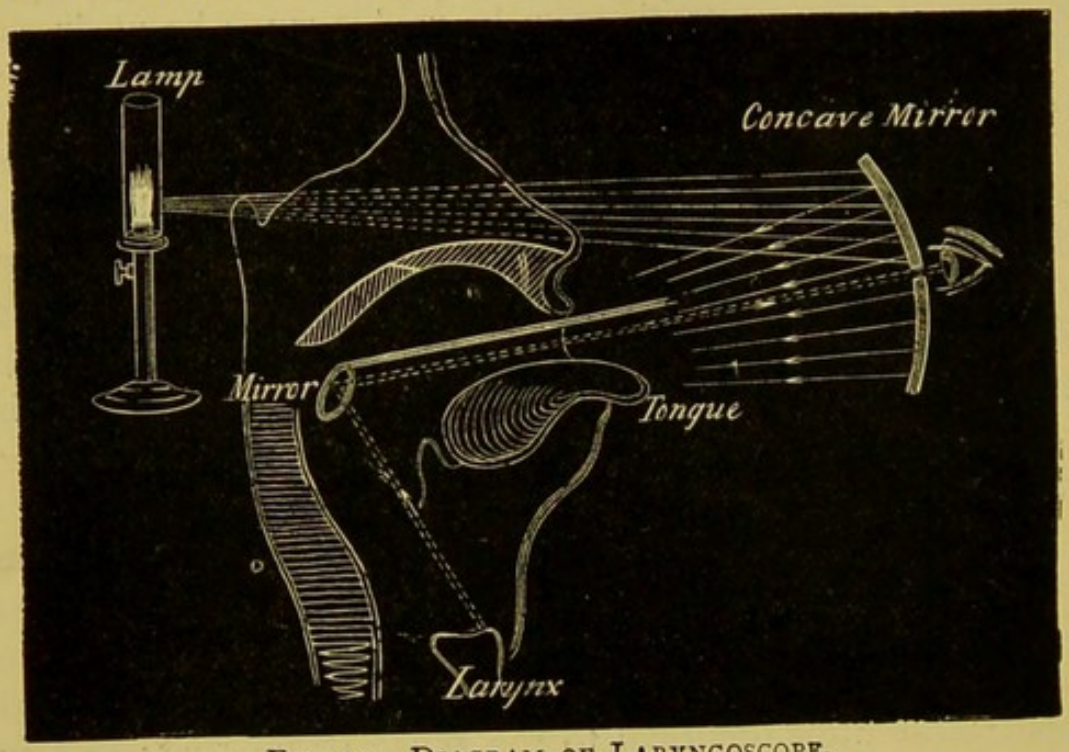


FIG. 93.—DIAGRAM OF LARYNGOSCOPE.

A great deal of our knowledge as to the mode and mechanism of the production of voice has been acquired by means of the *laryngoscope* (Fig. 93). This consists of a small plane mirror mounted on a handle, which is held at the back of the mouth in such a position that a beam of light, reflected from a larger concave mirror fastened on the forehead of the observer, is thrown into the larynx of the patient. The observer looks through a hole in the centre of the large mirror; and an image of the interior of the larynx is seen in the small mirror, in which the parts that are anterior appear as posterior, the arytenoid cartilages in front, the thyroid behind, and the vocal cords stretching between. The small mirror is warmed to body

temperature before being introduced, so as to prevent the condensation of moisture on it. And the tendency to retch which is caused by contact of the instrument with the soft palate may be removed or lessened by the application of a solution of cocaine.

Examined with the laryngoscope during quiet respiration, the glottis is seen to be moderately, though not widely, open, and the vocal cords almost motionless. Although the portion between the arytenoid cartilages has received the name of glottis respiratoria, in contradistinction to the glottis vocalis between the vocal cords, the rima in its whole

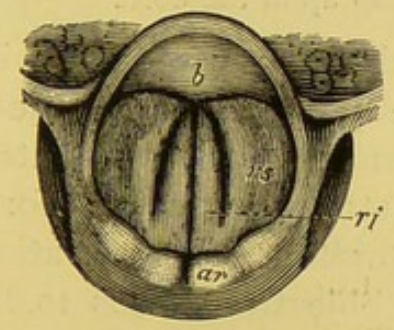


FIG. 94.—POSITION OF THE GLOTTIS PRELIMINARY TO THE UTTERANCE OF SOUND.

rs, false vocal cord; *ri*, true vocal cord; *ar*, arytenoid cartilage; *b*, pad of the epiglottis.

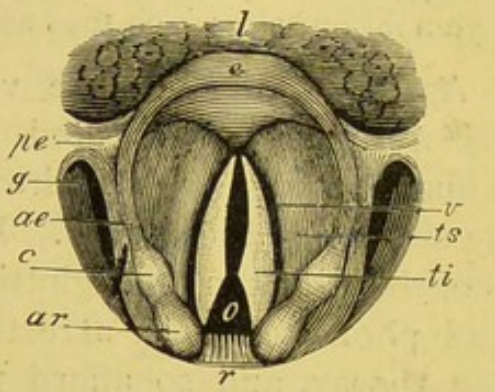


FIG. 95.—POSITION OF OPEN GLOTTIS.

l, tongue; *e*, epiglottis; *ae*, ary-epiglottidean fold; *c*, cartilage of Wrisberg; *ar*, arytenoid cartilage; *o*, glottis; *v*, ventricle of Morgagni; *ti*, true vocal cord; *ts*, false vocal cord.

extent from front to back is really concerned in the respiratory act. In deep expiration the vocal cords come nearer to the middle line, and the glottis is narrowed; in deep inspiration they are widely separated, and the rings of the trachea, and even its bifurcation, may be disclosed to view. When a sound is produced, a note sung, for example, the cords are approximated (Figs. 94 and 95); and with a high note more than with a low.

The essential difference between the production of notes in the lower register, or chest voice, and in the higher register, or falsetto, has been much debated. The lowest notes which can be uttered by any given voice are chest notes, the highest are falsetto notes; but there is a debatable land common to both registers, and medium notes can be sung either from the chest or from the head. Chest notes impart a vibration or *fremitus* to the thoracic walls, from the resonance of the lower air-chambers, the trachea and bronchi; and

this can be distinctly felt by the hand. In head notes or falsetto the resonance is chiefly in the upper cavities, the pharynx, mouth, and nose. As to the mechanical conditions in the larynx, there is a pretty general agreement that during the production of falsetto notes the vocal cords are less closely approximated than in the sounding of chest notes. The escape of air is consequently more rapid in the head voice, and a falsetto note cannot be maintained so long as a note sung from the chest. But it is only the anterior part of the rima glottidis that is wider in the falsetto voice; the whole of the glottis respiratoria, and even the posterior portion of the glottis vocalis, are closed during the emission of falsetto notes.

Oertel has stated, and the statement has been confirmed by others, that the free edge of the vocal cord alone vibrates in the falsetto voice, one or more nodes or motionless lines parallel to the edge being formed by the contraction of the internal part of the thyro-arytenoid muscle, which thus acts like a stop upon the cord.

Approximation of the vocal cords may take place in certain acts unconnected with the production of voice. Thus, a cough, as has already been mentioned, is initiated by closure of the glottis. During a strong muscular effort, too, the chink of the glottis is obliterated, and respiration and phonation both arrested. The object of this is to fix the thorax, and so afford points of support for the action of the muscles of the limbs and abdomen. But considerable efforts can be made even by persons with a tracheal fistula.

Speech. — Ordinary speech is articulated voice — voice shaped and fashioned by the resonance of the upper air cavities, and *jointed* together by the sounds or noises to which the varying form of these cavities gives rise. Here we come upon the fundamental distinction between vowels and consonants. Vowels are musical sounds; consonants are not musical sounds, but noises—that is to say, they are due to irregular vibrations, not to regularly recurring waves, the frequency of which the ear can appreciate as a definite pitch. This difference of character corresponds to a difference of origin: the vowels are produced by the vibrations of the vocal cords; the consonants are due to the rushing of the expiratory blast through certain constricted portions of the buccal chamber, where a kind of temporary glottis is established by the approximation of its walls. One of these 'positions of articulation' is the orifice of the lips; the

consonants formed there, such as *p* and *b*, are called labials. A second articulation position is between the anterior part of the tongue and the teeth and hard palate. Here are formed the dentals, *t*, *d*, etc. The ordinary English *r*, and the *r* of the Berwickshire and East Prussian 'burr,' also arise in this position through a vibratory motion of the point of the tongue. The third position of articulation is the narrow strait formed between the posterior portion of the arched tongue and the soft palate. To the consonants arising here the name of gutturals has been given. They include *k*, *g*, the Scottish *ch*, and the uvular German *r*. The latter is produced by a vibration of the uvula. The aspirated *h* is a noise set up by the air rushing through a moderately wide glottis, and some have therefore included the glottis as a fourth articulation position for consonants. Certain sounds like *n*, *m*, and *ng*, when final (as in *pen*, *dam*, *ring*), although produced at the glottis, are intensified by the resonance of the air in the nose and pharynx, and are sometimes spoken of as nasal consonants.

As we have said, the vowels are produced by vibrations of the vocal cords, but they owe their special timbre to the reinforcement of certain overtones by the resonating cavities, the shape and fundamental tone of which are different for each vowel. When a vowel is whispered, the mouth assumes a characteristic shape, and emits the fundamental tone proper to the form and size of the particular 'vowel-cavity,' not as a reinforcement of a tone set up by the vibrations of the vocal cords, but in response to the rush of air through the cavity; just as a bottle of given shape and size gives out a definite note when the air which it contains is set in vibration, by blowing across its mouth. A whisper, in fact, is speech without voice; the larynx takes scarcely any part in the production of the sounds; the vocal cords remain apart and comparatively slack; and the expiratory blast rushes through without setting them in vibration.

The fundamental tone of the 'vowel-cavity' may be found for each vowel by placing the mouth in the position necessary for uttering it, then bringing tuning-forks of different period in front of it, and noting which of them sets up sympathetic

resonance in the air of the mouth, and so causes its sound to be intensified. The fundamental tone is lowest for *u* (as in *lute*). Next comes *o*; then *a* (as in *path*); then *a* (as in *fane*); then *i*; while *e* is highest of all. A simple illustration of this may be found in the fact that when the vowels are whispered in the order given, the pitch rises.

Such is the explanation of the difference of the vowels in quality which was first given by Helmholtz. Universally accepted for a time, it has been in recent years assailed by Hermann, who bases his criticisms (1) on microscopic examination of curves obtained by the Edison phonograph, and (2) on the results of his phono-photographic method. (The record of an Edison phonograph is magnified by a system of levers, the last of which carries a small mirror, on which a beam of light is allowed to strike. The reflected beam falls on a moving drum covered with sensitive paper. Thus the movements of the mirror are greatly exaggerated and photographed.) Hermann has come to the conclusion that the mouth does not act as a mere resonator, but that for each vowel, in addition to the fundamental note due to the vibration of the vocal cords, the pitch of which is, of course, variable, one or, it may be, two other notes, not necessarily harmonics of the laryngeal note, but separated from it by a constant or nearly constant musical interval, are directly produced by the passage of the expiratory blast through the mouth. The fact that it is by no means difficult to sing and whistle at the same time shows the possibility of Hermann's view, that a fixed tone can be generated in the mouth by the intermittent stream of air issuing from between the vibrating vocal cords, just as a tone is generated in a pipe by blowing into or over it (Grützner). McKendrick has also made important investigations on this subject, and has obtained curves by enlarging the phonographic records by mechanical means.

When *u* or *o* is sounded, the buccal cavity has the form of a wide-bellied flask, with a short and narrow neck for *u*, a still shorter but wider neck for *o*. For *e* the tongue is raised and almost in contact with the palate, and the cavity of the mouth is shaped like a flask with a long narrow neck and a very short belly. For *i* the shape is similar, but the neck is not so narrow. For *a* (as in *path*) the vowel-cavity is intermediate in form between that of *u* and *e*, being roughly funnel-shaped, and the mouth is rather widely opened. For *u* (*oo*) the resonating cavity is made as long as possible, the larynx being depressed and the lips protruded; for *e* the resonating cavity is at its shortest, the larynx being raised as much as possible and the lips retracted (Figs. 96 to 98).

When the vowels are being uttered, the soft palate closes the entrance to the nasal chambers completely, as may be shown by holding a candle in front of the nose, or trying to inject water through the nares. If the cavities of the nose

are not completely blocked off, the voice assumes a *nasal* character in pronouncing certain of the vowels; and in some languages this is the ordinary and correct pronunciation.

Many animals have the power of emitting articulated sounds; a few have risen, like man, to the dignity of sentences, but these only by imitation of the human voice. Both vowels and consonants can be distinguished in the notes of birds, the vocal powers of which are in general higher than those of mammalian animals. The latter, as a rule, produce only vowels, though some are able to form consonants too.

The **nervous mechanism of voice and speech** will have to be

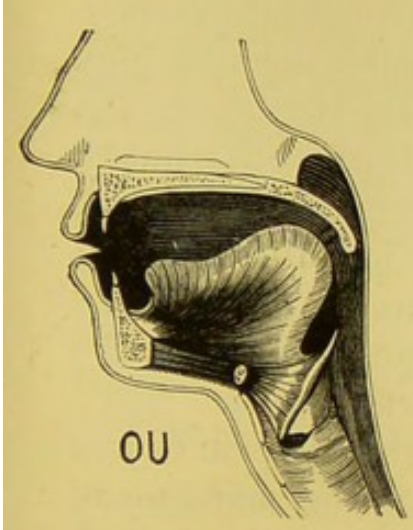


FIG. 96.

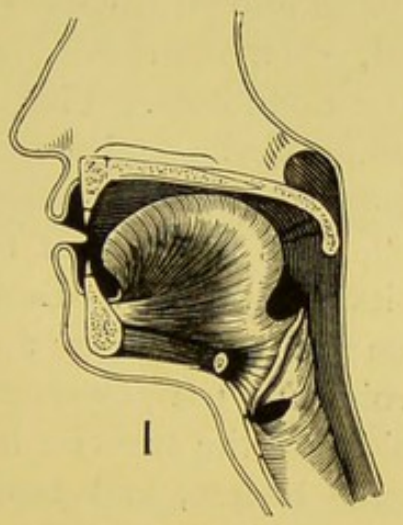


FIG. 97.

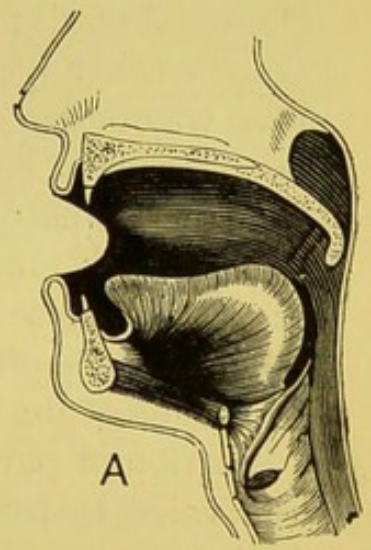


FIG. 98.

again considered when we come to study the physiology of the brain and spinal cord. But the curious physiological antithesis between the functions of abduction and of adduction of the vocal cords may be mentioned here. The abductor muscles are not employed in the production of voice; they are associated with the less specialized, the less skilled and purposive function of respiration. The adductor muscles are not brought into action in respiration; they are associated with the highly-specialized function of speech. Corresponding to this difference of function, we find that the adductors only are represented in the cortex of the brain, the abductors in the medulla oblongata. Stimulation of an area in the lower part of the ascending frontal convolution, near the fissure of

Rolando, in the macaque monkey, causes adduction of the vocal cords, never abduction. Stimulation of the medulla oblongata (accessory nucleus) causes abduction, never adduction (Horsley and Semon). The skilled adductor function is, therefore, placed under control of the cortex. The vitally important, but more mechanical, abductor function is governed by the medulla. The abductor movements are more likely to be affected by organic disease, the adductor movements by functional changes. But the distinction between the two groups of muscles is not entirely due to a difference of central connections; for Hooper has found that in an animal deeply narcotized with ether, stimulation of the recurrent laryngeal nerve causes invariably abduction of the vocal cords; in an animal slightly narcotized, adduction. On the other hand, when the nerve is cooled the abductors give way before the adductors. The same is true when it is allowed to become dry. And after death in a cholera patient it was observed that the posterior crico-arytenoid, an abductor muscle, was the first of the intrinsic laryngeal muscles to lose its excitability. Lesions of the medulla oblongata are often accompanied by marked changes in the character of the voice and the power of articulation.

Section or paralysis of the superior laryngeal nerve causes the voice to become hoarse, and renders the sounding of high notes an impossibility, owing to the want of power to make the vocal cords tense. Stimulation of the vagus within the skull causes contraction of the crico-thyroid muscle and increased tension of the cords. Section or paralysis of the inferior laryngeal nerves leads to loss of voice or aphonia, and dyspnœa (Fig. 99). Both adductor and abductor muscles are paralyzed; the vocal cords assume their mean position—the position they have in the dead body—and the glottis can neither be narrowed to allow of the production of a note, nor widened during inspiration. It is said, however, that young animals, in which the structures around the glottis are more yielding than in adults, can still utter shrill cries after section of the inferior laryngeals, the contraction of the crico-thyroid muscle alone being able, while increasing the tension of the cords, to draw them together. Strong

stimulation of the inferior laryngeal causes closure of the glottis, for although it supplies both abductors and adductors, the latter prevail. With weak stimulation, and in young animals, the abductors carry off the victory, and the glottis is opened (Risien Russell).

Interference with the connections on one side, between the higher cerebral centres and the medulla oblongata, as by rupture of an artery and effusion of blood into the posterior portion of the internal capsule (giving rise to hemiplegia, or paralysis of the opposite side of the body), is not followed

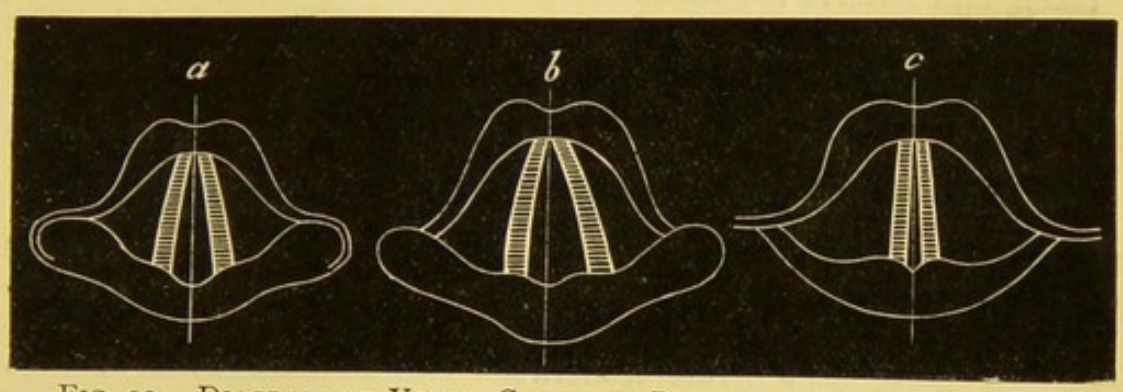


FIG. 99.—DIAGRAM OF VOCAL CORDS IN PARALYSES OF THE LARYNX.

a, Paralysis of both inferior laryngeal nerves. The vocal cords have taken up the 'mean' position. *b*, Paralysis of right inferior laryngeal nerve. An attempt is being made to narrow the glottis for the utterance of sound. The right cord remains in its 'mean' position. *c*, Paralysis of the abductor muscles only, on both sides. The cords are approximated beyond the 'mean' position by the action of the adductors.

by loss of voice; the laryngeal muscles on both sides are still able to act.

PRACTICAL EXERCISES ON CHAPTER III.

1. **Tracing of the Respiratory Movements.**—(*a*) Set up the arrangement shown in Fig. 100, and test whether it is air-tight. Have also in readiness an induction machine and electrodes arranged for an interrupted current. Anæsthetize a rabbit with chloral (Experiment 24, p. 190), or a small dog* with morphia and ether

* If a large dog is used the bottle may be omitted, the tracheal cannula being connected with the stem of a T-tube. One end of the horizontal limb of the T-tube is connected with the tambour; the other is provided with a rubber tube which can be partially closed by a screw clamp to regulate the excursion.

or ACE mixture. Insert a cannula into the trachea (p. 177), and connect it with the large bottle by a tube. Connect the bottle with a recording tambour adjusted to write on a drum, and regulate the amount of the excursion of the lever by slackening or tightening the screw-clamp. Set the drum off at slow speed, and take a tracing.

(*b*) Then disconnect the cannula from its tube. Dissect out the vagus in the lower part of the neck, pass a ligature under it, but do not tie it. Connect the cannula again with the bottle, and while a tracing is being taken ligature the vagus. Then stimulate its central end with weak shocks, marking the time of stimulation on the drum. Repeat the stimulation with strong shocks, and observe the results.

(*c*) Apply a strong solution of potassium chloride with a camel's-hair brush to the central end of the vagus while a tracing is being taken, and observe the effect.

(*d*) Isolate the sciatic nerve (p. 185), ligature it, and cut below the ligature. Stimulate its central end while a tracing is being taken. The respiratory movements will be increased.

(*e*) Disconnect the cannula, and isolate the vagus on the other side. While a tracing is being taken, divide it. The respiratory movements will probably at once become deeper and less frequent.

(*f*) Again disconnect the cannula. Isolate the superior laryngeal branch of the vagus, which will be found coursing inwards to the larynx at the level of the upper edge of the thyroid cartilage. Ligature the nerve, and divide it between the larynx and the ligature. Reconnect the cannula. Take a tracing first with weak and then with strong stimulation of the central end of the superior laryngeal.

(*g*) Insert a cannula into the carotid artery. While a tracing is being taken, allow the blood to flow. Dyspnœa and exaggeration of the respiratory movements will be seen when a considerable quantity of blood has been lost. Mark and varnish the tracings. In the whole of this experiment the cannula is to be disconnected, except when the lever is actually writing on the drum, in order that the period during which the animal must breathe into the confined space of the bottle may be diminished as much as possible.

2. **The Effect of Temperature on the Respiratory Centre—Heat Dyspnœa.**—Set up an arrangement for taking a respiratory tracing as in 1. Anæsthetize a dog, and fasten it, back downward, on a holder. Make an incision in the middle line of the neck, commencing a little below the cricoid cartilage, and extending down for 4 or 5 inches. Insert a cannula into the trachea. Isolate both carotid arteries for as great a distance as possible, and arrange them on the brass tubes shown in Fig. 100*a*. Connect two adjacent ends of the tubes by a short rubber tube. Connect one of the remaining ends to a funnel, supported on a stand, and the other to a rubber tube hanging over the table above a large jar. Slip two or three folds of paper between the tubes and the vagus nerves. Heat two or three litres of water to 55° or 60° C. Now connect the tracheal cannula with the bottle. As soon as the tracing is under way, let the hot water run through the funnel and tubes into the jar. Mark on the tracing the point at which the flow of the hot water was begun, and go on

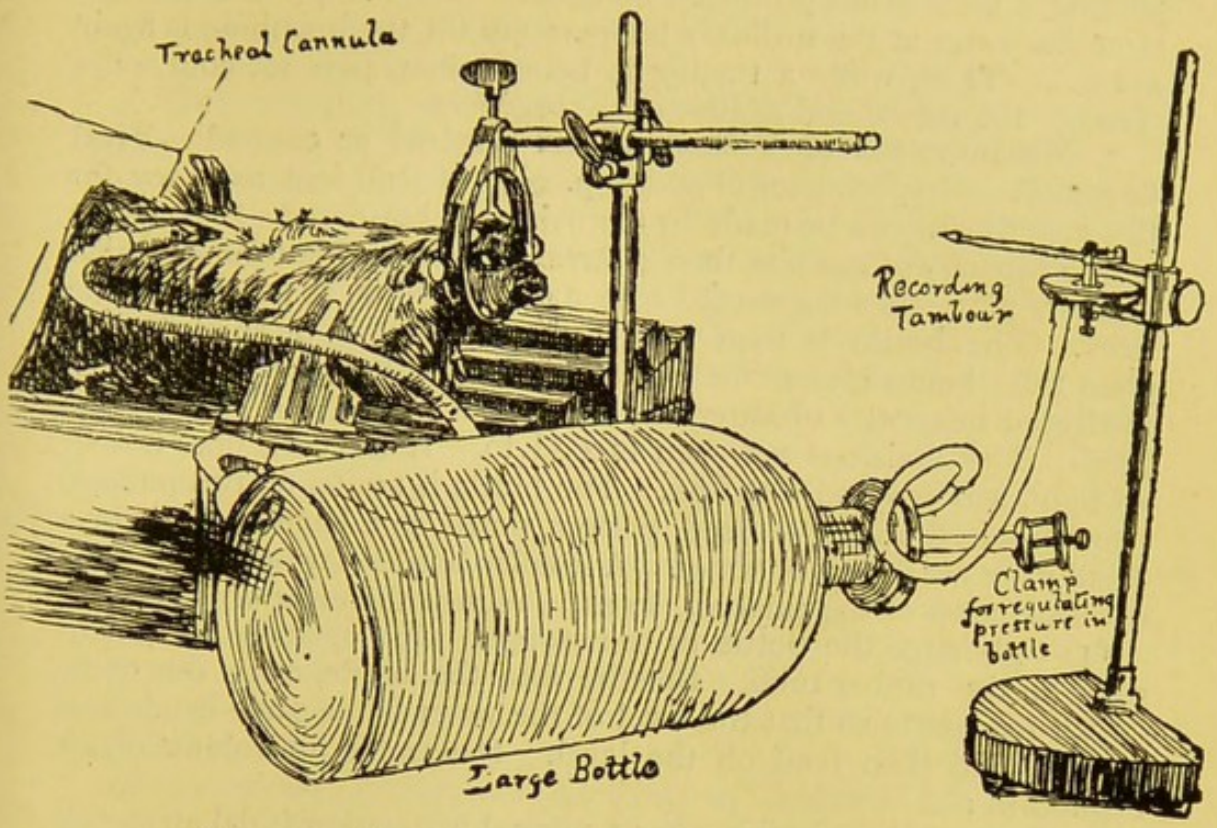


FIG. 100.—ARRANGEMENT FOR RESPIRATORY TRACING.

Two glass tubes are inserted through a cork in the mouth of the large bottle. One of them has a small piece of indiarubber tubing on it, which is closed or opened, as may be required, by a screw-clamp. The other is connected by a rubber tube with a recording tambour. The tubulure at the bottom of the bottle is closed by a cork, through which passes a glass tube, connected by a rubber tube with the tracheal cannula. If no bottle with tubulure is available, it is only necessary to pass through the cork, down to the bottom of the bottle, a third glass tube, which is connected with the tracheal cannula. While a tracing is being taken the animal breathes the air contained in the bottle. When this becomes vitiated the respiratory movements are exaggerated and a normal tracing is no longer obtained. For this reason the tracheal cannula must be connected with the bottle only at the moment when a tracing is to be taken. The arrangement is most suitable for a small animal.

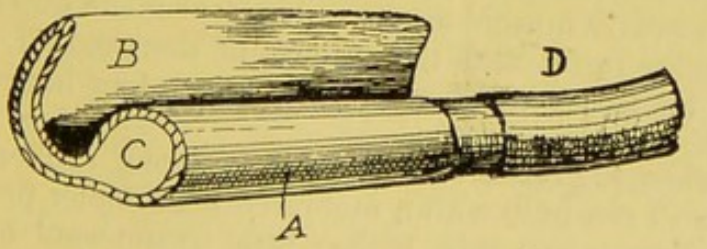


FIG. 100*a*.—ARRANGEMENT FOR HEATING OR COOLING THE BLOOD IN THE CAROTID ARTERIES.

A, cylindrical portion of tube; B, flattened portion in the groove between which and A the artery lies; C, cross-section, showing the lumen extending into B; D, rubber tube attached to a brass tube soldered into A. The other end of A has a similar brass tube soldered into it (not shown in the figure). This is connected by a rubber tube with a similar apparatus, on which the other carotid lies. D is connected with a funnel containing hot or cold water or with the outflow tube, as the case may be.

passing it until it has produced an effect. Then stop the drum, and circulate water at the ordinary temperature till the breathing is again normal. Then, while a tracing is being taken, pass ice-cold water through the tubes, and again notice the effect.

3. **Measurement of Volume of Air inspired or expired.—Vital Capacity.**—A spirometer (Fig. 79, p. 207) of sufficient accuracy for this experiment can be made by removing the bottom of a large bottle with a capacity of not less than 4 litres. A good cork, through which passes a glass tube connected with a rubber tube, is fitted into the neck. The bottle is then fixed vertically, mouth downwards, the glass tube being closed for the time, and graduated by pouring in measured quantities of water, say 100 c.c. at a time, and marking the level. The divisions are then etched in. If the cork does not fit air-tight, it is covered with wax. The bottle is swung on two pulleys, counterpoised and immersed, bottom down, in a large glass jar or a small cask nearly full of water. A smaller bottle may be used for the determination of the tidal air, so as to reduce the error of reading.

(1) Submerge the bottle to the stopper, after opening the pinch-cock on the rubber tube. Breathe into the bottle, close the cock, adjust the bottle so that the level of the water is the same inside and outside, and then read off the level. Determine the volume of air expired in :

(*a*) A normal expiration after a normal inspiration (tidal air) ;

(*b*) The greatest possible expiration after a normal inspiration (supplemental air) ;

(*c*) The greatest possible expiration after the greatest possible inspiration (vital capacity).

(2) Open the cock, and raise the bottle till it is nearly full of air. Determine the volume of air inspired in :

(*a*) A normal inspiration after a normal expiration (tidal air) ;

(*b*) The greatest possible inspiration after a normal expiration (complemental air) ;

(*c*) The greatest possible inspiration after the greatest possible expiration (vital capacity).

Make several observations of each quantity, and take the mean.

(3) Count the rate of respiration for three minutes, keeping the breathing as nearly normal as possible ; repeat the observation ; and from the mean result and the amount of the tidal air calculate the quantity of air taken into the lungs in twenty-four hours (pulmonary ventilation).

4. **Respiratory Pressure.**—Connect a strong rubber tube with a glass bulb, and the bulb with a mercurial manometer provided with a scale. (1) Fasten the tube with a little cotton-wool in one nostril, breathe through the other with closed mouth, and observe the amount by which the level of the mercury is altered in ordinary inspiration and expiration.

(2) Repeat the observation with forced breathing, pinching the tube at the height of inspiration and expiration, and reading off the maximum inspiratory and expiratory pressure.

(3) Repeat (1) with the tube connected to the mouth by a glass tube held between the lips, and the nostrils open.

(4) Repeat (2) with the tube in the mouth and nostrils closed.

5. **Determination of Carbon Dioxide and Oxygen in Inspired and Expired Air**—(1) **Estimation of Carbon Dioxide.**—Fill a burette with water, and close the pinchcock on the rubber tube. Immerse the wide end of the burette in a large vessel of water, and fill it with carbon dioxide by putting into it below the water a tube connected with a bottle in which carbon dioxide is being evolved by the action of hydrochloric acid on marble chips. See that gas has been coming off freely from the bottle for a little time before the tube is put under the burette. Do not fill the burette with gas beyond the graduated part. Hold the burette in the vertical position, its mouth being still immersed, make the level of the water the same inside and outside, and read off the meniscus. Then introduce a piece of stick sodium hydrate, close the burette with a finger or the palm of the hand, lift it out of the water, and by a sort of see-saw movement shake the sodium hydrate repeatedly from end to end of it. Again immerse the burette, and read the level of the meniscus. Most of the gas will be absorbed. Repeat the shaking. If the reading is still the same, absorption is now complete.

(2) **Estimation of Oxygen (Analysis of Inspired Air).**—Fill the burette with the air of the laboratory. Open the pinchcock, and immerse the wide end of the burette till the water reaches the graduation. Then close the cock, and read off the meniscus. Introduce a piece of sodium hydrate, and proceed as in (1). Notice that there is no appreciable absorption. (This method is not suitable for the measurement of the small quantity of carbon dioxide in ordinary air.) Now introduce, under water, some pyrogallic acid. This can be done conveniently by wrapping up some of the crystals in thin paper so as to form a kind of small cigarette, which is pushed up into the burette. A little more sodium hydrate may also be added, if the piece first introduced is entirely dissolved. Shake as described in (1), till no more absorption takes place. Then read off the meniscus again (always making the level the same inside and outside the burette). The difference in the two readings gives the amount of oxygen present. What remains in the burette is nitrogen (and a little argon). Its amount is, of course, equal to the reading of the burette, plus the capacity of the ungraduated part at the narrow end of the burette, which must be determined once for all by a separate measurement.

(3) **Analysis of Expired Air.**—(*a*) Fill the spirometer with water, breathe into it several times in your ordinary way, but be careful not to inspire any air from the spirometer; then fill the burette with the expired air from it. Or simply expire several times through the burette, seeing that none of the inspired air comes through it. Determine, as in (1) and (2), the percentage amount of carbon dioxide, oxygen and nitrogen. (*b*) Repeat (*a*) with air expired after the lungs have been thoroughly ventilated by taking a number of deep breaths in succession, and determine whether there is any difference in the percentage amounts.

6. **Estimation of the Quantity of Water and of Carbon Dioxide given off by an Animal** (*Haldane's Method*).—(1) Connect the apparatus shown in Fig. 101 with the water-pump. Allow a negative pressure of 5 or 6 inches of water to be established in it, as shown

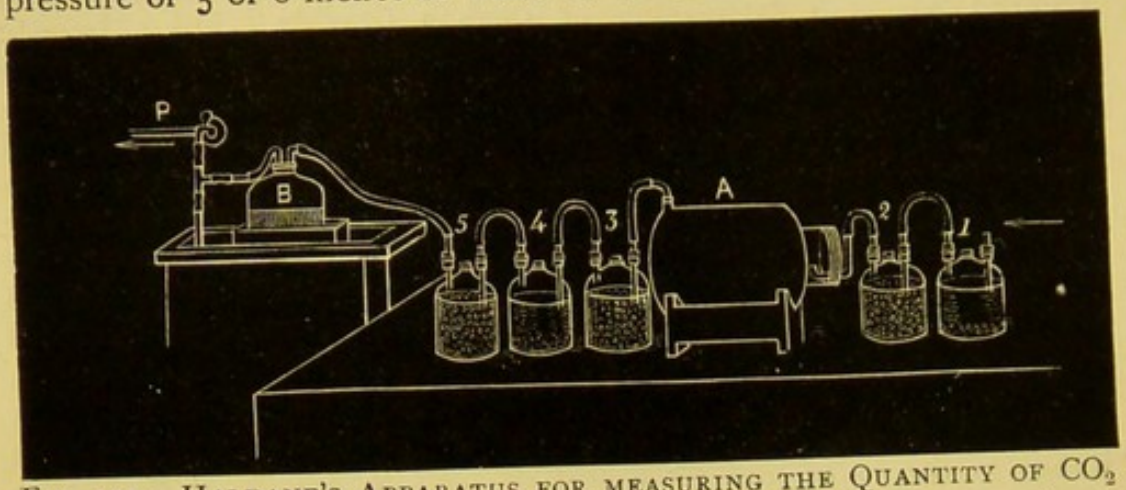
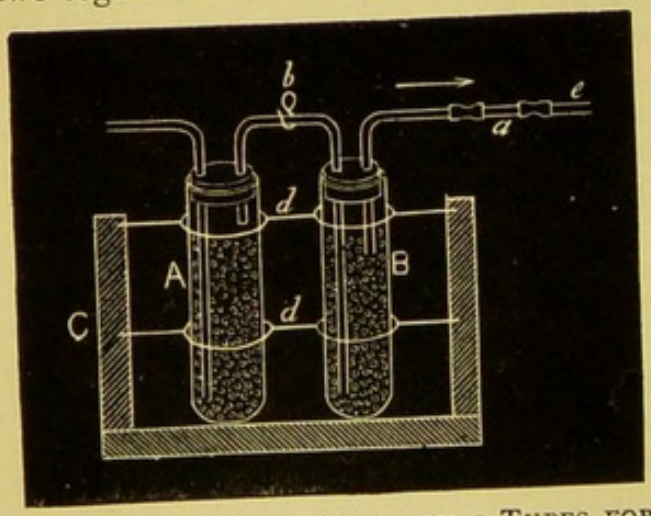


FIG. 101.—HALDANE'S APPARATUS FOR MEASURING THE QUANTITY OF CO_2 AND AQUEOUS VAPOUR GIVEN OFF BY AN ANIMAL.

A, chamber into which the animal is put; 1 and 4, Woulff's bottles filled with soda-lime to absorb carbon dioxide; 2, 3, and 5, Woulff's bottles filled with pumice-stone soaked in sulphuric acid to absorb watery vapour; B glass bell-jar suspended in water, by means of which the negative pressure is known; P, water-pump which sucks air through the apparatus; 1 and 2 are simply for absorbing the carbon dioxide and water of the ingoing air.

by the rise of water in the bell-jar, B. Then close the open tube of carbon dioxide bottle 1, and clamp the tube between the water-pump and the bell-jar. If the negative pressure is maintained, the arrangement is air-tight. Now weigh bottle 3 and bottles 4 and 5, the last two together. Place a cat in the respiratory chamber A, connect the



A, soda-lime tube; B, sulphuric acid tube; C, wooden frame, in which A and B are supported by wires *d*; *b*, wire hook, which grips the glass tube firmly, and by means of which the tubes are lifted out of the frame in order to be weighed; *a*, short piece of glass tubing, by taking out which the absorption tubes are disconnected from the rest of the apparatus; *e*, glass tube going off to animal chamber. The right-hand glass tube of B should not touch the sulphuric acid as depicted.

FIG. 102.—ABSORPTION TUBES FOR CO_2 AND MOISTURE.

chamber directly with the water-pump, and test whether it is tight. Then take the stopper out of bottle 1, and adjust the rate at which air is drawn through the apparatus. Let the ventilation go on for a few minutes, then insert bottles 3, 4, and 5 again. Note the time exactly at this point, and after an hour disconnect 3, 4, and 5, and again weigh. The difference of the two weighings of 3 shows the

quantity of water given off by the animal in an hour; the difference in the combined weight of 4 and 5, the quantity of carbon dioxide. Weigh the cat, and calculate the amount of water and of carbon dioxide given off per kilo per hour.

(2) For the student it is more convenient to use smaller animals. The mouse may be taken as an example of a warm-blooded animal, and the frog of a cold-blooded. Instead of the Woulff's bottles use wide test-tubes connected as in Fig. 102, and for the animal chamber a small beaker, closed with a very carefully-fitted cork which has been boiled in paraffin. The inlet and outlet tubes of the chamber are to be introduced through this cork. The holes for these are to be bored with the greatest care, and the tubes to be put in while the cork is still hot from boiling in paraffin. Also insert a thermometer about 6 inches long registering from 0° C. to 45° C. Modeller's wax is to be used finally to render all the junctions air-tight.

Add to the series of tubes described in the apparatus a single tube containing baryta-water. This is placed after the tube 5, and so arranged that the air-current bubbles through the water. As long as the absorption of carbon dioxide is complete, the baryta-water remains clear. Beyond this a water-bottle should be placed to act as a valve and to indicate the negative pressure in the apparatus. It can be most simply constructed by using a cylinder of stout glass tubing in a wide-mouthed bottle containing some water, the inlet and outlet tubes passing through a paraffined cork which seals the upper end of the cylinder.

Before making an observation, test whether the apparatus is air-tight, as explained above, after introducing the animal into the chamber, sealing the latter with wax, and connecting it with the absorption tubes. But a negative pressure of 2 or 3 inches of water is a sufficient test for the small apparatus.

To make an observation, set the air-current going at the desired rate. Allow it to run for a few minutes till the carbon dioxide, which has accumulated during the testing, has been swept out. At a time which has been decided on and noted, stop the current by disconnecting the water-pump. Disconnect and stopper up the animal chamber, and weigh it as quickly as possible. Connect up again, using only recently-weighed absorption-tubes, and finally connect with the water-pump and allow the current to pass for a definite period, say an hour. If a consecutive series of observations is to be made, two sets of tubes should be prepared for use during alternate periods. Use in each case two soda-lime tubes, the most recently filled one being placed second of the two.

The soda-lime should not be too dry, or absorption is not sufficiently rapid. The following facts are made out in the observation :

(*a*) The loss of weight by the animal chamber (chiefly loss by the animal). (*b*) The gain of the sulphuric acid tube in water. (*c*) The gain of the soda-lime tubes in carbon dioxide.

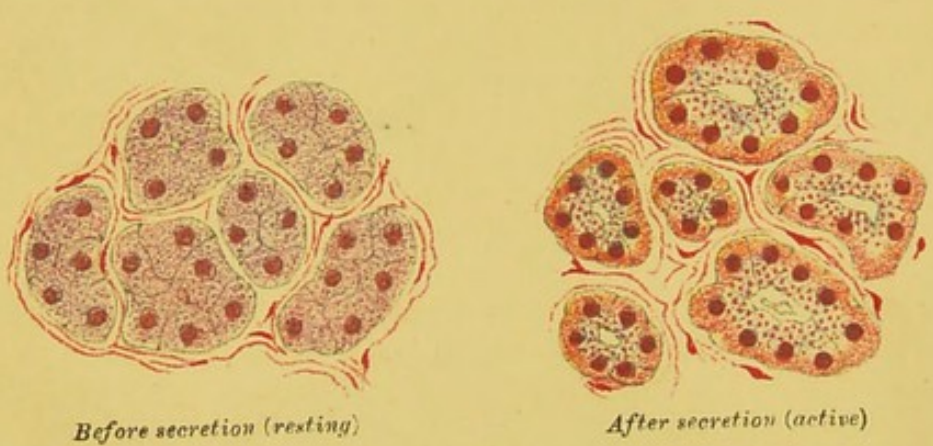
If we compare total loss and total gain, we find they do not correspond, the gain being always greater than the loss. The surplus can only be oxygen which has been absorbed by the animal and added to

the hydrogen and carbon of its substance to form water and carbon dioxide. Calculate the respiratory quotient (p. 225).

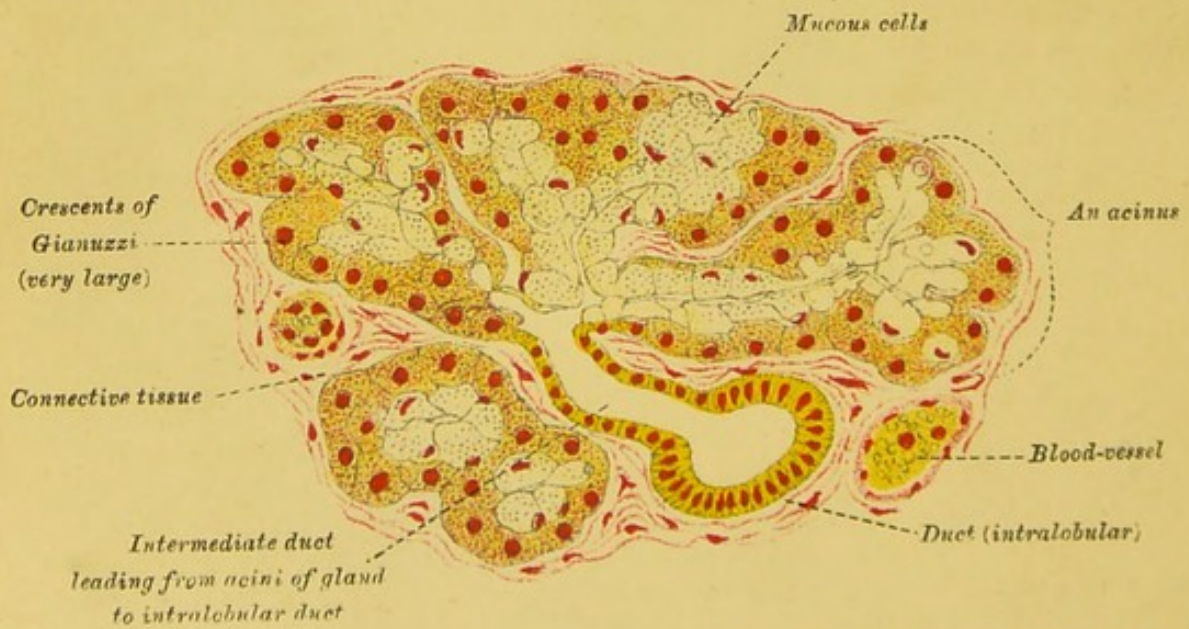
7. **Section of both Vagi.**—Proceed as in experiment 24, p. 190, but use an ordinary rabbit; and instead of cutting the sympathetic, pass threads under both vagi, divide them, and sew up the wound. An induction coil is not required, unless the student has any difficulty in deciding which nerve is the vagus. The point may be at once settled by stimulating the nerves before division. Stimulation of the vagus will cause slowing or stoppage of the heart, and therefore of the pulse in the carotid, and quickening of respiration. Stimulation of the sympathetic will have neither of these effects. A dog may also be used, and the vago-sympathetics divided. Count the pulse and the rate of respiration before and after the section of each nerve, and observe carefully any change that may occur. Also note whether the depth of the breathing is affected. The animal must be looked at once at least on the day of the operation, and its behaviour carefully observed. It should be seen daily thereafter so long as it survives. A rabbit does not usually live much more than twenty-four hours.

As soon after death as possible, make an autopsy, observing especially the state of the lungs. Harden portions of the lungs that appear to contain the most exudation in Müller's fluid (ten times as much fluid as tissue). Change the fluid next day, and again at the end of a week. In three or four weeks wash out the Müller's fluid under the tap, and transfer the tissue to 90 per cent. alcohol. After a few days it is to be prepared for cutting by being passed successively through absolute alcohol (two days), absolute alcohol and ether mixture (two days), thin celloidin (two or three days), thick celloidin (one day). Fasten on vulcanized wood-fibre and cut sections with a sliding microtome, moistening the knife with 80 per cent. alcohol. Stain, mount, and examine under the microscope. Note the exudation in the alveoli, and make drawings. Write a report of your complete experiment.

1. Section of submaxillary gland showing both mucous and serous alveoli, × 250. (Stained with hæmatoxylin.)



2. Section of serous gland, × 300 (Stained with borax carmine.)



3. Section of mucous gland (after secretion), × 300. (Stained with picrocarmine.)

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CHAPTER IV.

DIGESTION.

In the last chapter we have described the manner in which the interchange of gases between the tissues and the air is carried out. We have now to consider the digestion and absorption of the solid and liquid food, its further fate in relation to the chemical changes or metabolism of the tissues, and finally the excretion of the waste products by other channels than the lungs.

Logically, we ought to take metabolism after absorption and before excretion, tracing the food through all its vicissitudes from the moment when it enters the blood or lymph till it is cast out as useless matter by the various excretory organs. Unfortunately, however, the steps of the process are as yet almost entirely hidden from us; we know only the beginning and the end. We can follow the food from the time it enters the alimentary canal till it is taken up by the tissues of absorption; and we have really a fair knowledge of this part of its course. We can collect the end products as they escape in the urine, or in the breath, or in the sweat; and our knowledge of them and of the manner in which they are excreted is considerable. But of the wonderful pathway by which the dead molecules of the food mount up into life, and then descend again into death, we catch only a glimpse here and there. Only the introduction and the conclusion of the story of metabolism are at present in our possession in fairly continuous and legible form. We will read these before we try to decipher the handful of torn leaves which represents the rest.

Comparative. — In the lowest kinds of animals, such as the Amœba, there is neither mouth, nor alimentary canal, nor anus: the food, wrapped round by pseudopodia, is taken in at any part of the animal with which it happens to come in contact. A vacuole is formed around it. Acid is secreted into the vacuole, the food is digested within the cell-substance, and the part of it which is useless for nutrition is cast out again at any part of the surface.

Coming a little higher, we find in the Cœlenterates a mouth and alimentary tube, which opens into the body-cavity, where a certain amount of digestion seems to take place, and from which the food is absorbed either through the cells of the endoderm, or, as in Medusa, by means of fine canals, which radiate from the body-cavity into its walls, and form part of the so-called gastro-vascular system. In the Echinodermata we have a further development, a complete alimentary canal with mouth and anus, and entirely shut off from the body-cavity. In many Arthropods it is possible already to distinguish parts corresponding to the stomach, and the small and large intestines of higher forms, the digestive glands being represented by organs which in some groups seem to be homologous with the liver, and in others with the salivary glands of the higher vertebrates. A few Molluscs seem in addition to possess a pancreas.

Among Vertebrates fishes have the simplest, and birds and mammals the most complicated, alimentary system. In the lowest fishes the stomach is only indicated by a slight widening of the anterior part of the digestive tube. In water-living Vertebrates there are no salivary glands. In Birds the œsophagus is generally dilated to form a crop, from which the food passes into a stomach consisting of two parts, one pre-eminently glandular (proventriculus), the other pre-eminently muscular (ventriculus). Among Mammals a twofold division of the stomach is distinctly indicated in rodents and cetaceæ, but this organ reaches its greatest complexity in ruminants, which possess no fewer than four gastric pouches. The differentiation of the intestine into small and large intestine and rectum is more distinct, both anatomically and functionally, in Mammals than in lower forms; but there are marked differences between the various mammalian groups both in the relative size of the several parts of the digestive tube, and in the proportion between the total length of the alimentary canal and the length of the body. In general, the canal is longest in herbivora, shortest in carnivora. Thus, the ratio between length of body and length of intestine is in the cat 1 : 4, dog 1 : 6, man 1 : 5 or 6, horse 1 : 12, cow 1 : 20, sheep 1 : 27. The relative capacity of the stomach, small intestine, and large intestine, is in the dog 6 : 2 : 1·5, in the horse 1 : 3·5 : 7, in the cow 7 : 2 : 1. The area of the mucous surface of the alimentary canal is very considerable, in the dog more than half that of the skin, the surface of the small intestine being three times that of the stomach and four times that of the large intestine. In the horse the mucous surface has twice the area of the skin.

Anatomy of the Alimentary Canal in Man.—The alimentary canal is a muscular tube, which, beginning at the mouth, runs under the

various names of pharynx, œsophagus, stomach, small intestine, large intestine, and rectum, till it ends at the anus. Its walls are largely composed of muscular fibres ; its lumen is clad with epithelium, and into it open the ducts of glands, which, morphologically speaking, are involutions or diverticula formed in its course. In virtue of its muscular fibres it is a contractile tube ; in virtue of its epithelial lining and its special glands it is a secreting tube ; in virtue of both it is fitted to perform those mechanical and chemical actions upon the food which are necessary for *digestion.* Its inner surface is in most parts richly supplied with bloodvessels, and in special regions beset with peculiarly-arranged lymphatics ; by both of these channels the alimentary tube performs its function of *absorption.* From the beginning of the œsophagus to the end of the rectum the *muscular wall* consists, broadly speaking, of an outer coat of longitudinally-arranged fibres, and a thicker inner coat of fibres running circularly or transversely around the tube. Between the layers lies a plexus of non-medullated nerves and nerve-cells (Auerbach's plexus). In the stomach the longitudinal fibres are found only on the two curvatures, and a third incomplete coat of oblique fibres makes its appearance internal to the circular layer. In the large intestine, again, the longitudinal fibres are chiefly collected into three isolated strands. In the pharynx the typical arrangement is departed from, inasmuch as there is no regular longitudinal layer ; but the three constrictor muscles represent to a certain extent the great circular coat. The muscles of the mouth and of the pharynx are of the striped variety. So is the muscle of the upper half of the œsophagus in man and the cat, and of the whole œsophagus in the dog and the rabbit. In the rest of the alimentary canal the muscle is smooth, except at the very end, where the external sphincter of the anus is striped. In certain situations the circular coat is developed into a regular anatomical sphincter, a definite muscular ring, whose function it is to shut one part of the tube off from another (sphincter pylori), or to help to close the external opening of the tube (internal sphincter of anus). Elsewhere a tonic contraction of a portion of the circular coat, not anatomically developed beyond the rest, creates a functional sphincter (cardiac sphincter of stomach).

Throughout the greater part of the digestive tract the peritoneum forms a thin serous layer, external to the muscular coat. Internally the muscular coat is separated from the *mucous membrane*, the lining of the canal, by some loose areolar tissue containing bloodvessels, lymphatics and nerves (Meissner's plexus), and called the *submucous coat.* Between the mucous and submucous layers, but belonging to the former, in the whole canal below the beginning of the œsophagus, is a thin coat of smooth muscular fibre, the muscularis mucosæ, consisting in some parts, *e.g.*, in the stomach, of two, or even three, layers. Between this and the lumen of the canal lie the ducts and alveoli of glands, surrounded by bloodvessels and embedded in adenoid or lymphoid tissue, which in particular regions is collected into well-defined masses (solitary follicles, Peyer's patches, tonsils), extending, it may be, into the submucous tissue. In the mouth,

pharynx and œsophagus, the glands lie in the submucosa, as do the glands of Brunner in the duodenum; everywhere else they are confined to the mucous membrane proper. Between the openings of the glands the mucous membrane is lined with a single layer of columnar epithelial cells, sometimes (in the small intestine) arranged along the sides of tiny projections or villi. At the ends of the alimentary canal, viz., in the mouth, pharynx and œsophagus, and at the anus, the epithelium is stratified squamous, and not columnar.

The purpose of food is to supply the waste of the tissues and to maintain the normal composition of the body. In the body we find a multitude of substances marked off from each other, some by the sharpest chemical differences, others by characters much less distinct, but falling upon the whole into a few fairly definite groups. Thus, there are bodies like serum-albumin, serum-globulin, myosin, and so on, which are so much alike that they can all be placed in one great class, as *proteids*. Then we have substances like glycogen and dextrose, vastly simpler in their composition, and belonging to the group of *carbo-hydrates*. Then, again, *fats* of various kinds are widely distributed in normal animal bodies; and *inorganic materials*, such as water and salts, are never absent.

Now, although it is by no means necessary that a substance in the body belonging to one of these great groups should be derived from a substance of the same group in the food, it has been found that no diet is sufficient for man unless it contains representatives of all; a proper diet must include proteids, carbo-hydrates, fats, inorganic salts and water. These proximate principles have to be obtained from the raw material of the food-stuffs; it is the business of digestion to sift them out and to prepare them for absorption. This preparation is partly mechanical, partly chemical.

The water and salts and some carbo-hydrates, such as dextrose, are ready for absorption without change. Fats are, probably, for the most part, only mechanically altered. Indiffusible carbo-hydrates, like starch and dextrin, are changed into diffusible sugar, and the natural proteids into diffusible peptones. Mechanical division of the food is an important aid to the chemical action of the digestive juices. We shall see that this mechanical division forms a great part of the

work of the stomach, but it is normally begun in the mouth, and it is of consequence that this preliminary stage should be properly performed.

I. The Mechanical Phenomena of Digestion.

Mastication. — It is among the mammalia that regular mastication of the food first makes its appearance as an important aid to digestion. The amphibian bolts its fly, the bird its grain, and the fish its brother, without the ceremony of chewing. In ruminating mammals we see mastication carried to its highest point; the teeth work all day long, and most of them are specially adapted for grinding the food. The carnivora spend but a short time in mastication; their teeth are in general adapted rather for tearing and cutting than for grinding. Where the diet is partly animal and partly vegetable, as in man, the teeth are fitted for all kinds of work; and the process of mastication is in general neither so long as in the purely vegetable feeders, nor so short as in the carnivora.

In man there are two sets of teeth: the temporary or milk teeth, and the permanent teeth. The milk-teeth are twenty in number, and consist on each side of four incisors or cutting-teeth, two canines or tearing-teeth, and four molars or grinding-teeth. The central incisors emerge at the seventh month from birth, the other incisors at the ninth month, the canines at the eighteenth, and the molars at the twelfth and twenty-fourth month respectively. Each tooth in the lower jaw appears a little before the corresponding one in the upper jaw. Each of the milk-teeth is in course of time replaced by a permanent tooth, and in addition the vacant portion of the gums behind the milk set is now filled up by twelve teeth, six on each side, three above and three below. These twelve are the permanent molars; they raise the number of the permanent teeth to thirty-two. The permanent teeth which occupy the position of the milk molars now receive the name of premolars. The first tooth of the permanent set (the first true molar) appears at the age of 6½ years; the last molar, or wisdom tooth, does not emerge till the seventeenth to the twenty-fifth year.

In mastication the lower jaw is moved up and down, so as to alternately separate and approximate the two rows of teeth. It has also a certain amount of movement from side to side, and from front to back. The masseter, temporal and internal pterygoid muscles raise, and the digastric, with the assistance of the mylo- and genio-hyoid, depresses, the lower jaw. The external pterygoids pull it forward when both contract, forward and to one side when only one contracts. The lower fibres of the temporal muscle retract the jaw. The buccinator and orbicularis oris muscles prevent the food from passing between the teeth and the cheeks and lips. The tongue keeps the food in motion, works it up with the saliva, and finally gathers it into a bolus ready for deglutition.

Deglutition.—This act consists of a voluntary and an involuntary stage. During the former the anterior part of the tongue is pressed against the hard palate so as to thrust the bolus through the isthmus of the fauces. As soon as this has happened and the food has reached the posterior portion of the tongue, it has passed beyond the control of the will, and the second or involuntary stage of the process begins.

This stage may be divided into two parts: (1) pharyngeal, (2) œsophageal—both being reflex acts. During the first the food has to pass through the pharynx, the upper portion of which forms a part of the respiratory tract, and is in free communication with the larynx during ordinary breathing. It is therefore necessary that respiration should be interrupted and the larynx closed while the food is being moved through the pharynx. But that the interruption may be short, the food must be rapidly passed over this perilous portion of its descent. The pharynx is accordingly provided with rapidly-contracting striped muscle; and that none of its purchase may be lost, the pharyngeal cavity is cut off from the nose and mouth as soon as the bolus has entered it. The soft palate is raised by the levator palati; at the same time the upper part of the pharynx, narrowed by the contraction of the superior constrictor, comes forward to meet the soft palate, closes in upon it, and so prevents the food from passing into the nasal cavities. The pharynx is cut off from the mouth by the closure of the fauces through

the contraction of the palato-pharyngeal muscles which lie in their posterior pillars. The larynx is pulled upwards and forwards by the contraction of the thyro-hyoid muscle, and the elevation of the hyoid bone by the muscles which connect it to the lower jaw. The glottis is closed by the approximation of the vocal cords and the arytenoid cartilages, assisted it may be by the folding down of the epiglottis like a lid. But this organ can hardly play the great part which has been assigned to it in closing the larynx, since swallowing proceeds in the ordinary way when it is absent. The morsel of food, grasped by the middle and lower constrictors as it leaves the back of the tongue, passes rapidly and safely over the closed larynx, the process being accelerated by the pulling up of the lower portion of the pharynx over the bolus by the action of the palato- and stylo-pharyngei.

The second or œsophageal portion of the involuntary stage is a more leisurely performance. The bolus is carried along by a peculiar contraction of the muscular wall of the œsophagus, which travels down as a wave, pushing the food before it. When the food reaches the lower end of the gullet the tonic contraction of that part of the tube is for a moment relaxed, apparently by reflex inhibition, and the morsel passes into the stomach.

Such is the view of the mechanism of deglutition that has hitherto commanded the largest amount of support; and when the bolus is of such consistence and of such size that it actually distends the œsophagus, there is little doubt that this view is substantially correct. But it has been shown that liquid or semi-solid food is swallowed in a different way. The food lying on the dorsum of the tongue is suddenly put under pressure by the sharp contraction of the mylo-hyoid muscles in the floor of the mouth. Prevented from passing forwards by the contact of the tip of the tongue with the palate, it is shot rapidly in the direction of least resistance down to the lower part of the lax œsophagus, its movement in this direction being accelerated by the simultaneous contraction of the two hyoglossi which pull the tongue backward and downward. So far the whole process has only occupied one-tenth of a second. But it is only after about six seconds that the food is forced through the cardiac sphincter into the stomach by the arrival of the tardy peristaltic contraction of the œsophageal wall (Kronecker and Meltzer). (See also p. 349.)

There are certain remarkable peculiarities which distinguish this peristaltic movement of the œsophagus from that of

other parts of the alimentary canal. It is far more closely related to the central nervous system, and, unlike the peristaltic contraction of the intestine, can pass over any muscular block caused by ligature, section, or crushing, so long as the nervous connections are intact. But division of the œsophageal nerves causes, as a rule, stoppage of œsophageal movements; although under certain circumstances an excised portion of the tube may go on contracting in the characteristic way after removal from the body. Again, the peristaltic wave when artificially excited seems always under normal conditions to travel *down* the œsophagus, never to spread upwards or in both directions, as may happen in the intestine. Stimulation of the mucous membrane of the pharynx will cause reflex movements of the œsophagus, while stimulation of its own mucous membrane is ineffective. From these facts we learn that although the muscle of the œsophagus may possess a feeble power of spontaneous peristaltic contraction, yet this is usually in abeyance, or at least overmastered by nervous control; so that impulses, passing from a nerve centre and travelling down in regular progression along the œsophageal nerves, excite the muscular fibres in succession from the upper to the lower end of the tube.

The centre for the whole involuntary stage (both pharyngeal and œsophageal) of deglutition lies in the upper part of the medulla oblongata. When the brain is sliced away above the medulla deglutition is not affected, but if the upper part of the medulla is removed, the power of swallowing is abolished. In man disease of the spinal bulb interferes far more with deglutition than disease of the brain proper.

Normally the afferent impulses to the centre are set up by the contact of food or saliva with the mucous membrane of the posterior part of the tongue, the soft palate and the fauces, the nerve-channels being the superior laryngeal, the pharyngeal branches of the vagus, and the palatal branches of the fifth nerve. A feather has sometimes been swallowed involuntarily by a reflex movement of deglutition set up while the soft palate or pharynx were being tickled to produce vomiting. Artificial stimulation of the central end of the superior laryngeal will cause the movements of degluti-

tion independently of the presence of food or liquid; but if the central end of the glosso-pharyngeal nerve be stimulated at the same time, the movements do not occur. The glosso-pharyngeal is therefore able to inhibit the deglutition centre, and it is probably owing to the action of this nerve that in a series of efforts at swallowing, repeated within less than a certain short interval (about a second), only the last is successful.

The efferent nerves of the reflex act of deglutition are the hypoglossal to the tongue and the thyro-hyoid and other muscles concerned in raising the larynx; the glosso-pharyngeal, vagus, facial and fifth to the muscles of the palate, fauces, and pharynx; the fifth to the mylo-hyoid; and the vagus to the larynx and œsophagus. Section of the vagus interferes with the passage of food along the œsophagus; stimulation of its peripheral end causes œsophageal movements.

Movements of the Stomach and Intestines.—The whole of the stomach does not take part equally in the movements associated with digestion. We may divide the organ, both anatomically and functionally, into two portions—a pyloric portion, or *antrum pylori*, and a larger cardiac portion, or *fundus*.* At the junction of the antrum and the fundus the circular muscular coat is thickened into a ring called the 'transverse band,' or 'sphincter of the antrum.' When the stomach is empty it is contracted and at rest. A few minutes after food is taken contractions begin in the antrum, and run on in constricting undulations (in the cat at the rate of six in the minute) towards the pyloric sphincter. Feeble at first, they become stronger and stronger as digestion proceeds, and gradually come to involve the portion of the fundus next the sphincter of the antrum, but apparently their direction is always towards the pylorus, never, in normal digestion, away from it. The food is thus subjected to energetic churning movements in the pyloric end of the

* Here 'fundus' is used in the sense in which it is generally employed in speaking of the stomach of the dog or cat as signifying the whole of the organ with the exception of the antrum pylori. The fundus of the human stomach is, properly speaking, only the cul-de-sac at the cardiac end; the portion intervening between it and the antrum pylori is often termed the body of the stomach.

stomach, and worked up thoroughly with the gastric juice. Kept in constant circulation, it gradually becomes reduced to a semi-liquid mass, the chyme, which is at intervals driven against the pylorus by strong and regular peristaltic contractions of the lower end of the stomach, the sphincter relaxing from time to time by a sort of reflex inhibition to admit the better-digested portions into the duodenum, but tightening more stubbornly at the impact of a hard and undigested morsel. The cardiac end, with the exception of the portion that borders the transverse band, appears to take no share in these peristaltic movements. And, indeed, it is far more difficult to cause such contractions by artificial stimulation in the fundus than in the pylorus. The two portions of the stomach seem to be partially, or in certain animals from time to time completely, cut off from each other by the contraction of the sphincter of the antrum. The fundus, so far as its mechanical functions are concerned, appears to act chiefly as a reservoir for the food, which it gradually passes into the antrum as digestion goes on, by a tonic contraction of its walls. These facts have been mainly ascertained by observations on animals, such as the dog and the cat, either by direct inspection after opening the abdomen (Rossbach), or in the intact body by means of the Röntgen rays (Cannon). In the latter method the food is mixed with subnitrate of bismuth, which is opaque to these rays, so that when the animal is looked at through a fluorescent screen the stomach appears as a dark shadow in the field.

In the intestine two kinds of movements are to be seen: (1) Gentle, swaying, 'pendulum' movements, sometimes irregular, but often recurring rhythmically at the rate (in the dog) of 10 or 12 in the minute. Both the longitudinal and the circular muscular coats contract, causing slight waves of constriction, which may originate at any part of the gut, but nearly always travel from above downwards, with a velocity of 2 to 5 centimetres per second. (2) True peristaltic movements, in which a ring of constriction, obliterating the lumen, moves slowly down the tube, with a speed, it may be, no greater than 1 mm. per second. The portion of the intestine immediately below the advancing constriction is

relaxed and motionless, so that we may say that a wave of inhibition precedes the wave of contraction. The peristaltic movements of the small intestine, the most typical of their kind, are most easily excited by mechanical stimulation of the mucous membrane, as by the contact of a morsel of food or an artificial bolus of cotton-wool. Travelling, under normal conditions, always downwards, the constriction squeezes the contents of the tube before it, and the wave usually ends at the ileo-cæcal valve, which separates the small intestine from the large. The cause of the definite direction of the peristaltic wave is grounded in the anatomical relations of the intestinal wall. For when a portion of the intestine is resected, turned round in its place and sutured, so that what was before its upper is now its lower end, the contraction wave appears to be unable to pass, and the obstruction to the onward flow of the intestinal contents causes marked dilatation of the gut, and sometimes serious disturbance of nutrition. The most probable explanation is that the peristalsis is governed by a local reflex nervous mechanism (Auerbach's plexus), the stimulation of which by the contact of the food with the mucous membrane or by the distension of the gut causes excitation of the circular muscular fibres above the point of stimulation and inhibition of them below it. On the other hand, the pendulum movements appear to be myogenic in origin and independent of the nervous system (Bayliss and Starling). This distinction is borne out by the difference in the effect of poisons like cocaine and nicotine, which paralyze the local nervous mechanism,on the two kinds of contractions. The pendulum movements are, if anything, increased in intensity and made more regular. But the peristaltic waves, although they can be locally excited by direct stimulation of the muscular fibres, are no longer propagated, and a bolus introduced into the intestine remains at rest where it is placed. Under certain conditions it appears that a reverse or anti-peristalsis can be set up in the intact body, *e.g.*, in the case of obstruction of the intestine leading to vomiting of its contents. But such a reversal of the normal direction is not easy to realize by artificial stimulation, and even when an antiperistaltic

wave is started it travels up the intestine only for a short distance and then dies out. The movements of the large intestine do not differ essentially from those of the small. They start at the ileo-cæcal valve and travel downwards, but do not normally reach the rectum, which, except during defæcation, remains at rest.

Influence of the Central Nervous System on the Gastro-intestinal Movements.—As we have already said, these movements are much less closely dependent on the central nervous system than are those of the œsophagus; they can not only go on, but are in general better marked when the extrinsic nervous connections are cut; they cannot spread when the continuity of the tube is destroyed, and the mere presence of food will excite them when other than local reflex action has been excluded by section of the nerves. Nevertheless, the central nervous system does exercise some influence in the way of regulation and control, if not in the way of direct initiation of the movements, and the swallowing or even the smell of food has been observed to strengthen the contractions of a loop of intestine severed from the rest, but with its nerves still intact. The vagus is the efferent channel of this reflex action: stimulation of its peripheral end may cause movements of all parts of the alimentary canal from œsophagus to large intestine, except the cardiac end of the stomach (Meltzer), and may strengthen movements already going on; but section of it does not stop them, nor hinder the food from causing peristalsis wherever it comes. The vagus also contains inhibitory fibres for the lower end of the œsophagus and the whole of the stomach, including the cardiac sphincter. The splanchnic nerves contain fibres by which the intestinal movements can be inhibited, and they appear to be always in action, for after section of these nerves the movements are strengthened. On the other hand, stimulation of the peripheral end of the cut splanchnic causes arrest of the movements. Occasionally, however, it has the opposite effect. Contractions of the small intestine are more easily caused by excitation of the vagus after the inhibitory splanchnic nerves have been cut.

The lower part of the large intestine is influenced by the sacral nerves (second, third and fourth sacral in the rabbit), and by certain

lumbar nerves, in the same way as the higher parts of the alimentary canal, and particularly the small intestine, are influenced by the vagus and the splanchnics. Stimulation of these sacral nerves within the spinal canal causes contraction, tonic or peristaltic, of the descending colon and rectum; stimulation of the lumbar nerves or of the portions of the sympathetic into which their visceral fibres pass (lumbar sympathetic chain from second to sixth ganglia, or the rami from it to the inferior mesenteric ganglia) causes inhibition of the movements, preceded, it may be, by a transient increase.

Stimulation of the sacral nerves causes or increases the contraction of both coats of the descending colon and rectum; stimulation of the lumbar nerves inhibits both. And in the small intestine the same law holds good; the two coats are contracted together by the action of the vagus, or inhibited together by that of the splanchnics. With the establishment of these facts an ingenious theory, originated by v. Basch, falls to the ground. He supposed that the same nerve which causes contraction of the circular coat in all tubes whose walls are made up of two layers of muscle also contains fibres that bring about inhibition of the longitudinal coat, and *vice versâ*. It was suggested that in this way antagonism between the two coats was prevented.

Some drugs, such as strychnia, stimulate peristaltic movements by acting through the central nervous system; others, like muscarine, by acting directly on the local nervous mechanism of the intestine. Atropia antagonizes the action of muscarine by local influence. Morphia, which is much used in medicine to diminish intestinal movements, also appears to act locally, although it is said that after this drug the intestinal walls are steadily contracted, not relaxed. Venous blood in some animals, but apparently not in all, has a stimulating effect, causing movements which much surpass the normal movements, both in their vigour and in the speed with which they travel. For this reason the peristaltic contractions seen on opening the abdomen in a recently killed rabbit give an exaggerated picture of what actually occurs in the intact body.

Defæcation is partly a voluntary and partly a reflex act. But in the infant the voluntary control has not yet been developed; in the adult it may be lost by disease; in an animal it may be abolished by operation, and in each case the action becomes wholly reflex. In the normal course of events, the rectum, which is empty and quiescent in the intervals of defæcation, is excited to contraction as soon as

fæces begin to enter it through the sigmoid flexure, and the sensations caused by their presence give rise to the desire to empty the bowels. This desire may for a time be resisted by the will, or it may be yielded to. In the latter case the abdominal muscles are forcibly contracted, and the glottis being closed, the whole effect of their contraction is expended in raising the pressure within the abdomen and pelvis, and so driving the fæces from the colon to the rectum. The sphincter ani is now relaxed by the inhibition of a centre in the lumbar portion of the spinal cord, through the activity of which the tonic contraction of the sphincter is normally maintained. This relaxation is partly voluntary, the impulses that come from the brain acting probably through the medium of the lumbar centre; but in the dog, after section of the cord in the dorsal region, the whole act of defæcation, including contraction of the abdominal muscles and relaxation of the sphincter, still takes place, and here the process must be purely reflex. The contraction of the levatores ani helps to resist over-distension of the pelvic floor and to pull the anus up over the fæces as they escape.

Vomiting.—We have seen that under normal conditions the movements of the alimentary canal always tend to carry the food in one definite direction, along the tube from the mouth to the rectum. The peristaltic waves generally run only in this direction, and, further, regurgitation is prevented at three points by the cardiac and pyloric sphincters of the stomach and the ileo-cæcal valve. But in certain circumstances the peristalsis may be reversed, one or more of the guarded orifices forced, and the onward stream of the intestinal contents turned back. In obstruction of the bowel, the fæcal contents of the large intestine may pass up beyond the ileo-cæcal valve, and, reaching the stomach, be driven by an act of vomiting through the cardiac orifice; in what is called 'a bilious attack,' the contents of the duodenum may pass back through the pylorus and be ejected in a similar way; or, what is by far the most common case, the contents of the stomach alone may be expelled.

Vomiting is usually preceded by a feeling of nausea and a rapid secretion of saliva, which perhaps serves, by means of the air carried down with it when swallowed, to dilate the

cardiac orifice of the stomach, but may be a mere by-play of the reflex stimulation bringing about the act. The diaphragm is now forced down upon the abdominal contents, the glottis closed, and the abdominal muscles strongly contracted. At the same time the stomach itself, and particularly the antrum pylori, contracts, the cardiac orifice relaxes, and the gastric contents are shot up into the pharynx, and issue by the mouth or nose. Either the diaphragm and abdominal muscles alone, without the stomach, or the diaphragm and stomach together, without the abdominal muscles, can carry out the act of vomiting. For an animal whose stomach has been replaced by a bladder filled with water can be made to vomit by the administration of an emetic (Magendie); and Hilton saw that a man who lived fourteen years after an injury to the spinal cord at the height of the sixth cervical nerve, which caused complete paralysis below that level, could vomit, though with great difficulty. In a young child, in which very slight causes will induce vomiting, the stomach alone contracts during the act. But in the adult such a contraction is ineffectual, and the same is the case in animals, for a dog under the influence of a moderate dose of curara, which paralyzes the voluntary muscles but not the stomach, cannot vomit.

The nerve centre is in the medulla oblongata. It may be excited by many afferent channels: the sensory nerves of the fauces or pharynx, of the stomach or intestines (as in strangulated hernia), of the liver or kidney (as in cases of gallstone or renal calculi), of the uterus or ovary, and of the brain (as in cerebral tumour), are all capable, when irritated, of causing vomiting by impulses passing along them to the vomiting centre.

The vagus nerve in man certainly contains afferent fibres by the stimulation of which this centre can be excited, for it has been noticed that when the vagus was exposed in the neck in the course of an operation, the patient vomited whenever the nerve was touched (Boinet, quoted by Gowers). In meningitis, vomiting is often a prominent symptom, and is sometimes due to irritation of the vagus nerve by the inflammatory process.

Some drugs act as *emetics* by irritating surfaces in which

efficient afferent impulses may be set up, the gastric mucous membrane, for example; sulphate of zinc and sulphate of copper act mainly in this way. Apomorphia, on the other hand, stimulates the centre directly, and this is also the mode in which vomiting is produced in certain diseases of the medulla oblongata. The efferent nerves for the diaphragm are the phrenics, for the abdominal muscles the intercostals. The impulses which cause contraction of the stomach pass along the vagi. Dilatation of the cardiac orifice is brought about partly by the shortening of muscular fibres, which spread out upon the stomach from the lower end of the œsophagus, perhaps partly by nervous inhibition.

II. The Chemical Phenomena of Digestion.

The chemical changes wrought in the food as it passes along the alimentary canal are due to the secretions of various glands, which line its cavities, or pour their juices into it through special ducts. These secretions owe their power for the most part to substances present in them in very small amount, but which, nevertheless, act with extraordinary energy upon the various constituents of the food, causing profound changes without being themselves used up, or their digestive power affected. These marvellous and as yet mysterious agents are the unformed or unorganized ferments—unorganized because, unlike some other ferments, such as yeast, their action does not depend upon the growth of living cells. Their chemical nature has not been exactly made out; some of them at least do not appear to be proteids. But it is doubtful whether even one of the ferments of the digestive juices has as yet been satisfactorily isolated, and at present it is only by their effects that we recognise them. Some of them act best in an alkaline, some in an acid medium; they all agree in having an 'optimum' temperature, which is more favourable to their action than any other; a low temperature suspends their activity, and boiling abolishes it for ever. The action of all of them seems to be *hydrolytic; i.e.*, it is accompanied with the taking up of the elements of water by the substance acted upon. The accumulation of the products of the action first checks and then arrests it.

Besides these unformed ferments, certain formed ferments, or micro-organisms, are present in parts of the alimentary canal, and even in normal digestion contribute to the changes brought about in the food; while under abnormal conditions they may awaken into troublesome, and even dangerous, activity. It is possible that many of these act by producing unorganized ferments, and that the distinction between the two kinds of ferments is rather superficial.

It is now necessary to consider in detail the nature of the various juices yielded by the digestive glands, and the mechanism of their secretion, so far as it is known to us. Since it is along the digestive tract that glandular action is seen on the greatest scale, this discussion will practically embrace the nature of secretion in general. And here it may be well to say that, although in describing digestion it is necessary to break it up into sections, a true view is only got when we look upon it as a single, though complex, process, one part of which fits into the other from beginning to end. It is, indeed, the duty of the physiologist, wherever it is possible to insert a cannula into a duct and to drain off an unmixed secretion, to investigate the properties of each juice upon its own basis; but it must not be forgotten that in the body digestion is the joint result of the chemical work of five or six secretions, the greater number of which are actually mixed together in the alimentary canal, and of the mechanical work of the gastro-intestinal walls.

The Chemistry of the Digestive Juices.

(1) **Saliva.**—The saliva of the mouth is a mixture of the secretions of three large glands on each side, and of many small ones. The large glands are the parotid, which opens by Stenson's duct opposite the second upper molar tooth; the submaxillary, which opens by Wharton's duct under the tongue; and the sublingual, opening by a number of ducts near and into Wharton's. The small glands are scattered over the sides, floor, and roof of the mouth, and over the tongue.

Two types of salivary glands, the *serous* or *albuminous* and the *mucous*, are distinguished by structural characters and by the nature of their secretion; and the distinction has

been extended to other glands. The parotid of many, if not all, mammals is a purely serous gland; it secretes a watery juice with a general resemblance in composition to dilute blood-serum. The submaxillary of the dog and cat is a typical mucous gland; its secretion is viscid, and contains mucin. The submaxillary gland of man is a mixed gland; mucous and serous alveoli, and even mucous and serous cells, are intermingled in it (Plate II., Fig. 1). The submaxillary of the rabbit is purely serous. The sublingual is in general a mixed gland, but with far more mucous than serous alveoli.

The mixed saliva is a somewhat viscous, colourless liquid of low specific gravity (average about 1005), alkaline to litmus, acid to phenolphthalein. Besides water and salts, it contains mucin (entirely from the submaxillary, the sublingual and the small mucous glands of the mouth), to which its viscidity is due, traces of serum-albumin and serum-globulin (chiefly from the parotid), and a ferment—ptyalin. The salts are calcium carbonate and phosphate (often deposited as 'tartar' around the teeth, occasionally as salivary calculi in the glands and ducts), sodium bicarbonate, sodium and potassium chloride, and almost always, a trace of sulphocyanide of potassium, detected by the red colour which it strikes with ferric chloride.* The total solids amount only to five or six parts in the thousand. A great deal of carbon dioxide can be pumped out from saliva, as much as 60 to 70 c.c. from 100 c.c. of the secretion, *i.e.*, more than can be obtained from venous blood. Only a small proportion of this is in solution, the rest existing as carbonates. A very small quantity of oxygen (about 0·5 volume per cent.) appears also to be present even in saliva which has not come into contact with the air (Pflüger). Under the microscope epithelial scales, leucocytes (the so-called salivary corpuscles), bacteria, and portions of food, may be found. All these things are as accidental as the last—they are mere flotsam and jetsam, washed by the saliva from the inside of the mouth. But greater significance

* In 100 students the saliva only once failed to give the reaction, and in this individual a trace of sulphocyanide was present 3 days later. It is absent from the saliva of many animals. In 25 dogs submaxillary saliva obtained by stimulation of the chorda tympani only once contained a trace of it.

attaches to certain peculiar bodies, either spherical or of irregular shape, that are seen in the viscid submaxillary saliva of the dog or cat. They appear to be masses of secreted material. The quantity of saliva secreted in the twenty-four hours varies a good deal. On an average it is from 1 to 2 litres. (Practical Exercises, p. 375.)

Besides its functions of dissolving sapid substances, and so allowing them to excite sensations of taste, of moistening the food for deglutition and the mouth for speech, and of cleansing the teeth after a meal, saliva, in virtue of its ferment, ptyalin, is amylolytic; that is, it has the power of digesting starch and converting it into maltose, a reducing sugar. In man the secretion of any of the three great salivary glands has this power, although that of the parotid is most active. In the dog, on the other hand, parotid saliva has little action on starch, and submaxillary none at all; while in animals like the rat and the rabbit the parotid secretion is highly active. In the horse, sheep, and ox, the saliva secreted by all the glands seems equally inert. A watery or glycerine extract of a gland whose natural secretion is active also possesses amylolytic power.

Starch-grains consist of granulose enclosed in envelopes of cellulose. Only the granulose is acted upon by ptyalin, and hence unboiled starch, in which the cellulose envelopes are intact, is but slowly affected by saliva. When starch is boiled, the envelopes are ruptured, and the granulose passes into imperfect solution, yielding an opalescent liquid. If a little saliva be added to some boiled starch solution which is free from sugar, and the mixture be set to digest at a suitable temperature (say 40° C.), the solution in a very short time loses its opalescence and becomes clear. It still, however, gives the blue reaction with iodine; and Trommer's test (p. 23) shows that no sugar has as yet been formed. The change is so far purely a physical one; the substance in solution is soluble starch. Later on the iodine reaction passes gradually through violet into red; and finally iodine causes no colour change at all, while maltose is found in large amount, along with isomaltose, a sugar having the same formula as maltose, but differing from it in the melting point of the crystalline compound formed by it with phenyl

hydrazine (p. 431). Traces of dextrose, a sugar which rotates the plane of polarization less than maltose, but has greater reducing power, are produced by the further action of the saliva on maltose itself. When a small quantity of ferment acts for a short time, the production of isomaltose is favoured. The production of maltose and dextrose is favoured by the prolonged action of a large quantity of ferment.

The red colour indicates the presence of a kind of dextrin called erythrodextrin; the violet colour shows that at first this is still mixed with some unchanged starch. Soon the erythrodextrin disappears, and is succeeded by another dextrin, which gives no colour with iodine, and is therefore called achroodextrin. This is partly, but in artificial digestion never completely, converted into maltose, and can always at the end be precipitated in greater or less amount by the addition of alcohol to the liquid. It is probable that a whole series of dextrins is formed during the digestion of starch. Some of these may appear as forerunners of the sugar, others merely as concomitants of its production. The latter may never pass into sugar; and it is certain that sugar may appear before all the starch has been converted into achroodextrin. When the sugar is removed as it is formed, as is approximately the case when the digestion is performed in a dialyser, the residue of unchanged dextrin is less than when the sugar is allowed to accumulate (Lea). In ordinary artificial digestion, for instance, under the most favourable circumstances at least 12 to 15 per cent. of the starch is left as dextrin; in dialyser digestions the residue of dextrin may be little more than 4 per cent. This goes far to explain the complete digestion of starch which takes place in the alimentary canal, a digestion so exhaustive that, although soluble starch and dextrin may be found in the stomach after a starchy meal, they do not occur in the intestine, or only in minute traces. Here the amylolytic ferment of the pancreatic juice, which is essentially the same in its action as ptyalin, only more powerful, must effect a very complete conversion of the starch molecules accessible to its attack. It is not inconsistent with this, that unchanged starch granules may sometimes be excreted in the fæces, especially when imbedded in raw vegetable structures.

It is impossible with our present knowledge to represent the entire process by a chemical equation. If we look only to the final product, the equation

$$(C_6H_{10}O_5)_a + \frac{a}{2}H_2O = \frac{a}{2}(C_{12}H_{22}O_{11})$$

Starch. Water. Maltose.

or

$$2(C_6H_{10}O_5)_a + aH_2O = aC_{12}H_{22}O_{11}$$

will represent the change in natural and complete digestion. The molecule of starch being taken as some unknown multiple, a, of the group $C_6H_{10}O_5$, the first equation suits the case of a being an even number, and the second that of a being an odd number.

If we accept 4 per cent. as the minimum residue of unchanged dextrin in the best artificial digestion, or, in other words, if we suppose that of 25 parts of starch 24 are changed into maltose, and 1 remains as dextrin, our equation, taking the dextrin molecule as a multiple b of $C_6H_{10}O_5$, will be:

$$25(C_6H_{10}O_5)_a + 12aH_2O = 12a(C_{12}H_{22}O_{11}) + \frac{a}{b}(C_6H_{10}O_5)_b$$

Starch. Water. Maltose. Dextrin.

for the case where $\frac{a}{b}$ is a whole number. If $\frac{a}{b}$ is not a whole number, we should have to clear of fractions by multiplying both sides by $\frac{b}{m}$, where m is the greatest common measure of a and b. We should thus get:

$$25\frac{b}{m}(C_6H_{10}O_5)_a + 12a\frac{b}{m}H_2O = 12a\frac{b}{m}(C_{12}H_{22}O_{11}) + \frac{a}{m}(C_6H_{10}O_5)_b.$$

Starch. Water. Maltose. Dextrin.

It is a notable fact that amylolytic ferments are not confined to the animal body. Diastase, which is present in all sprouting seeds, and may be readily extracted by water from malt, forms maltose and dextrin from starch. Its optimum temperature, however, is about 65° C., while that of ptyalin is about 40° C.

While a neutral or weakly alkaline reaction is not unfavourable to salivary digestion, it goes on best in a slightly acid medium (Kübel). But an acidity equal to that of a ·1 per cent. solution of hydrochloric acid stops it completely, although the ferment is still for a time able to act when the acidity is sufficiently reduced. Strong acids or alkalies permanently destroy it. These facts show that in the mouth, where the reaction is weakly alkaline, the conditions are comparatively favourable to the action of the ptyalin. They

are still more favourable in the stomach for some time after the beginning of a meal, while the reaction is yet weakly acid. But during the greater part of gastric digestion the degree of acidity is such that the ptyalin must be hindered. Although the food stays but a short time in the mouth, there is no doubt that, in man at least, some of the starch is there changed into sugar (p. 376). But this does not seem to be the case in all animals. Something depends on the amylolytic activity of the saliva, and something upon the form in which the starchy food is taken, whether it is cooked or raw, enclosed in vegetable fibres or exposed to free admixture with the secretions of the mouth.

It is important to note here that hydrolytic changes of very much the same nature as those produced by ptyalin can be brought about in other ways. If starch is heated for a time with dilute hydrochloric or sulphuric acid, it is changed first into dextrin, and then into a form of reducing sugar, which, however, is not maltose, but dextrose. If maltose is treated with acid in the same way, it is also changed into dextrose. When glycogen (p. 446) is boiled with dilute oxalic acid at a pressure of three atmospheres, isomaltose and dextrose are formed (Cremer). We shall see later on that the action of other ferments can also be to a certain extent imitated by purely artificial means. In fact, some of the ferments accomplish at a comparatively low temperature what can be done in the laboratory at a higher temperature, and by the aid of what we may call more violent methods.

(2) **Gastric Juice.**—The Abbé Spallanzani, although not, perhaps, the first to recognise, was the first to study systematically, the chemical powers of the gastric juice, but it was by the careful and convincing experiments of Beaumont that the foundation of our exact knowledge of its composition and action was laid.

It is difficult to speak without enthusiasm of the work of Beaumont, if we consider the difficulties under which it was carried on. An army surgeon stationed in a lonely post in the wilderness that was then called the territory of Michigan, a thousand miles from a University, and four thousand from anything like a physiological laboratory, he was accidentally called upon to treat a gun-shot wound of the stomach in a Canadian voyageur, Alexis St. Martin.

When the wound healed a permanent fistulous opening was left, by means of which food could be introduced into the stomach and gastric juice obtained from it. Beaumont at once perceived the possibilities of such a case for physiological research, and began a series of experiments on digestion. After a while, St. Martin, with the wandering spirit of the voyageur, returned to Canada without Dr. Beaumont's consent and in his absence. Beaumont traced him, with great difficulty, by the help of the agents of a fur-trading company, induced him to come back, provided for his family as well as for himself, and proceeded with his investigations. A second time St. Martin went back to his native country, and a second time the zealous investigator of the gastric juice, at heavy expense, secured his return. And although his experiments were necessarily less exact than would be permissible in a modern research, the modest book in which he published his results is still counted among the classics of physiology. The production of artificial fistulæ in animals, a method that has since proved so fruitful, was first suggested by his work.

Gastric juice when obtained pure, as it can be from an accidental fistula in man, or by mechanically stimulating the mucous membrane of the stomach of a fasting dog through an artificial gastric fistula, or, better, by giving a dog with an œsophageal as well as a gastric fistula a 'sham-meal' (p. 343), is a thin, colourless liquid of low specific gravity (1002 to 1005) and distinctly acid reaction. The total solids average about 5 parts per thousand, about one half being inorganic salts, chiefly sodium and potassium chloride. Two ferments are present: pepsin, which changes proteids into peptones; and rennin, which curdles milk. The acidity is due to free hydrochloric acid, the proportion of which in man is usually something like ·2 per cent., but more in the dog (·3 to ·5 per cent.). Often but not always (Kocher) in cancer of the stomach the free hydrochloric acid is replaced by lactic acid, and it is known that in health some lactic acid is often present when the stomach contains food, being produced from the carbo-hydrates by the action of a ferment or ferments, not specific to gastric juice, but found everywhere in the alimentary canal. That in normal gastric juice the acidity is not due to lactic acid can be shown by Uffelmann's test (Practical Exercises, p. 380).

More than this, it is not due to an organic, but to an inorganic acid, for healthy gastric juice causes such an alteration in the colour of aniline dyes like congo-red and methyl violet, as would be produced by dilute mineral acids,

and not by organic acids, even when present in much greater strength.* Finally, when the bases and acid radicles of the juice are quantitatively compared, it is found that there is more chlorine than is required to combine with the bases; the excess must be present as free hydrochloric acid. The quantity of gastric juice secreted is very great; it has been estimated at as much as 5 to 10 litres in twenty-four hours, or five times as much as the quantity of saliva secreted in the same time. But such estimates are loose and uncertain.

The great action of gastric juice is upon proteids. In this two of its constituents have a share, the pepsin and the free acid. One member of this chemical copartnery cannot act without the other; peptic digestion requires the presence both of pepsin and of acid; and, indeed, an active artificial juice can be obtained by digesting the gastric mucous membrane with ·2 per cent. hydrochloric acid. A glycerine extract of a stomach which is not too fresh also possesses peptic powers; but it requires the addition of a sufficient quantity of acid to render them available.

Well-washed fibrin obtained from blood is a convenient proteid for use in experiments on digestion. Since the blood contains traces of pepsin, the fibrin should be boiled to destroy any which may be present.

If we place a little fibrin in a beaker, cover it with ·2 per cent. hydrochloric acid, add a small quantity of pepsin or of a gastric extract, and put the beaker in a water-bath at 40° C., the fibrin soon swells up and becomes translucent, then begins to be dissolved, and in a short time has disappeared (see Practical Exercises, p. 378). If we examine the liquid before digestion has proceeded very far, we shall find chiefly acid-albumin in solution; later on, chiefly albumoses; still later, peptones will be present along with the albumoses. From this we conclude that acid-albumin is a stage in the conversion of fibrin into albumose, and albumose a half-way house between acid-albumin and peptone. Similar, but not identical, intermediate substances occur in the digestion of the other proteids, as well as in that of bodies like gelatin, which are not true proteids, but which pepsin can digest. The generic name of proteose properly includes all bodies of the albumose type, the term 'albumose' itself being sometimes reserved for such intermediate products of the digestion of albumin;

* A dilute solution of congo-red is turned violet by organic and blue by inorganic acids; the gastric juice turns it blue. Methyl violet is rendered blue by an inorganic acid like hydrochloric acid, and green if more of the acid be added. It is not altered by organic acids. Gastric juice turns it blue.

while those of fibrin are called fibrinoses ; of globulin, globuloses ; of casein, caseoses ; and so on. Probably the peptones produced from different proteids are also not absolutely identical.

Beyond peptone gastric digestion does not go. Indeed, in no case does the whole, and only under very favourable conditions even the half, of the original proteid in an artificial digestion ever reach the stage of peptone. The pancreatic juice, as we shall see later on, not only effects a more complete conversion into peptone, but can split up peptone itself into substances which are no longer proteid. Since the subject of proteid digestion must come up again, it will be well to postpone any closer discussion of the process till we can view it as a whole. In the meantime it is only necessary to repeat that pepsin alone cannot digest proteids at all. Its action requires the presence of an acid ; in a neutral or alkaline medium peptic digestion stops. As in the case of other ferments, there is a certain temperature at which pepsin acts best, an 'optimum' temperature (35° to 40° C., or about that of the body). At 0° C. it is inactive, except in cold-blooded animals (frog). Boiling destroys it.

Dilute acid alone does not dissolve coagulated proteids like boiled fibrin, or does so only with extreme slowness. Uncoagulated proteids, however, are readily changed by it into acid-albumin; and by the prolonged action of acids, especially at a high temperature, further changes may be caused in all proteids, apparently of much the same nature as those produced in peptic digestion. But under the ordinary conditions of natural or artificial gastric digestion, it may be said that the acid alone does little until it is aided by the ferment, just as the ferment alone does nothing without the aid of the acid. One striking difference, however, there is: the acid is used up during the process ; the ferment is little, if at all, affected. Although hydrochloric acid acts most powerfully, other acids, such as lactic, phosphoric, or sulphuric, can replace it.

The milk-curdling ferment, *rennin*, is contained in large amount in an extract of the fourth stomach of the calf, which has long been used in the manufacture of cheese. It exists in the healthy gastric juice of man, but disappears in cancer of the stomach and in chronic gastric catarrh.

It can be separated from pepsin by precipitating an acid extract of calf's stomach with magnesium carbonate in powder, and some neutral acetate of lead. The pepsin is mechanically carried down with the precipitate, but most of the rennin remains in solution. The curdling of milk by rennin is essentially a coagulation of casein. It seems to be produced by the splitting up of a more complex body, *caseinogen*, into two substances, one of which, *casein*, is insoluble (in the presence of calcium phosphate, but not otherwise), and forms the curd; while the other, *whey-proteid*, is soluble, and passes into the whey. Dilute acid will of itself precipitate casein, and the presence of acid, and particularly hydrochloric acid, in the gastric juice helps the action of the milk-curdling ferment. That a ferment is really concerned in the process is, however, shown by the fact that the juice, after being made neutral or alkaline, still curdles milk, and that this power is destroyed by boiling. The optimum temperature is the same as that of the other ferments of the digestive tract, about 40° C. (p. 379).

As to the exact function which the milk-curdling ferment of the gastric juice performs in digestion, we have no precise knowledge. It seems superfluous if we suppose that the free acid is able of itself to do all that the ferment does along with it. But there is evidence that the curd produced by the ferment is more profoundly changed than the precipitate caused by dilute acids; for the latter may be redissolved, and then again curdled by rennin, while this cannot be done with the former. We may suppose, then, that the ferment is capable of effecting changes more favourable to the subsequent action of the pepsin upon the casein than those which the acid alone would effect. Or it may be that the ferment acts in the early stages of digestion before much acid has been secreted. We do not know whether the curdling of milk renders it easier for the watery portion to be absorbed by the walls of the stomach. If this were the case, it would be a *raison d'être* for early curdling, since milk is a very dilute food, and the immense proportion of water in it might weaken the gastric juice too much for rapid digestion of the proteids.

On fats gastric juice has no action, although it will dissolve the proteid constituents of fat-cells, and the proteid substances

which keep the fat-globules of milk apart from each other. As regards the carbo-hydrates the swallowed saliva will continue to act on starch in the stomach, so long as the acidity is not too great; while the hydrochloric acid of the gastric juice is able to invert cane-sugar, changing it into a mixture of dextrose and levulose* ('invert' sugar).

(3) **Pancreatic Juice.**—Pancreatic juice, bile, and intestinal juice, of which the first two are the most important, are all mingled together in the small intestine, and act upon the food, not in succession, but simultaneously. But by artificial fistulæ in animals they can all be obtained separately; and occasionally some of them can be procured through accidental fistulæ in the human subject.

Pancreatic juice, as obtained from a dog, by means of a cannula tied in the duct of Wirsung through an opening in the linea alba, is a clear, viscid liquid of distinctly alkaline reaction. It differs notably from saliva and gastric juice in its high specific gravity (about 1030), and the large proportion of solids in it, which may be as much as 10 per cent., or, roughly speaking, about the same as in blood-plasma. About nine-tenths of the solids consist of proteids, and rather less than one-tenth of inorganic material (chiefly sodium carbonate, to which the alkaline reaction is due, and sodium chloride). Traces of fats, soaps and leucin may also be present. When the juice is heated to near the boiling-point, a copious precipitate of coagulated albumin is formed. The fresh juice coagulates spontaneously, especially at a low temperature; but the coagulum is soon digested. Possibly cold hinders the destructive power of the juice on the factors necessary for coagulation more than it restrains the process of clotting. The quantity of pancreatic juice secreted during the twenty-four hours in an average man has been estimated at 200 to 300 c.c. An artificial pancreatic juice can be made by extracting the pancreas, which must not be too fresh (p. 380), with water or glycerine.

* These are both reducing sugars, but, as their names indicate, they rotate the plane of polarization in opposite directions. The specific rotatory power of levulose is greater than that of dextrose, so that when cane-sugar is completely inverted, although equal quantities of dextrose and levulose are produced, the plane of polarization is rotated to the left. Cane-sugar itself rotates it to the right.

Pancreatic juice contains four ferments: (1) A proteolytic or proteid-digesting ferment, *trypsin*; (2) an amylolytic ferment, *amylopsin*; (3) a fat-splitting or lipolytic ferment, *steapsin*, also called *pialyn*; (4) a milk-curdling ferment.

The last cannot be considered as taking any practical share in digestion, since it can hardly ever happen that milk passes through the stomach without being curdled.

Trypsin, to a certain extent, corresponds with pepsin in its action on proteids. But it acts energetically in an alkaline as well as in a not too acid medium (a very slight amount of digestion may go on in distilled water); and its action does not stop at the peptone stage—it can split up peptones into leucin, tyrosin, arginine, aspartic acid, and other nitrogenous substances simpler than proteids.

If fibrin is digested at a temperature of 40° C. with a 1 per cent. solution of sodium carbonate, to which a little pancreatic extract or juice has been added, along with a trace of thymol to prevent putrefaction, it is gradually eaten away without swelling up and becoming transparent as it does in peptic digestion; but some granular débris is always left (p. 380). This undigested residue is soluble in 1 per cent. sodium hydrate, but it is never entirely dissolved in any artificial digestion. In natural digestion, on the contrary, it is never found; just as some dextrin always remains when ptyalin has done its utmost upon starch outside the body, while in the intestine little or no dextrin can be detected. When the undigested residue is filtered off, the solution may still contain: (1) a substance resembling alkali-albumin, which is present only in small amount, as it is rapidly changed into (2) albumoses, (3) peptone, (4) leucin, tyrosin, and similar products. It will depend on how far the digestion has been carried whether, and in what quantity, any one of these bodies is present.

The order in which they appear and their relative amount at different stages of the digestion show that the alkali-albumin and albumoses are, like the acid-albumin and albumoses of peptic digestion, mainly, at any rate, intermediate substances through which proteid passes on its way to peptone; and there is no reason to believe that up to

this point there are any essential differences between the action of trypsin and pepsin.* In both cases the action seems to consist in a splitting up of the complex proteid with assumption of water, so that each successive product is further hydrated than the last; nor is it, as yet at least, possible to point out any radical distinction between the peptone of gastric and the peptone of pancreatic digestion. It is not necessary to suppose that the further splitting up of some of the peptone by trypsin into leucin, tyrosin, etc., is an action differing in kind so much as in degree from that which leads to the formation of peptone both in tryptic and in gastric digestion. Trypsin is a more powerful ferment than pepsin. And when we find, as we are apt to do, that a pancreatic digest contains less albumose and more peptone than a peptic digest made under similar conditions, we ascribe this not to a peculiar property possessed by the trypsin and lacking in the pepsin, but to a more energetic action of the former along the common lines. So when this action suffices to push the peptone still farther along the downward path, it is not necessary to assume that an influence radically different from that of pepsin is at work. This argument is strengthened when we find that without a ferment at all, by the prolonged action of various agents which cause hydration (dilute acids or alkalies, or superheated steam, or oxidizing substances like ozone), albumoses and peptones first, and ultimately leucin and tyrosin, may be formed from ordinary proteids. In fact, it would seem that when the complex proteid molecule is split up by proteolytic ferments, or by other and not too violent agents, there are certain favourite 'sets' or combinations into which its constituents are apt to fall, no matter how the decomposition may be brought about, bodies of the fatty and of the aromatic series being especially constant and conspicuous among the products. Leucin, $C_6H_{11}(NH_2)O_2$, for instance, is amido-caproic acid, in which amidogen (NH_2) has replaced one H in caproic acid ($C_6H_{12}O_2$), one of the

* It is scarcely a fundamental distinction that in a peptic digest several albumoses (proto-, hetero-, and deutero-albumose) may be found, and in a tryptic digest only deutero-albumose; for the other albumoses are readily converted into deutero-albumose.

fatty acid series. Tyrosin, $C_3H_4(C_6H_4OH)(NH_2)O_2$, is related to propionic acid ($C_3H_6O_2$), another of the fatty acids. If one H in propionic acid is replaced by NH_2 we get amido-propionic acid, $C_3H_5(NH_2)O_2$. If another H is replaced by oxyphenyl ($C_6H_4.OH$), an aromatic radicle, we get tyrosin.

As much as 8 to 10 per cent. of leucin, and 2 to 4 per cent. of tyrosin, may be produced in artificial tryptic digestion of fibrin (Lea, Kühne), but only a portion (about the half) of the peptones formed ever undergoes this change, no matter how long the digestion.

This and other facts have led to the theory that every natural proteid consists of two elements as regards the products into which it may be split by digestion—a *hemi* element and an *anti* element. Thus, albumin is supposed to consist of hemi-albumin and anti-albumin. When digested by trypsin, the hemi-albumin gives rise eventually to hemi-peptone, and the anti-albumin to anti-peptone. The hemi-peptone is comparatively unstable, and is further split up into leucin and tyrosin; the anti-peptone is comparatively stable, and resists further change.

As to the method in which the ferments bring about these profound changes, and the rôle played by the auxiliary acid or alkali, we are almost completely in the dark. Wurtz has supposed that papain, a ferment obtained from the juice of the fruit of the *Carica papaya*, which acts powerfully on proteids in much the same way as trypsin, unites temporarily with the proteid—with fibrin, for instance—and after the hydration of the latter is complete, is again set at liberty, and free to act on some more of the unchanged fibrin. He compares its action with that of some inorganic bodies, such as sulphuric acid, a small quantity of which may cause the hydration of a large amount of certain substances by forming temporary compounds with them, and being then set free to act again. In peptic digestion, however, the hydrochloric acid seems certainly to be used up. In the gastric juice it is perhaps united to the pepsin; and it is capable of forming combinations with all proteids, the lower proteids, such as peptone, combining with a greater proportion of the acid than the higher, such as fibrin or albumin.

In all that we have hitherto said regarding tryptic digestion we have supposed that putrefaction has been entirely prevented. If no antiseptic is added to a tryptic digest, it rapidly becomes filled with micro-organisms, and emits a very disagreeable fæcal odour; and now various bodies which are not found in the absence of putrefaction make their appearance, such as indol, skatol, and other substances to which the fæcal odour is due. They are not true products of tryptic digestion, but are formed by the putrefactive micro-organisms, which can themselves break up proteids into leucin and tyrosin, and change tyrosin into indol.

Amylopsin, the sugar-forming ferment of pancreatic juice, changes starch into dextrin and maltose, just as ptyalin does; but it is more powerful, and readily acts on raw starch as well as boiled.

Steapsin splits up neutral fats into glycerine and the corresponding fatty acids. The latter unite with the alkalies of the pancreatic juice and the bile to form soaps. In this important process, bile acts as the helpmate of pancreatic juice; together they effect much more than either or both can accomplish by separate action.

(4) **Bile.**—Bile is a liquid the colour of which varies greatly in different groups of animals, and even in the same species is not constant, depending on the length of time the bile has remained in the gall-bladder and other circumstances. When it is recognised that the colour depends on a series of pigments, which are by no means stable, and of which one can be caused to pass into another by oxidation or reduction, this want of uniformity will be easily intelligible. The fresh bile of carnivora is golden red; the bile of herbivorous animals is in general of a green tint, but, when it has been retained long in the gall-bladder, may incline to reddish-brown. Human bile is generally described as being of a reddish or golden-yellow colour, but it is doubtful whether this is true of the perfectly fresh secretion, for while Beaumont speaks of the yellowish bile which he could press into the stomach of St. Martin by manipulating the abdomen, bile flowing from a fistula has been observed to be green (Robson, Copeman and Winston). That of a monkey taken from the gall-bladder immediately after death is dark green, but if left a few hours in the gall-bladder it is brown, the green pigment having been reduced. This would seem to indicate that human bile, originally green, may alter its colour in the interval which must elapse before it can usually be obtained after death. Bile, as obtained from accidental fistulæ in otherwise healthy persons, has a much lower specific gravity than pancreatic juice (1008 to 1010). In the gall-bladder water is absorbed from the bile and mucin added to it, so that the specific gravity of bladder bile is as high as 1030 to 1040. The reaction is feebly alkaline. The composition of human bile from a fistula was approximately as follows:

Water		982 parts in 1,000	
Solids:			
Mucin and pigments	1·5		
Bile-salts	7·5		
Lecithin and soaps	1	18	„ „
Cholesterin	·5		
Inorganic salts	7·5		

It will be observed that no proteids are enumerated in this table; bile contains none, and it is unlike all the other digestive juices in this respect.

Mucin is scarcely to be looked upon as an essential constituent of bile; it is not formed by the actual bile-secreting cells, but by mucous glands in the walls and goblet-cells in the epithelial lining of the larger bile-ducts, and especially of the gall-bladder. The mucin of human bile is a true mucin, but that of ox-bile is a nucleo-albumin (p. 17). It may be removed by precipitation with alcohol or dilute acetic acid.

Bile-pigments.—It has been said that these form a series, but only two of the pigments of that series appear to be present in normal bile, bilirubin and biliverdin. In human bile as usually obtained, the former, in herbivorous bile and that of some cold-blooded animals, such as the frog, the latter, is the chief pigment. But in fresh human bile biliverdin may be chiefly present, and bilirubin can be extracted in large amount from the gallstones of cattle; while in the placenta of the bitch biliverdin is present in quantity, although, as in all carnivora, it is either absent from the bile or exists in it in comparatively small amount. All these facts show that the two pigments are readily interchangeable.

Bilirubin is best prepared from powdered red gallstones by dissolving the chalk with hydrochloric acid, and extracting the residue with chloroform, which takes up the pigment. From this solution, on evaporation, beautiful rhombic tables or prisms of bilirubin separate out; and the crystals are finer when the solution also contains cholesterin than when it is pure.

Biliverdin can be obtained from the placenta of the bitch by extraction with alcohol. It is insoluble in chloroform, and by means of this property it may be separated from bilirubin when the two happen to be present together in bile. Biliverdin can also be formed from bilirubin by oxidation. By the aid of active oxidizing agents, such as yellow nitric acid (which contains some nitrous acid), a whole series of oxidation products of bilirubin is obtained, beginning with biliverdin, and passing through bilicyanin, a blue pigment, to choletelin, a yellow substance. It is possible that there are other intermediate bodies. This is the foundation of *Gmelin's test for bile-pigments* (see Practical Exercises, p. 381). The same substances are produced, and in the same order, when a solution of bilirubin in chloroform is treated with a dilute alcoholic solution of iodine.

The positive pole of a galvanic current causes the same oxidative changes, the same play of colours, while the reducing action of the

negative pole reverses the effect, if the action of the positive electrode has not gone too far. Starting from biliverdin, the negative pole causes the green to pass through yellowish-green into golden-yellow, and ultimately into pale yellow, indicating a series of bodies formed by reduction of the biliverdin. These reactions can also be used for the detection of bile-pigments.

By the reducing action of sodium amalgam, or of tin and hydrochloric acid, on bilirubin, but not apparently by electrolysis, hydrobilirubin is obtained. This is identical with the 'febrile' urobilin of some pathological urines, and with stercobilin, a pigment found in the fæces from birth onwards, although not in the meconium (pp. 359, 390), and therefore probably derived from the normal bile-pigment by reduction in the intestine itself, where reducing substances due to the action of micro-organisms are never absent in extra-uterine life. The changes occurring in oxidation and reduction of the bile-pigment may be partially represented as follows:

$$(\underset{\text{Bilirubin.}}{C_{32}H_{36}N_4O_6}) + O_2 = (\underset{\text{Biliverdin.}}{C_{32}H_{36}N_4O_8}), + 2O_2 = (\underset{\text{Choletelin.}}{C_{32}H_{36}N_4O_{12}})$$

$$2(\underset{\text{Bilirubin.}}{C_{32}H_{36}N_4O_6}) - O_2 + 4H_2O = 2(\underset{\text{Hydrobilirubin.}}{C_{32}H_{36}N_4O_5.2H_2O}).$$

Judging from the analogy of the blood-pigment—from which, as we shall see, the bile-pigment is derived, and the changes in which, through oxidation and reduction, have a certain superficial resemblance to those which bilirubin undergoes when it is converted into biliverdin, and which biliverdin undergoes when it passes back again to bilirubin—we might have expected bile to possess a characteristic spectrum.

This, however, is not the case. The bile of most animals shows no bands at all. The fresh bile of certain animals, the ox, for instance, does show bands—a strong one over C, and two weaker bands, one of which is just to the left of D, and the other to the right of it, but nearer D than E. The two last bands grow stronger when the bile is allowed to stand for twenty-four hours, and in about three days, in warm weather, a fourth sharp band may appear between C and B. But none of these bands are due to the normal bile-pigment, and they are not essentially changed when this is oxidized or reduced by electrolysis. MacMunn attributes the spectrum of the bile of the ox and sheep to a body which he calls cholohæmatin, and which does not belong to the bile-pigments proper. Of the derivatives of the bilirubin set, only the lowest and the highest members, hydrobilirubin and choletelin, are described as giving absorption spectra.

The Bile-salts.—These are the sodium salts of two acids, glycocholic and taurocholic. In human bile both are present, but the former in greater quantity than the latter; sometimes taurocholic acid is entirely absent. In the bile of the dog and cat only taurocholic acid is found; in that of the carnivora generally it is by far the more important of the two acids; in the bile of most herbivora there is much more glycocholic than taurocholic acid.

Both acids are made up of a non-nitrogenous body, cholic or

cholalic acid, and a nitrogenous body, glycin in glycocholic, and taurin in taurocholic acid.

The decomposition of the bile-acids into these substances is effected by boiling them with dilute acid or alkali, a molecule of water being taken up; thus—

$$\underset{\text{Glycocholic acid.}}{C_{26}H_{43}NO_6} + H_2O = \underset{\text{Glycin.}}{C_2H_5NO_2} + \underset{\text{Cholic acid.}}{C_{24}H_{40}O_5};$$

$$\underset{\text{Taurocholic acid.}}{C_{26}H_{45}NSO_7} + H_2O = \underset{\text{Taurin.}}{C_2H_7NSO_3} + \underset{\text{Cholic acid.}}{C_{24}H_{40}O_5}.$$

Taurocholic acid is much more easily broken up than glycocholic; even boiling with water is sufficient.

Glycin is amido-acetic acid, taurin is amido-isethionic acid, an atom of the hydrogen of the acid being in each case replaced by NH_2. A notable difference between glycocholic and taurocholic acid is that the latter contains sulphur. The whole of this belongs to the taurin.

Traces of cholic acid, formed by hydrolysis from the bile-acids, probably by the action of putrefactive bacteria, are found in the intestines, especially in the lower portion.

Pettenkofer's test for bile-acids (Practical Exercises, p. 381), accidentally discovered in examining the action of bile upon sugar, depends upon three facts: (1) That cholic acid and furfurol give a purple colour when brought together; (2) that the bile-salts yield cholic acid when acted upon by sulphuric acid; (3) that when cane-sugar is decomposed by strong sulphuric acid, furfurol is formed.

Since a similar colour is given when the same reagents are added to a solution containing albumin, it is necessary to remove this, if present, from any liquid which is to be tested for bile-acids.

Lecithin and *cholesterin* are by no means peculiar to bile. They are found in almost all the liquids of the body, and are especially important constituents of the nervous substance. The former is a crystallizable fat of a peculiar nature, containing nitrogen and phosphorus. It is unstable, and when heated with baryta-water it yields a soap, barium stearate, which is precipitated, and two other substances, choline and glycero-phosphoric acid, which remain in solution.

Cholesterin is a triatomic alcohol. It is best obtained from white gallstones, of which it is the chief, and sometimes almost the sole, constituent (see Practical Exercises, p. 382).

The chief inorganic salts of bile are sodium chloride, sodium carbonate, and alkaline sodium phosphate. The phosphoric acid of the ash comes partly from the phosphorus of organic compounds (lecithin and bile-mucin), the sulphuric acid from the sulphur of taurocholic acid, the sodium largely from the bile-salts. Iron is a notable inorganic constituent of bile, although it exists only in traces, in the form of phosphate of iron. Manganese is also present. 100 c.c. of fresh bile yields 50 to 100 c.c. of carbon dioxide, part of which is in solution and part combined with alkalies.

The quantity of bile secreted in twenty-four hours in an average man is probably from 750 c.c. to a litre.

The great **action of the bile in digestion** is undoubtedly the preparation of the fats for absorption. In this preparation two processes are important: a chemical process, *saponification*, or the formation of soaps from the fatty acids of decomposed neutral fats, and a physical process, *emulsification*, or the formation of a mechanical suspension of such fine globules of unaltered neutral fat as exist in milk. While there has been much discussion as to the relative share taken by saponification and emulsification in the *absorption* of fat (p. 370), there is no doubt that they are both concerned in the *digestion* of fat or the preparation of it for absorption. In this, indeed, the two processes are complementary, for an essential preliminary to emulsification in the intestine seems to be the formation of a certain amount of soaps, while the formation of an emulsion at least increases the surface of contact between the unaltered fat and the digestive juices, and so favours more rapid saponification. In both processes the bile plays a part, though not an independent one; it acts always in conjunction with the pancreatic juice.

No completely satisfactory explanation has been given of the precise nature of this partnership, but it is certain that the fat-splitting ferment of the pancreatic juice, on the one hand, and the bile-salts on the other, contribute largely to the total action. An alkaline solution, a solution of sodium carbonate, *e.g.*, is unable of itself to emulsify a perfectly neutral oil; but if some free fatty acid be added, emulsification is rapid and complete. Now, there is no doubt that here a soap is formed by the action of the alkali on the fatty acid, and there is equally little doubt that the formation of the soap is an essential part of the emulsification. But it is not clear in what manner the soap acts, whether by forming a coating round the oil-globules, or by so altering the surface tension, or other physical properties of the solution in which it is dissolved, that they no longer tend to run together. However this may be, in pancreatic juice we have the two factors present which this simple experiment shows to be necessary and sufficient for emulsification; we have a

ferment which can split up neutral fats and set free fatty acids, and an alkali which can combine with those acids to form soaps. Accordingly, pancreatic juice is able of itself to form emulsions with perfectly neutral oils. It is possible that the proteid constituents of pancreatic juice may have a share in emulsification. In bile, on the contrary, although the alkali is present, there is no fat-splitting ferment, and according to the best experiments, bile alone has no emulsifying power. But we now come to a remarkable fact: this inert bile when added to pancreatic juice greatly intensifies its emulsifying action, and a solution of bile-salts has much the same effect as bile itself. The fact is undoubted, but the explanation is obscure. What it is that bile or bile-salts can add to the pancreatic juice which so increases its power of emulsification, we do not know. It is indeed true that the bile, presumably in virtue of its alkaline salts, can, in presence of a free fatty acid, rapidly form an emulsion. But the pancreatic juice itself contains a considerable quantity of sodium carbonate.

A part of the effect of the bile seems to be due to its favouring in some way the fat-splitting action of the pancreatic juice. The capacity of dissolving soaps, which is a property of the bile-salts, appears also to be important in supplementing the solvent power of the intestinal liquids for the soaps formed by the pancreatic juice. But however the mutual action of the two juices on the digestion of fats may be explained, there is no doubt that they are equally necessary. For in some diseases of the pancreas fat or fatty acid often appears in the stools, and this token of imperfect digestion of the fatty food may be confirmed by the wasting of the patient; and the same occurs when the bile is prevented by obstruction of the duct or by a biliary fistula from entering the intestine.

The white stools of jaundice owe their colour, not merely to the absence of bile-pigment, but also to the presence of fat. Their highly offensive odour used to be adduced as evidence that bile is the 'natural antiseptic' of the intestine. It seems rather to be due to the coating of the particles of food with undigested fat, which shields the proteids from the action of the digestive juices while

permitting the putrefactive bacteria to revel in them unchecked. As a matter of fact, the bile itself has little, if any, power of hindering the growth of micro-organisms, although the free bile-acids are tolerably active antiseptics. In suckling children it is not uncommon to see the fæces white with fat. This is a less serious symptom than in adults, and perhaps betokens merely that the milk in the feeding-bottle is undiluted cow's milk, which is richer in fat than human milk, and ought to be mixed with an equal quantity of water.

Bidder and Schmidt found that the chyle in the thoracic duct of a normal dog contained 3·2 per cent. of fat. In a dog with the bile-duct ligatured the proportion fell to 0·2 per cent.

Bile has been credited with a physical power of aiding the passage of fat through membranes, and it has been inferred that this has an important bearing on the absorption of fat from the intestine. But the inference does not follow from the statement, and the statement has been itself denied.

On proteids bile has no digestive action, although, according to Rachford, the addition of it to fresh pancreatic juice considerably increases the proteolytic power of that secretion. The addition of bile to a gastric digest causes a precipitate of acid-albumin (parapeptone), albumose, and pepsin. The precipitate is soluble in excess of bile, or of a solution of bile-salts, but the pepsin has no longer any power of digesting proteids. Part of the bile-acids and bile-mucin is also thrown down by the acid of the digest.

It has been vaguely, and almost helplessly, suggested, in the laudable endeavour to find functions for the bile, that by thus precipitating the chyme bile prepares it for the action of the pancreatic juice. But it is difficult to see how the precipitation of a substance can prepare the way for its digestion, and it is doubtful whether the excess of bile required to neutralize the chyme and re-dissolve the precipitated proteids actually exists. The whole discussion, is, indeed, an illustration of the hazard that is run in transferring without great care the results of digestion *in vitro* to the normal and natural processes in the alimentary canal.

Although bile has sometimes a feebly amylolytic action, this is not to be included among its specific powers, for a diastatic ferment in small quantities is widely diffused in the body.

(5) **Succus entericus.**—This is the name given to the special secretion of the small intestine, which is supposed to be a product of the Lieberkühn's crypts. In order to obtain it pure, it is of course necessary to prevent admixture with the bile, the pancreatic juice, and the food. This is done by dividing

a loop of intestine from the rest by two transverse cuts, the abdomen having been opened in the linea alba. The continuity of the digestive tube is restored by stitching the portion below the isolated loop to the part above it; one end of the loop is sutured to the lips of the wound in the linea alba, and the other being ligatured, the whole forms a sort of test-tube opening externally (Thiry's fistula). Or both ends are made to open through the abdominal wound (Vella's fistula). Another method is to make a single opening in the intestine, and by means of two indiarubber balls, one of which is pushed down, and the other up through the opening, and which are afterwards inflated, to block off a piece of the gut from communication with the rest. The intestinal juice so obtained is a thin yellowish liquid of alkaline reaction. Its specific gravity is about 1010. It contains a small amount of proteids, and about the same proportion of inorganic salts as most of the liquids and solids of the body, namely, ·7 or ·8 per cent.; but its composition seems to be far from constant. It has been credited with various digestive powers; in fact, according to one or two enthusiastic observers, it would almost seem to sum up in itself the actions of all the other digestive juices, and to possess besides a peculiar activity of its own. But we need not hesitate to say that in the work of digestion it plays a subordinate part. The sodium carbonate, in which it is exceedingly rich, will form soaps with fatty acids produced by the action of the pancreatic juice or of the fat-splitting bacteria in which the intestine abounds, and thus aid in the digestion of fats. That a great deal of fat may be split up in the alimentary canal in the absence both of bile and pancreatic juice is well ascertained. The alkali of the succus entericus will at the same time check the growing acidity of the intestinal contents. A ferment called invertin—which is not introduced with the food or formed by bacterial action as has been suggested, since it occurs in the aseptic intestine of the new-born child—changes cane sugar into a mixture of dextrose and levulose; some maltose may be changed into dextrose. Here, however, the catalogue of the powers of the succus entericus ceases; on proteids and starch it has little or no action. But the secretion of Brunner's glands in the duodenum, which resemble in structure the pyloric glands of the stomach, digests coagulated albumin, although its proteolytic powers are feebler than those of the pancreatic juice. And in all the young mammals hitherto investigated, including the new-born child, the small intestine throughout its whole extent contains a ferment which has the property of forming lactic acid from lactose. This is present also in some adult mammals, but it has not been shown that it is a constituent of the pure intestinal juice.

Having now finished our review of the chemistry of the digestive juices, our next task is to describe what is known as to their secretion—the nature of the cells by which it is effected and their histological appearance in activity and repose, and the manner in which it is called forth and controlled.

III. The Secretion of the Digestive Juices.

The digestive glands are formed originally from involutions of the mucous membrane of the alimentary canal, the salivary glands from the epiblast, the others from the hypoblast (Chap. XIV.). Some are simple unbranched tubes, in which there is either no distinction into body and duct, as in Lieberkühn's crypts in the intestines, or in which one or more of the tubes open into a duct, as in the glands of the cardiac end of the stomach. Some are branched tubes, several of which may end in a common duct; such are the glands of the pyloric end of the stomach, and the Brunner's glands in the duodenum. In others the main duct ramifies into a more or less complex system of small channels, into each of the ultimate branches of which one or more (usually several) of the secreting tubules or alveoli open. The salivary glands and the pancreas belong to this class of compound tubular or racemose glands, and so does the liver of such animals as the frog. But in the latter organ the typical arrangement is obscured in the higher vertebrates by the predominance of the portal bloodvessels over the system of bile-channels as a groundwork for the grouping of the cells.

In every secreting gland there is a vascular plexus outside the cells of the gland-tubes, and a system of collecting channels on their inner surface; and in a certain sense the cells of every gland are arranged with reference to the blood-vessels on the one hand, and the ducts on the other. But in the ordinary racemose glands the blood-supply is mainly required to feed the secretion; the cells of the alveoli have either no other function than to secrete, or if they have other functions, they are not such as to entail a great disproportion between the size of the cells and the lumen of the channels into which they pour their products. For both reasons the relation of the grouping of the cells to the duct-system is very obvious, to the blood-system very obscure. In the liver the conditions are precisely reversed. We cannot suppose that the manufacture of a quantity of bile less in volume than the secretion of the salivary glands, though doubtless containing far more solids, requires an immense organ like

the liver, and a tide of blood like that which passes through the portal vein. And, as we shall see, the liver has other functions, some of them certainly of at least equal importance with the secretion of bile, and one of them evidently requiring from its very nature a bulky organ. Accordingly, both the richness of the blood-supply and the size of the secreting cells are out of proportion to the calibre of the ultimate channels that carry the secretion away. The so-called bile-capillaries, which represent the lumen of the secreting tubules, are mere grooves in the surface of adjoining cells; and the architectural lines on which the liver lobule is built are: (1) the interlobular veins which carry blood to it; (2) the rich capillary network which separates its cells and feeds them; (3) the central intra-lobular vein which drains it. Thus a network of cells lying in the meshes of a network of blood-capillaries takes the place of a regular dendritic arrangement of ducts and tubules; and in accordance with this the bile-capillaries, instead of opening separately into the ducts, form a plexus with each other within the hepatic lobule.

The ducts and secreting tubules of all glands are lined by cells of columnar epithelial type, but the type is most closely preserved in the ducts. In none of the digestive glands is there more than a single complete layer of secreting cells. But the alveoli of the mucous salivary glands show here and there a crescent-shaped group of small deeply-staining cells (crescents of Gianuzzi) outside the columnar layer (Plate II., 1, 3), and between it and the basement membrane, while the gland-tubes of the cardiac end of the stomach have in the same situation a discontinuous layer of large ovoid cells, termed parietal from their position, oxyntic (or acid-secreting) from their supposed function (Fig. 104). The serous salivary glands, the pancreas, the pyloric glands of the stomach, the Lieberkühn's crypts, have but a single layer of epithelium; and since there is no hepatic cell which is not in contact with at least one bile-capillary, the liver may be regarded as having no more. Remarkable histological changes, evidently connected with changes in functional activity, have been noticed in most of the digestive glands. In discussing these,

it will be best to omit for the present any detailed reference to the liver, since, although there are histological marks of secretive activity in this gland as well as in others, and of the same general character, they are accompanied, and to some extent overlaid, by the microscopic evidences of other functions (p. 446). The serous salivary glands and the pancreas can be taken together; so can the cardiac and pyloric glands of the stomach; the mucous salivary glands must be considered separately.

Changes in the Pancreas and Parotid during Secretion.—The cells of the alveoli of the pancreas or parotid during rest, as can be seen by examining thin lobules of the former between

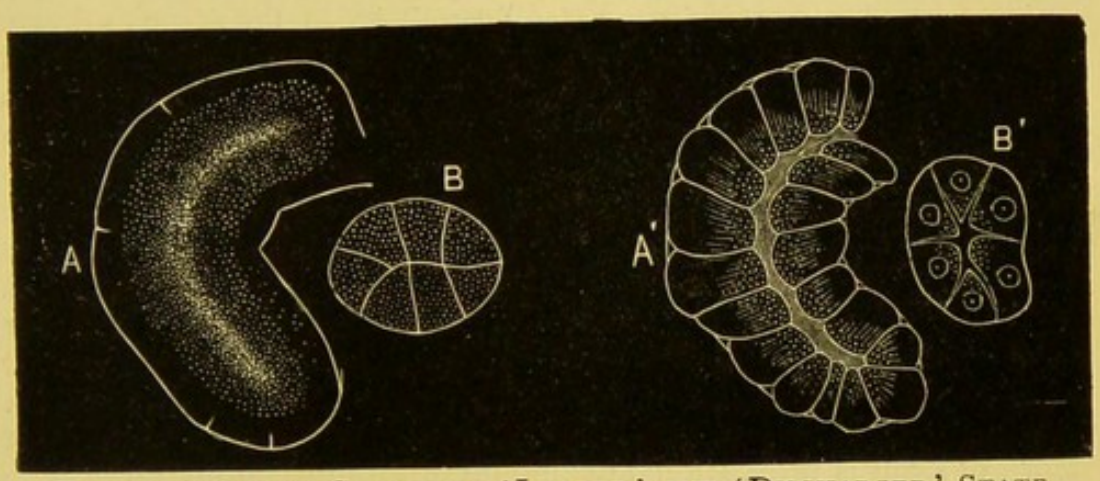


FIG. 103.—SEROUS GLANDS IN 'LOADED' AND 'DISCHARGED' STATE.

A, rabbit's pancreas, 'loaded' (resting); A', 'discharged' (active), observed in the living animal (Kühne and Lea). B, loaded, B', discharged, alveolus of parotid (fresh preparations), (Langley).

the folds of the mesentery in the living rabbit, or fresh teased preparations of the latter, are filled with fine granules to such an extent as to obscure the nucleus. In the parotid the whole cell is granular, in the pancreas there is still a narrow clear zone at the outer edge of the cell which contains few granules or none; in both, the divisions between the cells are very indistinct, and the lumen of the alveolus cannot be made out. During activity the granules seem to be carried from the outer portion of the cell towards the lumen, and there discharged; the clear outer zone of the pancreatic cell grows broader and broader at the expense of the inner granular zone, until at last the latter may in its turn be reduced to a narrow contour line around

the lumen. In the uniformly clouded parotid cell a similar change takes place; a transparent outer zone arises; and, after prolonged secretion, only a thin edging of granules may remain at the inner portion of the cell. In both glands the outlines of the cells become more clearly indicated, and a distinct lumen can be now recognised. The cells are smaller than they are during rest, and in the pancreas they stain more readily with carmine and other protoplasmic dyes, the outer zone always staining more deeply than the inner, as is the case with the same zone even in the resting pancreatic cell (Plate II., 2).

When the glands are hardened with alcohol, or most of the ordinary hardening reagents, the appearances in the serous salivary cells differ from those described, for the granules, unlike those of the pancreatic cells, are altered by the treatment, and the two zones in the discharged gland are not distinguishable by any difference in the depth of the carmine stain. But in the rabbit's parotid after the scanty secretion caused by prolonged stimulation of the sympathetic the whole cell stains more deeply than the loaded cell. Its protoplasm is turbid with fine and uniformly diffused granules; its nucleus is large and spherical, and contains well-marked nucleoli, in contrast to the pale and transparent protoplasm and the small shrivelled nucleus of the resting cell, in which nucleoli are indistinct or invisible. Now, carmine being a protoplasmic dye, it is fair to conclude that depth of stain is proportional to amount of protoplasm present. The deeper stain of the outer rim of the pancreatic cell during rest indicates that here the protoplasm predominates over the dead and unstained products of its activity, which are accumulated in the remainder of the cell. The increase of the deeply-staining zone during secretion shows that these products are being moved towards the lumen of the alveolus, and that the relative amount of protoplasm in the outer zone is being increased, although the absolute size of the cell may be diminished. The deeper stain of the parotid cell after sympathetic stimulation, as well as the changes in the nucleus, indicate regeneration of protoplasm as much as elimination of non-protoplasmic elements. For in the dog changes similar to those in the rabbit are caused, although the amount of secretion on stimulation of the sympathetic is very small, and generally only sufficient to block the ducts without appearing externally. The disappearance of granules from without inwards during activity suggests that these are manufactured products eliminated in the secretion.

Changes in the Glands of the Stomach during Secretion.—The mucous membrane of the stomach is covered with a single layer of columnar epithelium, largely consisting of mucigenous goblet-cells. It is studded with minute pits, into which open the ducts of the peptic and pyloric glands, the ducts being lined with cells just like

those of the general gastric surface. The peptic or cardiac glands have short ducts, into each of which open one to three gland-tubes seldom branched. The ducts of the pyloric glands are longer, and the secreting tubules, which also open by twos or threes into the ducts, are branched. The secreting parts of both kinds of glands are lined by short columnar, finely granular cells; and in the pyloric tubules no others are present. But, as we have said, in the peptic

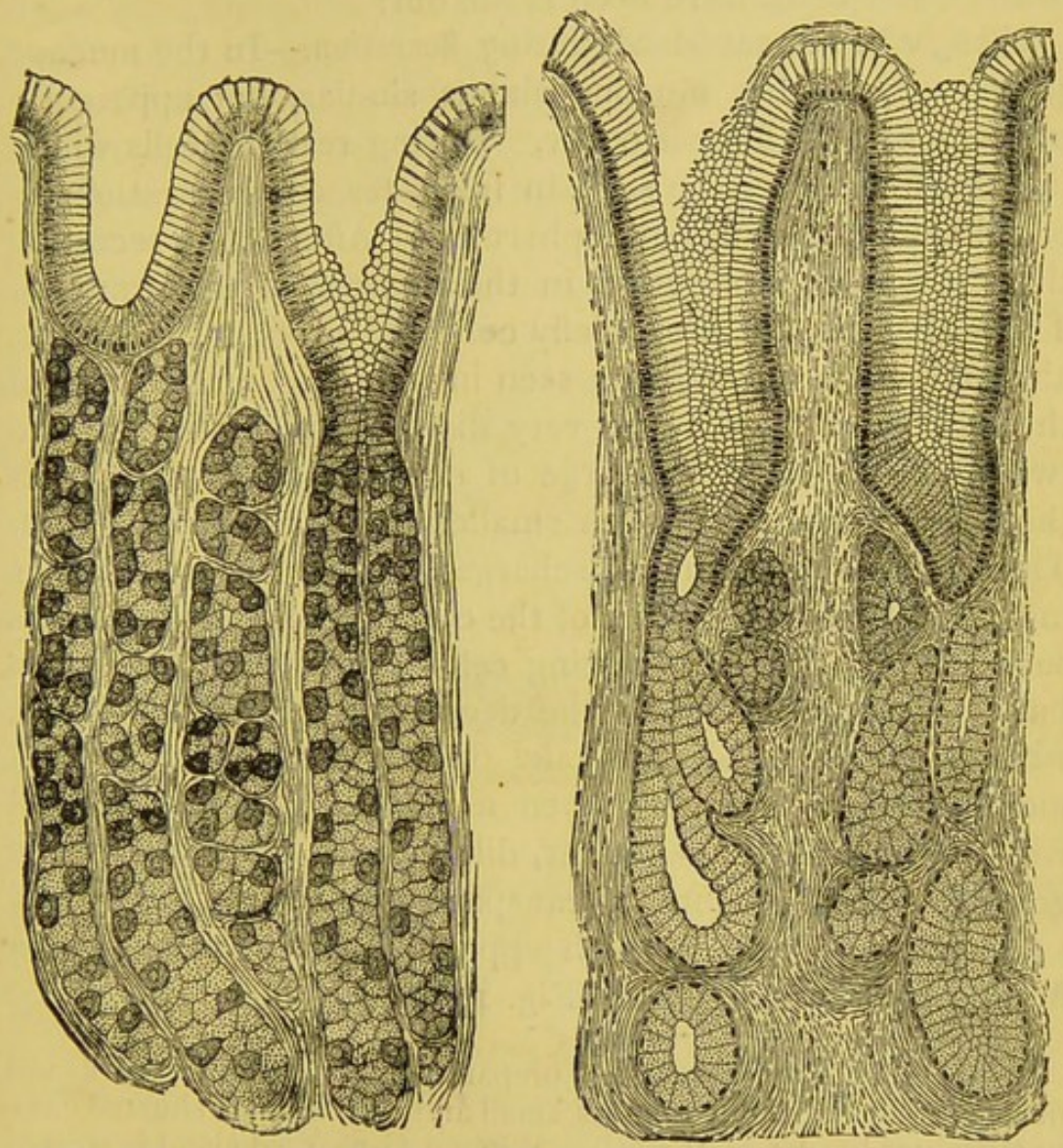


FIG. 104.—THE GASTRIC GLANDS.—On the left cardiac, right pyloric (Ebstein).

glands there are besides large ovoid cells scattered at intervals like beads between the basement membrane and the lining or chief cells.

The histological changes connected with secretion do not differ essentially from those described in the pancreas and the parotid, but there is much greater difficulty in making observations on the living, or at least but slightly altered, cells. During digestion the granules seem to disappear from

the outer part of the chief cells of the peptic glands, leaving a clear zone, the lumen being bordered by a granular layer. Or, more rarely, there may be a uniform decrease in the number of granules throughout the cell. The ovoid cells swell up, so as to bulge out the membrana propria, but no definite changes in their contents, such as those observed in the other cells, have been made out.

Changes in Mucous Glands during Secretion.—In the mucous salivary and other mucous glands similar, but apparently more complex, changes occur. During rest the cells which line the lumen may be seen in fresh, teased preparations to be filled with granules or 'spherules.' After active secretion there is a great diminution in the number of the granules. Those that remain are chiefly collected around the lumen, although some may also be seen in the peripheral portion of the cell; and there is no very distinct differentiation into two zones. That a discharge of material takes place from these cells is shown by their smaller size in the active gland. That the material thus discharged is not protoplasmic is indicated by the behaviour of the cells to protoplasmic stains such as carmine. The resting cells around the lumen stain but feebly, in contrast to the deep stain of the demilunes, while the discharged cells take on the carmine stain much more readily. Further, when a resting gland is treated with various reagents (water, dilute acids, or alkalies), the granules swell up into a transparent substance apparently identical with mucin, which appears to fill the meshes of a fine protoplasmic network (Fig. 105).

In ordinary alcohol-carmine preparations only the network and nucleus are stained; the nucleus, small and shrivelled, is situated close to the outer border of the cell. When a discharged gland is treated in the same way there is proportionally more 'protoplasm' and less of the clear material, what remains of the latter being chiefly in the inner portion of the cell, while the nucleus is now large and spherical, and not so near the basement membrane (Plate II., 1 and 3).

Everything, therefore, points to the granules in what we may now call the mucin-forming cells as being in some way or other precursors of the fully-formed mucin; manufactured during 'rest' by the protoplasm and partly at its expense,

moved towards the lumen in activity, discharged as mucin in the secretion. It has been asserted that not only is the protoplasm lessened in the loaded cell and renewed after activity, but that many of the mucigenous cells may be altogether broken down and discharged, their place being supplied by proliferation of the small cells of the demilunes. This conclusion, however, is not supported by sufficient evidence. But the fact on which we would specially insist is that the granules of the resting mucigenous cell may be looked upon as a mother-substance from which the mucin of the secretion is derived; they are not actual, but potential, mucin.

So in the pancreas, the serous or albuminous salivary

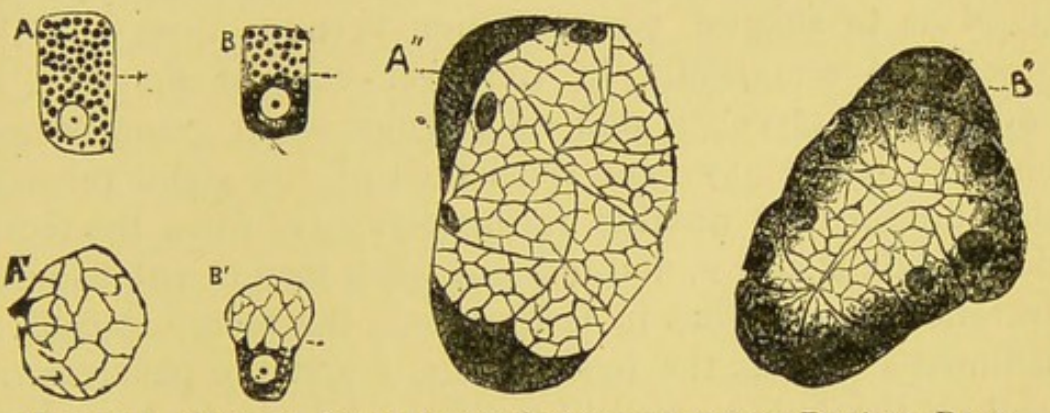


FIG. 105.—MUCOUS CELLS (FROM SUBMAXILLARY OF DOG) IN REST AND ACTIVITY (LANGLEY).

A, B, fresh; A′, B′, after treatment with dilute acetic acid; A″, B″, alveoli hardened in alcohol and stained with carmine. A, A′ and A″ represent the loaded; B, B′ and B″, the discharged condition.

glands, and the glands of the stomach, there is every reason to believe that the granules which appear in the intervals of rest, and are moved towards the lumen and discharged during activity, are the precursors, the mother-substances, of important constituents of the secretion. These granules are sharply marked off from the protoplasm in which they lie and by which they are built up. By every mark, by their reaction to stains, for instance, they are non-living substance, formed in the bosom of the living cell from the raw material which it culls from the blood, or, what is more likely, formed from its own protoplasm, then shed out in granular form and secluded from further change. The

proteolytic power of an extract of the pancreas, or the gastric mucous membrane, seems to be, roughly speaking, in proportion to the quantity of granules present in the cells. Therefore it is concluded that the granules are related in some way to trypsin and pepsin.

But we should greatly deceive ourselves if we supposed that granules of this nature in gland-cells are necessarily related to the production of ferments. The mucigenous granules have no such significance. Most digestive secretions contain proteid constituents, with which the granules may have to do, as well as with ferments. And bile, a secretion which contains no mucin, no proteids, and no ferments, as essential constituents, is formed in cells with granules so disposed and so affected by the activity of the gland as to suggest some relation between them and the process of secretion. In the liver-cells of the frog, in addition to glycogen and oil-globules, small granules may be seen, especially near the lumen of the gland tubules; they diminish in number during digestion, when the secretion of bile is active, and increase when food is withheld and secretion slow. And in fasting dogs the secreting cells of Brunner's glands, the pyloric glands and the pancreas, as well as the lining epithelium of the bile-ducts, have been found to contain many fatty granules. Possibly some of these represent the fat which is known to be excreted into the alimentary canal (pp. 372, 374, 455).

The granules in the ferment-forming glands are not composed of the actual ferments, and, indeed, the actual ferments are present in the secreting cells only in small amount, if at all, as is shown by the following facts:

A glycerine extract of a fresh pancreas has hardly any effect on proteids; a similar extract of a stale pancreas is very active. Therefore the fresh pancreas is devoid of trypsin. But it contains a substance which can readily be changed into trypsin; and this substance is soluble in glycerine, for the inert extract becomes active when it is treated with dilute acetic acid, or even when it is diluted with water and kept at the body-temperature. If the fresh pancreas be first treated with dilute acetic acid, and then with glycerine, the extract is at once active. All this goes

to show that in the fresh pancreas not trypsin, but a mother-substance, which has been named trypsinogen, is present, and that the latter yields trypsin, gradually when the pancreas is simply allowed to stand, more rapidly when the dilute acid is used. The natural secretion of the gland is active when the gland-cells contain no ferment, therefore during secretion the trypsinogen must be changed into trypsin.

Similarly, a glycerine extract of a fresh gastric mucous membrane is inert as regards proteids, or nearly so. But if the mucous membrane has been previously treated with dilute hydrochloric acid, the glycerine extract is active, as is an extract made with acidulated glycerine. Here we must assume the existence in the gastric glands of a mother-substance, pepsinogen, from which pepsin is formed. Only the chief cells of the cardiac, and the similar if not identical cells of the pyloric glands, are believed to manufacture the pepsin-forming substance. The ovoid cells of the former are supposed to secrete the hydrochloric acid. The evidence on which this belief is based is as follows:

The pyloric glands, in which in most situations no ovoid cells are to be seen, secrete pepsin, but no acid. The pyloric portion of the stomach has been isolated, the continuity of the alimentary canal restored by sutures, and the secretion of the pyloric pocket collected. It was found to be alkaline, and contained pepsin. The glands of the frog's œsophagus, which contain only chief cells, secrete pepsin, but no acid. It seems fair to conclude that the chief cells of the cardiac glands in the mammal secrete none of the free hydrochloric acid, but certainly some of pepsin. But it does not follow that all the pepsin is formed by these cells, although it would seem that all the hydrochloric acid must be secreted by the only other glandular elements present, the ovoid or 'border' cells. And, indeed, the glands in the fundus of the frog's stomach, which are composed only of ovoid cells, while secreting much acid, also form some pepsin, although far less than the œsophageal glands.

Attempts made to demonstrate an acid reaction in the border cells have hitherto failed, perhaps because the acid is poured into the

ducts as fast as it is formed. But it should be mentioned that some observers deny that the acid is secreted in the depths of any cell from the chlorides of the blood, and believe that it is formed at the surface of contact of the stomach-wall with the gastric contents from the sodium chloride of the food by an exchange of sodium ions (p. 362) for hydrogen ions from the blood or lymph. They point out in favour of this view that when, instead of sodium chloride, sodium bromide is given in the food, the hydrochloric acid in the stomach is to a large extent replaced by hydrobromic acid. And they argue that this cannot be due to the decomposition of the bromide by hydrochloric acid, since it occurs in animals deprived for a considerable time of salts, and in 'salt-hunger' the stomach contains no acid (Koeppe). It may be, however, that even in 'salt-hunger' the presence of sodium bromide in the stomach stimulates the secretion of hydrochloric acid, which then decomposes the bromide, with the formation of hydrobromic acid. The sodium chloride formed in the double decomposition might be re-absorbed, and the stock of chlorides in the blood remain undiminished. There are, besides, weighty theoretical objections to this hypothesis. On the other hand, it has been shown that mechanical stimulation of the stomach in a fasting individual, by a kind of rotatory sound, causes hydrochloric acid to appear in considerable amount, even when the viscus has been previously washed out so as to remove all the chlorides (Wesener). In this case the acid must be formed from the chlorides of the blood.

The rennet ferment of the gastric juice is formed in the chief cells, and has a precursor or zymogen like the other digestive ferments. A glycerine or watery extract of the salivary glands always contains active amylolytic ferment, if the natural secretion is active. So that if ptyalin is preceded by a zymogen in the cells, it must be very easily changed into the actual ferment.

The Quantitative Estimation of Ferment Action.—Since we have as yet no certain method of freeing ferments from impurities, our only quantitative test is their digestive activity. And since a very small quantity of ferment can act upon an indefinite amount of material if allowed sufficient time, we can only make comparisons when the time of digestion and all other conditions are the same. If we find that a given quantity of one gastric extract, acting on a given weight of fibrin, dissolves it in half the time required by an equal amount of another gastric extract, or dissolves twice as much of it in a given time, we conclude that the digestive activity of the pepsin is twice as great in the first extract as in the second, or, as it is sometimes more loosely put, that the one contains twice as much pepsin as the other. A convenient method of estimating the rate at which the fibrin disappears is to use fibrin stained with carmine. As solution goes on, the dye colours the liquid more and more deeply, and by comparing the depth of colour at any time with standard solutions of carmine, we get the quantity of dye set free, and therefore of fibrin digested. This method cannot be used for trypsin. As a test of the activity of a diastatic ferment, we take the amount of sugar formed in a given time in a given quantity of a standard starch solution.

We have spoken more than once of the gland-cells as *manufacturing* their secretions. It is an idea that rises naturally in the mind as we follow with the microscope the traces of their functional activity. And when we compare the composition of the digestive juices with that of the blood-plasma and lymph, the suggestion that the glands which produce them are not merely passive filters, but living laboratories, acquires additional strength. It is evident that everything in the secretion must, in some form or other, exist in the blood which comes to the gland, and in the lymph which bathes its cells. No glandular cell, if we except the leucocytes, which in some respects are to be considered as unicellular glands, dips directly into the blood; everything a gland-cell receives must pass through the walls of the bloodvessels. So that anything which we find in the secretion and do not find in the blood must have been elaborated by the gland from raw material brought to it by the latter.

Take, for example, the saliva or gastric juice. These liquids both contain certain things that also exist in the blood, but in addition they contain certain things specific to themselves: mucin in saliva, hydrochloric acid in gastric juice, ferments in both. It is true that a trace of pepsin and trace of a diastatic ferment may be discovered in blood; but there is no reason whatever to believe that this is the source of the pepsin of the gastric juice, or the ptyalin of the salivary glands. On the contrary, it is possible that the ferments of the blood may be in part absorbed from the digestive glands, the rest being formed by the leucocytes and liberated when they break down. The liver affords an even better example of this 'manufacturing' activity of gland-cells, and many facts may be brought forward to prove that the characteristic constituents of the bile, the bile-pigments and bile-acids, are formed in the liver, and not merely separated from the blood. Bile-pigment has indeed been recognised in the normal serum of the horse, and bile-acids in the chyle of the dog, but only in such minute traces as are easily accounted for by absorption from the intestine. Frogs live for some time after excision of the liver, but no bile-acids are found in the blood or tissues. But if the bile-duct be ligatured, bile-acids and pigments accumulate in the body, being absorbed by the lymphatics of the liver, as was shown by Ludwig and Fleischl in the dog. If the thoracic duct and the bile-duct are both ligatured, no bile-acids or pigments appear in the

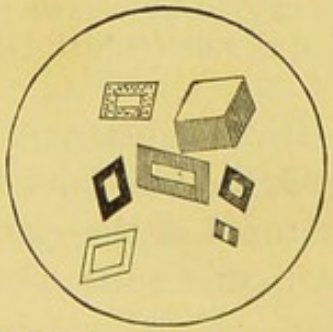


FIG. 106.—HÆMATOIDIN.

blood or tissues.* In mammals life cannot be maintained for any length of time after ligature of the portal vein, since this throws the whole intestinal tract out of gear. But after an artificial communication has been made between the portal and the left renal vein or the inferior cava, the portal may be tied and the animal live for months (Eck). The liver can now be completely removed, but death follows in a few hours. In birds there exists a communicating branch between the portal vein and a vein (the renal-portal) which passes from the posterior portion of the body to the kidney, and there breaks up into capillaries; and not only may the portal be tied, but the liver may be completely destroyed without immediately killing the animal. In the hours of life that still remain to it no accumulation of biliary substances takes place in the blood or tissues. A further indication that bile-pigment is produced in the liver is the fact that the liver contains iron in relative abundance in its cells (p. 382), and eliminates small quantities of iron in its secretion. Now bile-pigment, which contains no iron, is certainly formed from blood-pigment, which is rich in iron, for hæmatoidin (Fig. 106), a crystalline derivative of hæmoglobin found in old extravasations of blood, especially in the brain, is identical with bilirubin. The seat of formation of bile-pigment must therefore be an organ peculiarly rich in iron. The existence of hæmatoidin, however, shows that bile-pigment *may*, under certain conditions, be formed outside of the hepatic cells. The occurrence of biliverdin in the placenta of the bitch points in the same direction. But the pathological evidence in favour of the pre-formation of the biliary constituents tends rather to shrink than to increase. For many cases of what used to be considered 'idiopathic' or 'hæmatogenic' jaundice, *i.e.*, an accumulation of bile-pigments and bile-acids in the tissues, due to defective elimination by the liver, are now known to be caused by obstruction of the bile-ducts and consequent re-absorption of bile ('obstructive' or 'hepatogenic' jaundice).

But if substances such as the ferments, mucin, hydrochloric acid, the bile-salts and bile-pigments, are undoubtedly manufactured in the gland-cells, it is different with the water and inorganic salts which form so large a part of every secretion. No tissue lacks them; no physiological process goes on without them; they are not high and special products. As we breathe nitrogen which we do not need because it is mixed with the oxygen we require, the secreting cell passes through its substance water and salts as a sort of by-play or

* Wertheimer and Lepage state that bile or bilirubin injected into a bile-duct appears sooner in the urine than in the lymph of the thoracic duct, and therefore conclude that the bloodvessels are the most important channel of absorption. This conclusion, however, cannot be accepted until it is shown that in these experiments the injection did not cause rupture of some of the hepatic capillaries and direct entrance of the bile-pigment into the blood. It is not improbable that the pressure attained by the bile in the bile-capillaries is a factor in determining the path by which it is absorbed, and that when the pressure rises beyond a certain limit it may pass both into the bloodvessels and into the lymphatics.

adjunct to its specific work. But this is not the whole truth. The gland-cell is not a mere filter through which water and salts pass in the same proportions in which they exist in the liquids that the cell draws them from. The secretions of different glands differ in the nature, and especially in the relative proportions, of their inorganic constituents; and the secretion of one and the same gland is by no means constant in this respect, as we shall have to note more especially when we come to deal with the influence of the nervous system on secretion (p. 338).

The proteid substances, such as serum-albumin and globulin, common to blood and to some of the digestive secretions, take a middle place between the constituents that are undoubtedly manufactured in the cell and those which seem by a less special and laborious, though a selective, process to be passed through it from the blood. Their absence from bile, and, as we shall see, from urine, their abundance in pancreatic and scantiness in gastric juice, point to a closer dependence upon the special activity of the gland-cell than we can suppose necessary in the case of the salts.

Although it is in the cells of the digestive glands that the power of forming ferments is most conspicuous, it is by no means confined to them. It seems to be a primitive, a native power of protoplasm. Lowly animals, like the amœba, lowly plants, like bacteria, form ferments within the single cell which serves for all the purposes of their life. The ferment-secreting gland-cells of higher forms are perhaps only lop-sided amœbæ, not so much endowed with new properties as disproportionately developed in one direction. The contractility has been lost or lessened, the digestive power has been retained or increased; just as in muscle the power of contraction has been developed, and that of digestion has fallen behind. The muscle-cell and the cartilage-cell are parasites, if we look to the function of digestion alone. They live on food already more or less prepared by the labours of other cells; and it is a universal law that in the measure in which a power becomes useless it disappears. But the presence of pepsin in the white blood-corpuscles, the parasites as well as the scavengers of the blood, and of amylolytic ferments in many tissues, should

warn us not to conclude that the power of forming ferments belongs exclusively to any class of cells. And it is possible that food-substances absorbed from the blood are further elaborated by ferment action within the tissues themselves; while many facts show that the power of contraction is widely diffused among structures whose special function is very different, and a few point to its possession in some degree even by glandular epithelium. On the other hand, it must be remembered that none of the digestive glands absorb food directly from the alimentary canal to be then digested within their own cell-substance; the ferments which they form do their work outside of them; their cells feed also upon the blood.

Why are the Tissues of Digestion not affected by the Digestive Ferments?—This is the place to mention a point which has been very much debated, though never satisfactorily explained: Why is it that the stomach or the small intestine does not digest itself? This is really a part of a wider question: Why is it that living tissues resist all kinds of influences, which attack dead tissues with success? The living leucocyte destroys bacteria by which the dead leucocyte is broken up; it kills and digests them by substances formed within itself, but its own living protoplasm is not digested. Or if the battle goes the other way, the bacteria kill the leucocyte, and break it up, perhaps, by the aid of ferments of their own manufacture which affect it but not them. The amœba digests food in its cell-substance, but does not digest itself. The pancreatic juice acts with great intensity upon proteids, but not upon the proteids of the living pancreas and the living intestinal wall. When we ascribe these things to the resistance of living tissues, we play with words. And we have to inquire whether this is a general resistance of all living tissues, or a specific resistance of certain tissues to certain influences.

That *all* living tissues cannot withstand the action of the gastric juice has been shown by putting the leg of a living frog inside the stomach of a dog; the leg is gradually eaten away (Bernard). It is true that it has first been killed and then digested, but the question is, why the stomach-wall is not first killed and then digested? When the wall has been

injured by caustics or by an embolus, the gastric juice acts on it. But the living epithelium that covers it is able to resist the action of the acid and pepsin, which destroy the tissues of the frog's leg. The alkalinity of the blood has nothing to do with the explanation, for the frog's blood is also alkaline, and the cells that line the pancreatic ducts are preserved from the pancreatic juice, which is intensely active in an alkaline medium. A certain amount of protection may be afforded to the walls of the stomach by the thin layer of mucus which covers the whole cavity, for mucin is not affected by peptic digestion. And a mucous secretion seems in some other cases to act as a protective covering to the walls of hollow viscera, whose contents are such as would certainly be harmful to more delicate membranes, *e.g.*, in the urinary bladder, large intestine, and gall-bladder. Still, however important such a mechanical protection may be, it does not explain the whole matter, and it is necessary to suppose that the gastric epithelium has some special power of resisting the gastric juice, possibly by turning any of the ferment which may invade it into an inert substance like the zymogen, or by opposing its entrance as the epithelium of the bladder opposes the absorption of urea. In the gland-cells of the pancreas the protoplasm is, no doubt, shielded from digestion by the existence of the ferment in an inert form as zymogen; and it is possible that this is the reason, or at least one of the reasons, for the existence of the mother-substance. But this is not the whole explanation, for the living frog's leg is not harmed by a weakly alkaline pancreatic extract, which does not digest the epithelium, because it cannot kill it. On the other hand trypsin when injected below the skin causes the tissue to break down and ulcerate. And while an active solution of trypsin can be allowed to remain a long time in an isolated loop of small intestine without producing any ill effect, damage is soon caused not only to the intestinal wall, but also to the liver, when the mucous membrane of the loop has been injured before the introduction of the trypsin. We must suppose, then, that the normal mucous membrane of the intestine prevents the absorption of trypsin, or, if it absorbs any of it, renders it harmless. Indeed, it is impossible to escape the

conclusion that each membrane becomes accustomed, and, so to speak, 'immune,' to the secretion normally in contact with it, although not necessarily to other secretions. It is easy to multiply illustrations of this principle.

Few tissues but the lining of the urinary tract or of the large intestine could bear the constant contact of urine or fæces. When urine is extravasated under the skin, or the contents of the alimentary canal burst into the peritoneal cavity, they come into contact with tissues which, although alive, are much less fitted to resist them than the surfaces by which they are normally enclosed; and the consequences are often disastrous. Leucocytes thrive in the blood, but perish in urine; blood does not harm the endothelial cells of the vessels, but kills a muscle whose cross-section is dipped into it. The defensive, or in some cases offensive, liquids secreted by many animals are harmless to the tissues which produce and enclose them: a caterpillar investigated by Poulton secretes a liquid so rich in formic acid, that the mere contact of it would kill most cells. The so-called saliva of *Octopus macropus* contains a substance fatal to the crabs and other animals on which it preys. The blood of the viper contains an active principle similar to that secreted by its poison-glands, but its tissues are not affected by this substance, so deadly to other animals.

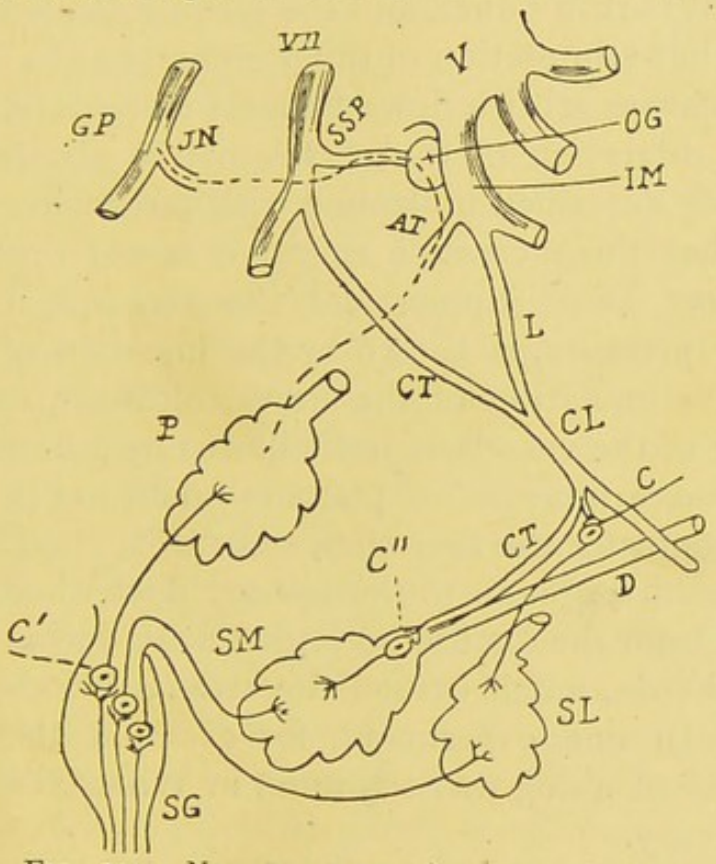
The Influence of the Nervous System on the Digestive Glands.

The greater part of our knowledge of this subject has been gained by the study of the salivary glands, and especially the submaxillary and sublingual, which lie superficially and are easily exposed.

(1.) **The Influence of Nerves on the Salivary Glands.**—All the salivary glands have a double nerve-supply, from the medulla oblongata through some of the cranial nerves, and from the spinal cord through the cervical sympathetic (Fig. 107).

In the dog the chorda tympani branch of the facial nerve carries the cranial supply of the sublingual and submaxillary glands. It joins the lingual branch of the fifth nerve, runs in company with it for a little way, and then, breaking off, after giving some fibres to the lingual, passes, as the chorda tympani proper, along Wharton's duct to the submaxillary gland. In the hilus of this gland most of its

fibres break up into fibrils around nerve-cells situated there and lose their medulla in doing so. A few fibres terminate in a similar manner before entering the hilus, and a few deeper in the gland. The nervous path is continued by the axis-cylinder processes (p. 662) of these nerve-cells, which, passing in as non-medullated fibres, end in a plexus on the basement membrane of the alveoli. From the plexus fibrils run in among the gland-cells, but do not seem to penetrate them. The lingual, the chorda tympani proper, and Wharton's duct form the sides of what is called the chordo-lingual triangle. Within this triangle are situated many ganglion cells, a special accumulation of which has received the name of the submaxillary ganglion. This, however, should rather be called the sublingual ganglion, since its cells, as well as the others in the chordo-lingual triangle, are the cells of origin of axis-cylinder processes, which proceed as non-



SM and SL, submaxillary and sublingual glands; P, parotid; V, fifth nerve; VII, facial; GP, glosso-pharyngeal; L, lingual; CT, chorda tympani; CL, chordo-lingual; D, submaxillary (Wharton's) duct; C, ganglion cell of so-called submaxillary ganglion in the chordo-lingual triangle, connected with a nerve fibre going to sublingual gland; C'', ganglion cell in hilus of submaxillary gland; SSP, small superficial petrosal branch of the facial; OG, otic ganglion; IM, inferior maxillary division of fifth nerve; AT, auriculo-temporal branch of fifth; JN, Jacobson's nerve; C' ganglion cells in superior cervical ganglion (SG) connected with sympathetic fibres going to parotid, submaxillary and sublingual glands. The figure is schematic.

FIG. 107.—NERVES OF THE SALIVARY GLANDS.

medullated fibres to the sublingual gland. The sublingual gland receives its cerebral fibres partly from branches given off from the lingual in the chordo-lingual triangle after the chorda tympani proper has separated from it, and ending around the nerve-cells within that triangle, partly from the chorda itself in the terminal portion of its course. These statements rest on anatomical and physiological evidence. The latter we shall return to.

The cerebral fibres for the parotid (in the dog) pass from the tympanic branch of the glosso-pharyngeal (Jacobson's nerve) through connecting filaments to the small superficial petrosal branch of the facial, with this nerve to the otic ganglion, and thence by the auriculo-temporal branch of the fifth to the gland.

The sympathetic fibres for all the salivary glands appear to arise from nerve-cells in the upper dorsal portion of the spinal cord.

Issuing from the cord in the anterior roots of the upper thoracic nerves (first to fifth, but mainly second thoracic for the submaxillary), they enter the sympathetic chain, in which they run up to the superior cervical ganglion. Here they break up into terminal twigs, and thus come into relation with ganglion cells, whose axis-cylinder processes pass out as non-medullated fibres, and, surrounding the external carotid, reach the salivary glands along its branches. Langley has shown, by means of nicotine (p. 157), that the sympathetic fibres for the submaxillary and sublingual, and, indeed, for the head in general in the dog and cat, are connected with nerve-cells in this ganglion, but not between it and their termination, or between it and their origin from the spinal cord.

Stimulation of the Cranial Fibres.—When in the dog a cannula is placed in Wharton's duct, and the saliva collected (p. 376), it is found that stimulation of the peripheral end of the divided chorda causes a brisk flow of watery saliva, and at the same time a dilatation of the vessels of the gland, which we have already described in dealing with vaso-motor nerves (p. 155). That the increased secretion is not due merely to the greater blood-supply, and the consequent increase of capillary pressure, is shown by the injection of atropia, after which stimulation of the nerve, although it still causes dilatation of the vessels, is not followed by a flow of saliva. Further, mere increase of pressure could not in any case of itself account for the secretion, since it has been found that the maximum pressure in the salivary duct when the outflow of saliva from the duct is prevented may, during stimulation of the chorda, much exceed the arterial blood-pressure (Ludwig). In one experiment, for example, the pressure in the carotid of a dog was 125 mm., in Wharton's duct 195 mm. of mercury.

Even in the head of a decapitated animal a certain amount of saliva may be caused to flow by stimulation of the chorda, but too much may easily be made of this. And since the blood is the ultimate source of the secretion, we could not expect a permanent or copious flow in the absence of the circulation, even if the gland-cells could continue to live. In fact, when the circulation is almost stopped by strong stimulation of the sympathetic, the flow of saliva caused by excitation of the chorda is at the same time greatly lessened or arrested, even though the sympathetic

itself possesses secretory fibres. So that, while there is no doubt that the chorda tympani contains fibres whose function is to increase the activity of the gland-cells, its vaso-dilator action is, under normal conditions, closely connected with, and, indeed, auxiliary to, its secretory action, although the former does not directly produce the latter. This is only a particular case of a physiological law of wide application, that *an organ in action in general receives more blood than the same organ in repose*, or, in other words, that *the tissues are fed according to their needs*. The contracting muscle, the secreting gland, is flushed with blood, not because an increased blood-flow can of itself cause contraction or secretion, but because these high efforts require for their continuance a rich supply of what blood brings to an organ, and a ready removal of what it takes away.

The quantity of blood passing through the parotid of a horse when it is actively secreting during mastication may be quadrupled (Chauveau). The parallel between the muscle and the gland is drawn closer when it is stated that electrical changes accompany secretion (p. 646), and that the rate of production of carbon dioxide and consumption of oxygen rises during activity. The temperature of the saliva flowing from the dog's submaxillary during stimulation of the chorda has been found to be as much as 1·5° C. above that of the blood of the cartoid, although with the gland at rest no constant difference could be detected (Ludwig). But such measurements are open to many fallacies; and while there is no doubt that more heat is produced in the active than in the passive gland, it will not be surprising, when the vastly increased blood-flow is remembered, that no difference of temperature between the incoming and outgoing blood has been satisfactorily demonstrated, although we must assume that such a difference exists.

It has already been mentioned that most of the fibres of the chorda tympani proper become connected with ganglion-cells, and lose their medulla inside the submaxillary gland, only a few having already lost it by a similar connection with ganglion-cells in the chordo-lingual triangle. These facts have been made out by means of the nicotine method previously described (p. 157). Thus, it is found that, after the injection of nicotine (5 to 10 mg. in a rabbit or cat, 40 or 50 mg. in a

dog), stimulation of the chorda tympani proper or of the chordo-lingual nerve causes no secretion from the submaxillary gland; but stimulation of the hilus of the gland is followed by a copious secretion—as much, if the stimulation is fairly strong, as was caused by excitation of the nerve before injection of nicotine. That this is due neither to any direct action on the gland-cells, nor to stimulation of the sympathetic plexus on the submaxillary artery, but to stimulation of chorda fibres beyond the hilus, is shown by the fact that after atropia has been injected in sufficient amount to paralyze the nerve endings of the chorda, but not of the sympathetic, stimulation of the hilus causes little or no flow of saliva. The application of nicotine solution to the chordo-lingual triangle does not affect the submaxillary secretion caused by stimulation of the chordo-lingual nerve, even in cases where a few secretory fibres for the submaxillary do not leave the chordo-lingual nerve in the chorda tympani proper, but are given off to the chordo-lingual triangle. This shows that none of the ganglion-cells in the triangle are connected with the cerebral secretory fibres of the submaxillary gland. By observations of the same kind they are known to be connected with fibres going to the sublingual. In a similar way, by observing the effects of stimulation of the chorda on the bloodvessels before and after the application of nicotine, it has been found that the vaso-dilator fibres are connected with ganglion-cells in the same positions as the secretory fibres (Langley).

Stimulation of the Sympathetic Fibres.—The sympathetic, as has been already indicated, contains both vaso-constrictor and secretory fibres for the salivary glands. If the cervical sympathetic in the dog is divided, and the cephalic end moderately stimulated, a few drops of a thick viscid and scanty saliva flow from the submaxillary and sublingual ducts, while the current of blood through the glands is diminished. As a rule, no visible secretion escapes from the parotid, but microscopic examination shows that many of the ductules are filled with fluid, which is apparently so thick as to plug them up (Langley); while the cells show signs of 'activity.'

Simultaneous Stimulation of Cranial and Sympathetic Fibres.—When the chorda and sympathetic are stimulated together, the former prevails so far, with moderate stimulation of the latter, that the submaxillary saliva is secreted in considerable quantity, and is not particularly viscid; it is, however, richer in organic matter than is the chorda saliva itself. When the chorda is weakly, and the sympathetic strongly excited, the scanty secretion (if there is any) is of sympathetic type,

thick and rich in organic matter. With strong stimulation of both nerves, the secretion, at first plentiful and watery, soon diminishes, even below the amount obtained by stimulation of the chorda alone, perhaps because of the diminution in the blood-flow produced by the vaso-constrictors of the sympathetic. With stimulation just strong enough to cause secretion when applied separately to either nerve, there is no secretion when it is applied simultaneously to both.

All this refers to the dog. In this animal, then, there seems to be a certain amount of physiological antagonism between the secretory action of the two nerves. But it differs in one respect from the antagonism between their vaso-motor fibres; for with strong stimulation the constrictors of the sympathetic always swamp the dilators of the chorda, while the secretory fibres of the chorda appear upon the whole to prevail over those of the sympathetic. And in all probability this apparent secretory antagonism is very superficial; and whatever interference there may be between the two nerves, apart from any possible effect of their vaso-motor interference, is not due to the one annulling the influence of the other on the gland-cells, but to the cells being called by them to different labours, in general complementary to each other, and only incompatible in so far as the working power of the cells may not be able to respond at the same time to large demands from both sides. For the sympathetic always adds something to the common secretion when there is a secretion at all, this something being represented by an increase in the percentage of organic matter. Not only so, but the sympathetic effect persists after stimulation has been stopped; and excitation of the chorda after previous stimulation of the sympathetic causes a flow of saliva richer in organic matter than would have been the case if the sympathetic had not been stimulated.

Indeed, the distinction between chorda and sympathetic saliva, which, by taking account of the parotid as well as the submaxillary and sublingual glands, has been generalized into a distinction between cerebral and sympathetic saliva,

and which holds good in the dog and the rabbit, breaks down before a wider induction. For in the cat the sympathetic saliva of the submaxillary gland, although much more scanty, is more watery than the chorda saliva (Langley), which, however, is by no means viscid; and the two secretions differ far less than in the dog. In accordance with this functional similarity, there is a much smaller difference in the action of atropia on the two sets of fibres in the cat than in the dog, although even in the cat the sympathetic is less readily paralyzed than the chorda.

In their secretory action there is not even an apparent antagonism in the cat, with minimal stimulation of both nerves, which causes as much secretion as would be produced if both were separately excited. Further, even in the dog, after prolonged stimulation of the sympathetic, the submaxillary saliva is no longer viscid, but watery, the proportion of solids, and especially of organic solids, being much lessened, as it also is in chorda saliva after long excitation. When the cerebral nerve of the resting gland is strongly excited, it is found that up to a certain limit the percentage of organic matter in a small sample of saliva subsequently collected during a brief weak excitation increases with the strength of the previous stimulation; this is also true of the inorganic solids. But there is a striking difference when the experiment is made on a gland after a long period of activity; here increase of stimulation causes no increase in the percentage of organic material, while the inorganic solids are still increased. In both cases the absolute quantity of water, and therefore the rate of flow of the secretion, is augmented.

All this points to the same conclusion as the microscopic appearances in the gland-cells, that the cells during rest manufacture the organic constituents of the secretion, or some of them, and store them up, to be discharged during activity. The water and the inorganic salts, on the other hand, seem rather to be secreted on the spur of the moment, so to speak, and not to require such elaborate preparation. And it has been stated that when the chorda tympani is stimulated with currents of varying strength, the quantity of

organic substances in small samples of saliva collected from a fresh gland is more nearly proportional to the rate of secretion than is the quantity of water and salts, which varies also with the blood-supply.

In order to explain the difference between the cerebral and sympathetic secretion, Heidenhain has supposed the existence of two kinds of secretory fibres: (1) secretory fibres proper, the excitation of which causes an actual outpouring of liquid from the gland-cells into the ducts; (2) 'trophic' fibres, which not only promote the changes by which already formed organic constituents of the secretion pass into solution, but also stimulate the growth of the glandular protoplasm. In such animals as the dog the cranial nerve (the chorda in the case of the submaxillary and sublingual glands) was supposed to contain many fibres of group (1), comparatively few of group (2); and the sympathetic few of (1) and more of (2). Since these trophic fibres, according to Heidenhain's original statement of his hypothesis, possess two distinct functions, his second group is sometimes subdivided into a set of katabolic fibres which favour the breaking down of material in the cell as a preliminary to its removal in the secretion, and a set of anabolic fibres which have to do with the building up of fresh substance. But it must be remembered that, although it may be convenient for certain purposes to make such a physiological classification, there is no proof of the existence of any corresponding anatomical distinction; and Langley has shown that in the cat's chorda atropia acts simultaneously on all the secretory fibres; the moment it paralyzes one group all are paralyzed. If they were anatomically distinct, it might have been supposed that atropia in a certain dose would pick out one or other group, and leave the rest still active.

It is conceivable that the differences between chorda and sympathetic saliva are due, not to the nerve-fibres, but to the end organs with which they are connected; that is, the two nerves may supply, not the same, but different gland-cells. And it is well known that even after prolonged stimulation of the chorda or chordo-lingual alone, some alveoli of the dog's submaxillary gland remain in the 'resting' state; after stimulation of the sympathetic alone, the number of unaffected alveoli is much greater; while after stimulation of both nerves, few alveoli seem to have escaped change. However suggestive these facts may be, they will not as yet bear the weight even of a hypothesis of salivary secretion. There must in any case be some overlapping in the nerve-supply; that is, some cells must be supplied by

both nerves, since excitation of the sympathetic influences the amount of organic material in the saliva obtained by subsequent stimulation of the chorda, and this organic matter certainly comes, for the most part at least, from substances stored up in the cells. And, indeed, we know nothing of a division of labour between the cells of a gland, except when there are obvious anatomical distinctions. Thus, the submaxillary gland in man contains both serous and mucous acini, and mucin-making cells are scattered over the ducts of most glands, and, indeed, on nearly every surface which is clad with columnar epithelium. In these cases we cannot doubt that one constituent—mucin—of the entire secretion is manufactured by a portion only of the cells. In the cardiac glands of the stomach, too, the ovoid cells, in all probability, yield the whole of the acid of the gastric juice. But, so far as we know, every hepatic cell is a liver in little. Every cell secretes fully-formed bile; every cell stores up, or may store up, glycogen. So it is with the secretory alveoli of the pancreas; one cell is just like another; all apparently perform the same work; each is a unicellular pancreas. (But see p. 484.)

Paralytic Secretion.—When the chorda tympani is divided, a slow 'paralytic' secretion from the submaxillary gland begins in a few hours, and continues for a long time accompanied by atrophy of the gland. There is also a secretion of the same kind from the submaxillary on the opposite side, but it is less copious. This is called the 'antilytic' secretion, which is most pronounced in the first few days after the operation, and seems to be a transient phenomenon. It can be at once abolished by section both of the chorda and the sympathetic on the corresponding side, and is therefore due to impulses arising in the central nervous system. The cause of the paralytic secretion has not been fully made out. If within two or three days of division of the chorda the sympathetic on the same side is cut, the secretion is greatly diminished or stops altogether; and it is concluded that up to this time it is maintained by impulses passing along the sympathetic to the gland from the salivary centre, the excitability of which has been in some way increased by division of the chorda. But if section of the sympathetic is not performed for several days, it has no effect on the paralytic secretion, which at this stage seems to depend on local changes in or near the gland itself, leading to a mild continuous excitation of those nerve-cells on the course of the fibres of the chorda to which reference has already been made. Section of the sympathetic

alone causes neither secretion nor atrophy, nor does removal of the superior cervical ganglion. The histological characters of the gland-cells during paralytic secretion are those of 'rest.'

Reflex Secretion of Saliva. — The reflex mechanism of salivary secretion is very mobile, and easily set in action by physical and mental influences. It is excited normally by impulses which arise in the mouth, especially by the contact of food with the buccal mucous membrane and the gustatory nerve-endings. The mere mechanical movement of the jaws, even when there is nothing between the teeth, or only a bit of a non-sapid substance like indiarubber, causes secretion. The vapour of glacial acetic acid or ether gives rise to a rush of saliva, as does gargling the mouth with distilled water. The smell, sight, or thought of food, and even the thought of saliva itself, may act on the salivary centre through its connections with the cerebrum, and make 'the teeth water.' A copious flow of saliva, reflexly excited through the gastric branches of the vagus, is a common precursor of vomiting; the introduction of food into the stomach also excites salivary secretion.

In most animals and in man the activity of the large salivary glands is strictly intermittent. But the smaller glands that stud the mucous membrane of the mouth never entirely cease to secrete, and the same is the case with the parotid in ruminant animals.

The centre is situated in the medulla oblongata, stimulation of which causes a flow of saliva. The chief afferent paths to the salivary centre are the lingual branch of the fifth and the glosso-pharyngeal; but stimulation of many other nerves may cause reflex secretion of saliva. In experimental stimulation, the sole efferent channel seems to be the cerebral nerve-supply of the glands. After section of the chorda, no reflex secretion by the submaxillary gland can be caused, although the sympathetic remains intact.

It was alleged by Bernard that, after division of the chordo-lingual, a reflex secretion could be obtained from the submaxillary gland by stimulating the central end of the cut lingual nerve between the so-called submaxillary ganglion and the tongue, the ganglion being supposed to act as

'centre.' It has been shown, however, that this is not a true reflex effect, but is due, mainly at least, to the excitation of certain secretory fibres of the chorda that run for some distance in the lingual, then bend back on their course and pass to the gland.

The salivary centre can also be inhibited, especially by emotions of a painful kind—for instance, the nervousness which often dries up the saliva, as well as the eloquence, of a beginner in public speaking, and the fear which sometimes made the medieval ordeal of the consecrated bread pick out the guilty.

In rare cases the reflex nervous mechanism that governs the salivary glands appears to completely break down; and then two opposite conditions may be seen—*xerostomia*, or 'dry mouth,' in which no saliva at all is secreted, and chronic ptyalism, or *hydrostomia*, where, in the absence of any discoverable cause, the amount of secretion is permanently increased. Both conditions are more common in women than in men.

(2) **The Influence of Nerves on the Gastric Glands.**—Like saliva, gastric juice is not secreted continuously, except in animals, such as the rabbit, whose stomachs are never empty. The normal and most efficient stimulus is the presence of food in the stomach. Faintly alkaline liquids, such as saliva, excite an active secretion, but it is only early in digestion, before the reaction of the gastric contents has become distinctly acid, that swallowed saliva can have any effect. Mechanical stimulation of the gastric mucous membrane also causes some secretion, although, it is true, not a great deal. So that at first thought there is much to suggest that the gastric glands are stimulated in a more direct manner than the salivary glands, as by the local action of food substances reaching the cells by a short-cut from the cavity of the stomach, or in a more roundabout way by the blood. And it might be very plausibly argued that the gastric glands are favourably situated for direct stimulation, while the salivary glands are not; and that the great function of saliva being to aid deglutition, an almost momentary, and at the same time a perilous act, it is necessary to provide by nervous mechanism for an immediate rush of secretion at any instant,

while it is not important whether the gastric juice is poured out a little sooner or a little later, and therefore it is left to be called forth by the more tardy and haphazard method of local action. Nevertheless, on looking a little closer, we find that this does not exhaust the subject, and that the gastric secretion can be influenced by events taking place in distant parts of the body, just as the salivary secretion can. In a boy whose œsophagus was completely closed by a cicatrix, the result of swallowing a strong alkali, and who had to be fed by a gastric fistula, it was found that the presence of food in the mouth, and even the sight or smell of food, caused secretion of gastric juice (Richet).

Here there must have been some nervous mechanism at work. The secretion cannot have been excited by the direct action of absorbed food products circulating in the blood—an explanation which has been given of the secretion seen in an isolated portion of the cardiac end of the stomach during the digestion of food in the rest. The efferent nervous channels through which these reflex effects are produced have been defined by Pawlow's experiments on dogs. He first made a gastric fistula, then a few days afterwards divided the œsophagus through a wound in the neck, and stitched the two cut ends to the edges of the wound. After the animals had recovered, it was observed that when meat was given to them by the mouth, a copious secretion of gastric juice followed in five or six minutes, notwithstanding the fact that in this 'sham feeding' the food immediately escaped from the opening in the upper portion of the divided œsophagus. Much the same result was seen when the food was simply shown to the animal. Division of the splanchnic nerves had no effect on this reflex secretion, while it could not be obtained after division of both vagi. Further, stimulation of the peripheral end of the vagus* caused secretion. These experiments accordingly show that secretory fibres for the gastric glands run in the vagi. But after division of the sympathetic fibres going to the stomach, and also the vagi, gastric secretion is still caused by the introduction of food into the stomach, so long as the vagi are cut below the origin of their cardiac and pulmonary branches, and disturbance of the heart and respiration thus avoided. And after section of both vagi in dogs, no marked qualitative or quantitative changes have been observed in the gastric juice. We must therefore suppose that the gastric glands, while under the control of a reflex nervous mechanism with its centre in the cerebrospinal axis, are also capable of being locally stimulated through the peripheral ganglia in the stomach walls, or directly by the mechanical contact of the food or the contraction of the muscular fibres of the viscus, or the chemical action of the products of digestion absorbed into the blood.

* The nerve was not stimulated till a few days after section, so as to allow the cardio-inhibitory fibres to degenerate. Otherwise the heart would have been stopped by the stimulation.

(3) **The Influence of Nerves on the Pancreas.**—Our scanty knowledge may be summed up thus. Stimulation of the medulla oblongata causes secretion, or increases it if already going on. Stimulation of the peripheral end of the vagus* excites secretion after a latent period of 2 to 3 minutes. Stimulation of the central end of the vagus and of other nerves inhibits the secretion; the inhibition caused by vomiting is probably due to impulses ascending the vagus. These facts show that a reflex mechanism governing the pancreatic secretion exists. The centre is probably in the medulla oblongata; the efferent fibres run in the vagus. Afferent impulses that increase the activity of the centre can be set up by stimulation of the gastric mucous membrane, by ether, *e.g.* There is some evidence that a local centre for the pancreatic secretion also exists, possibly in the semilunar ganglion. The natural secretion of pancreatic juice is by no means so intermittent as that of saliva. In the rabbit the pancreatic, like the gastric juice flows continuously. In a well-fed dog it is probable that the flow seldom stops altogether, for after a meal it has been seen to continue for 20 to 24 hours. It begins abruptly as soon as the food enters the stomach, doubtless through reflex impulses originating in the gastric mucous membrane, rises in two or three hours to a maximum, then falls till the fifth or sixth hour, after which it mounts again about the ninth or tenth hour to a second lower maximum, and then, gradually diminishing, ultimately stops. During activity the bloodvessels of the gland are dilated. When the nerves of the pancreas, which pass to it from the solar plexus along the vessels, are divided, 'paralytic' secretion of thin watery juice takes place. There is one remarkable difference between the normal secretion of

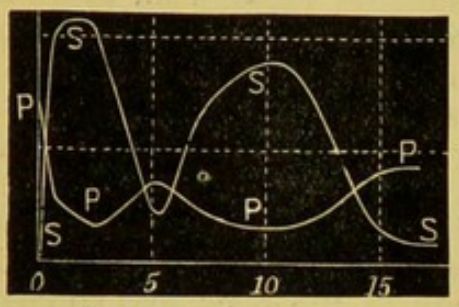


FIG. 108.—RATE OF SECRETION OF PANCREATIC JUICE.

S shows the variation in the rate of secretion of the pancreatic juice in a dog; P, the variation in the percentage of solids in the juice. It will be seen that the maxima of S fall at the same time as the minima of P. The numbers along the horizontal axis are hours since the last meal.

* Slowly recurring stimuli (*e.g.*, induction shocks at the rate of about one in the second) are used, so as to avoid stimulation of the vaso-constrictor fibres of the pancreas, which run in the vagus, since constriction of the bloodvessels hinders the secretion. (See also footnote on p. 343.)

pancreatic juice and of saliva: the pressure of the latter in the submaxillary duct may, as we have seen, greatly exceed the arterial blood-pressure, without reabsorption and consequent œdema of the gland occurring; but the secretory pressure of the pancreatic cells is very low, not more than a tenth of that of the salivary glands. Œdema begins before a manometer in the duct shows a pressure of 20 mm. of mercury.

(4) **The Influence of Nerves on the Secretion of Bile.**— Although bile is secreted constantly, it only passes at intervals into the intestine. For the liver in many animals, unlike every other gland except the kidney, has in connection with it a reservoir, the gall-bladder, in which its secretion accumulates, and from which it is only expelled occasionally. We have therefore to distinguish the bile-secreting from the bile-expelling mechanism. Of the direct influence of nerves on either we have scarcely any knowledge, scarcely even any guess which is worth mentioning here. It is true the secretion of bile may be distinctly affected by the section and stimulation of nerves which control the blood-supply of the stomach, intestines, and spleen, for the quantity of blood passing by the portal vein through the liver depends upon the quantity passing through these organs, and the rate of secretion is closely related to the blood-supply. In this way stimulation of the medulla oblongata, the spinal cord, and the splanchnic nerves stops or slows the secretion of bile by constricting the abdominal vessels; and the same effect can be reflexly produced by the excitation of afferent nerves.

The muscular fibres of the gall-bladder and the larger bile-ducts are thrown into contraction by stimulation of the spinal cord. It is possible that this takes place naturally in response to reflex impulses from the mucous membrane of the duodenum, for the application of dilute acid to the mouth of the bile-duct causes a sudden flow of bile, and the acid contents of the stomach, when projected through the pylorus into the intestine, have a similar effect.

The pressure under which the bile is secreted is remarkably small, the maximum being no more than 15 mm. of mercury. But small as this is, it is higher than the pressure of the portal blood, and therefore the liver ranges itself with the

high-pressure salivary glands rather than with the low-pressure pancreas. But although the biliary pressure is high relatively to that of the blood with which the secreting cells are supplied, it is absolutely very low; and this is a point of practical importance, for a comparatively slight obstruction to the outflow, even such as is offered by a congested or inflamed condition of the duodenal wall about the mouth of the duct, may be sufficient to cause reabsorption of the bile through the lymphatics, and consequent jaundice. Of course, complete plugging of the duct by a biliary calculus is a much more formidable barrier, and inevitably leads to jaundice, just as ligature of a salivary duct, in spite of the great secretory pressure, inevitably causes œdema of the gland.

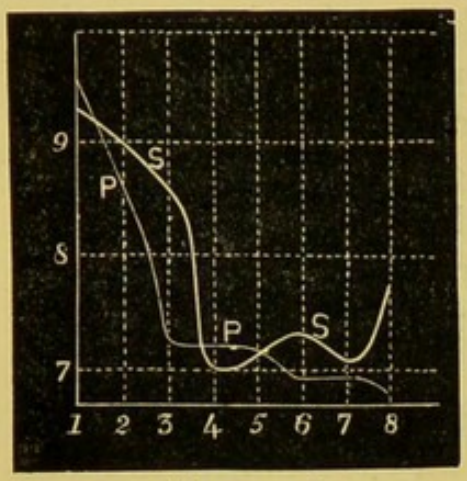


FIG. 109.—RATE OF SECRETION OF BILE.

S shows how the rate of secretion of bile falls in a dog when a biliary fistula is first made, and the bile thus prevented from entering the intestine; P shows the fall in the percentage of solids. The numbers along the horizontal axis are quarters of an hour since bile began to escape through the fistula. The numbers along the vertical axis refer only to curve S, and represent the rate of secretion in arbitrary units.

When food passes into the stomach, there is at once a sharp rise in the rate of secretion of bile. A maximum is reached from the fourth to the eighth hour—that is, while the food is in the intestine; there is then a fall, succeeded by a second smaller rise about the fifteenth or sixteenth hour, from which the secretion gradually declines to its minimum. Upon the whole, the curves of secretion of pancreatic juice and bile show a fairly close correspondence, which lends additional support to the view derived from their chemical and physical properties, that in digestion they are partners in a common work.

We do not know in what way the rate of secretion of bile is influenced by digestion, although it has been conjectured that the first abrupt rise may be started by reflex nervous action, and that later on absorbed food products may directly excite the hepatic cells. Rutherford found that when the mucous membrane of the stomach and duodenum is irritated

by a substance like gamboge, there is no increase in the rate of secretion of the bile, notwithstanding the greatly increased flow of blood through the intestinal vessels which the irritation causes. This tells in favour of the direct influence of substances derived from the food rather than of any important reflex action.

(5) **The Influence of Nerves on the Secretion of Intestinal Juice.**—As to the influence of nerves on the secretion of the succus entericus, our knowledge is almost limited to a single experiment, and that an inconclusive one. Moreau placed four ligatures on a portion of the small intestine, so as to form three compartments separated from each other and from the rest of the gut. The mesenteric nerves going to the middle loop were divided, and the intestine returned to the abdomen. After some time a watery secretion was found in the middle compartment, little or none in the others. This is a true 'paralytic' secretion, and not a mere transudation depending simply on the vascular dilatation caused by section of the vaso-constrictor nerves, for it has the same composition and digestive action as normal succus entericus obtained from a fistula.

Effect of Drugs on the Digestive Secretions.—A small dose of atropia, as has been said, abolishes the secretory action of the chorda tympani. This it does by paralyzing the nerve-endings. The gland-cells are not paralyzed, for the sympathetic can still cause secretion. The nerve-fibres are not paralyzed, because the direct application of atropia does not affect them; nor is the seat of the paralysis the ganglion-cells on the course of the fibres, for stimulation between those cells and the gland-cells is ineffective. Pilocarpine is the physiological antagonist of atropia, and restores the secretion which atropia has abolished. In small doses it causes a rapid flow of saliva, its action being certainly a peripheral action, and probably an action on the nerve-endings, for it persists after all the nerves going to the salivary glands have been divided, and after the ganglion-cells have been paralyzed by nicotine. Atropia and pilocarpine act similarly on some of the other digestive glands, the former paralyzing the pancreatic secretion, the latter increasing the secretion of gastric, and probably of intestinal, juice; but atropia does not stop the secretion caused by division of the intestinal nerves. Physostigmine and muscarine act on the whole like pilocarpine.

The action of a host of drugs on the secretion of bile has been investigated by various observers, but till something like unanimity has been reached, it would not be profitable to go into details here.

The only real cholagogues at present positively known appear to be the salts of the bile acids, which, given by themselves or in the bile, cause not only an increase in the volume of the biliary secretion, but also an increase in its solids. Certain compounds of salicylic acid, as salol (phenyl salicylate) and sodium salicylate, also appear to slightly increase the flow, while usually diminishing the concentration of the bile. The injection of hæmoglobin into the blood-stream, or its liberation there by substances, such as toluylene-diamin and arseniuretted hydrogen, which cause solution of the corpuscles, leads to an increased secretion of bile-pigment as well as a more rapid flow of bile.

Summary.—Here let us sum up the most important points relating to the secretion of the digestive juices. *They are all formed by the activity of gland-cells originally derived from the epithelial lining of the alimentary canal. The organic constituents or their precursors (including the mother-substances of the ferments) are prepared in the intervals of rest—absolute in some glands, relative in others—and stored up in the form of granules, which during activity are moved towards the lumen of the gland tubules, and there discharged.*

The nerves of the salivary glands are, as regards their origin, (a) cerebral, (b) sympathetic; the former group is vaso-dilator, the latter vaso-constrictor—both are secretory. Secretion of saliva depends strictly on the nervous system. That nerves influence the gastric and pancreatic secretions is also made out. As regards the intestinal glands and the liver, it has not been proved that their secretive activity is at all under the control of the nervous system, except in so far as the latter may indirectly govern it through the blood-supply, although various circumstances suggest the probability of a more direct action. In all the glands the blood-flow is increased during activity—in some (salivary glands) this is known to be caused through vasomotor nerves. In the salivary glands electromotive changes accompany the active state, while more heat is produced, more carbon dioxide given off, and more oxygen used up, during secretion than during rest. In the other glands we may assume that the same occurs.

IV. Digestion as a Whole.

Having discussed in detail the separate action of the digestive secretions, it is now time to consider the act of digestion as a whole, the various stages in which are

co-ordinated for a common end. The solid food is more or less broken up in the mouth and mixed with the saliva, which its presence causes to be secreted in considerable quantity. Liquids and perhaps small solid morsels are shot down the open gullet without contraction of the constrictors of the pharynx, and reach the lower portion of the œsophagus in a comparatively short time ($\frac{1}{10}$ second); while a good-sized bolus is grasped by the constrictors, then by the œsophageal walls, and passed along by a more deliberate peristaltic contraction. Beaumont saw, in the case of St. Martin, that the œsophageal orifice of the stomach contracted firmly

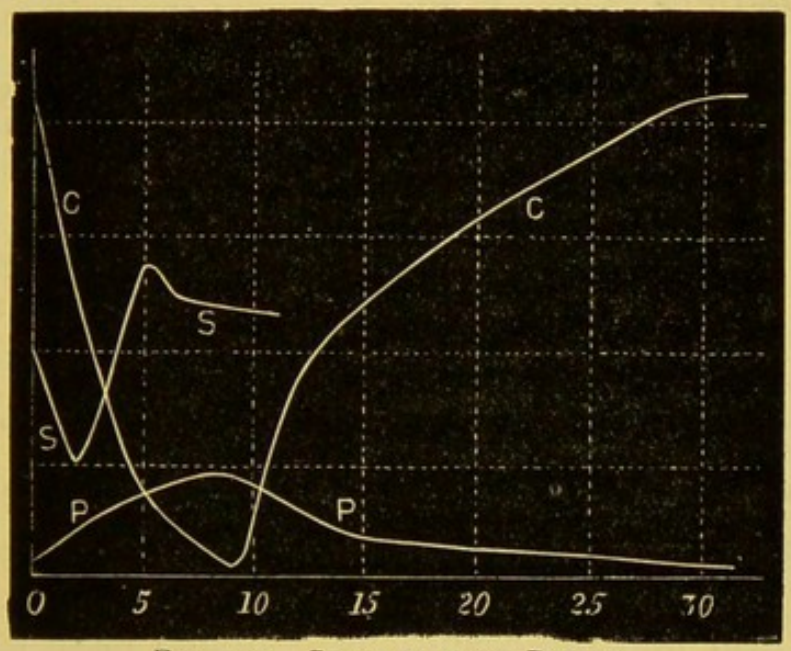


FIG. 110.—SECRETION OF PEPSIN.

C shows the quantity of pepsin in the mucous membrane of the cardiac end of the stomach at different times during digestion; P, the quantity of pepsin in the mucous membrane of the pyloric end; S, the quantity of pepsin in the *secretion* of the cardiac glands. The numbers marked along the horizontal axis are hours since the last meal. About five hours after the meal S reaches its maximum. From the very beginning of the meal C falls steadily down to the tenth hour, and then begins to rise, *i.e.*, the gland-cells of the cardiac end of the stomach become poorer in pepsin as secretion proceeds.

after each morsel was swallowed, and so did the gastric walls in the neighbourhood of the fistula when food was introduced by this opening. Two sounds may be heard in man on listening in the region of the stomach or œsophagus during deglutition of liquids, especially when, as generally happens, they are mixed with air. The first sound occurs at once, and is supposed to be due to the sudden squirt of the liquid along the gullet; the second, which is heard after a distinct interval (six seconds), seems to be caused by the

forcing of the fluid through the cardiac orifice of the stomach by the contraction of the œsophagus.

Chemical digestion in man begins already in the mouth, a part of the starch being there converted into dextrins and sugar (maltose), as has been shown by examining a mass of food containing starch just as it is ready for swallowing (p. 376). This process is no doubt continued during the passage of the food along the œsophagus.

The first morsels of a meal which reach the stomach find it free from gastric juice, or nearly so. They are alkaline from the admixture of saliva; and the juice which is now beginning to be secreted, in response to the presence of the food, and to reflex excitement starting in the mouth, is for a time neutralized, and amylolytic digestion still permitted to go on. For 20 to 40 minutes after digestion has begun there is no free hydrochloric acid in the stomach, although some is combined with proteids, and during this period the ptyalin of the swallowed saliva will be able to act even better than in the mouth, being favoured by the weakly acid reaction due to the lactic acid(and the traces of butyric and acetic acids) produced during the first part of the digestive period by the action of the *Bacillus acidi lactici* on the carbohydrates of the food. Indeed, for a time, as the meal goes on, the successive portions of food which arrive in the stomach will find the conditions more and more favourable for amylolytic digestion. But as the acidity continues to increase, the activity of the ptyalin will first be lessened, and ultimately abolished; and, upon the whole, a considerable proportion of the starches must usually escape complete conversion into sugar until they are acted upon by the pancreatic juice. This is particularly the case with unboiled starch, as contained in vegetables which are eaten raw; and, indeed, we know that sometimes a certain amount of starch may escape even pancreatic digestion, and appear in the fæces. Meanwhile, pepsin and hydrochloric acid are being poured forth; the latter is entering into combination with the proteids of the food; and before the end of an ordinary meal peptic digestion is in full swing. The movements of the pyloric end of the stomach increase, and eddies are set up in its contents, which carry the morsels of food with

them, and throw them against its walls. In this way not only are the contents thoroughly mixed, and fresh portions of food constantly brought into contact with the gastric juice secreted mainly in the more passive cardiac end, but a certain amount of mechanical disintegration is brought about; and this is aided by the digestion of the gelatin-yielding connective tissue which holds together the fibres of muscle and the cells of fat, and the digestible structures in vegetable tissue which enclose starch granules. If milk has formed a portion of the meal, the casein will have been curdled soon after its entrance into the stomach, by the action of the rennet ferment alone when the milk has been taken at the beginning of digestion before the gastric contents have become distinctly acid, by the acid and rennin together when it has been taken later. The casein and other proteids of milk, like the myosin and other proteids of meat, and the globulins, phytovitellins, and other proteids of bread and of vegetable food in general, are acted upon by the pepsin and hydrochloric acid, yielding ultimately peptones; while variable quantities of these proteids and of the acid-albumin and proteoses derived from them may escape this final change, and pass on as such into the duodenum. In the dog, indeed, a meal of flesh has been found to be almost entirely digested to the peptone stage while still in the stomach, leaving little for the pancreatic juice to do. But we may safely assume that, in the case of a man living on an ordinary mixed diet, much of the food proteids passes through the pylorus chemically unchanged, or having undergone only the first steps of hydration. For, even a few minutes after food has been swallowed, the pyloric sphincter may relax and allow the stomach to propel a portion of its contents into the intestine; and such relaxations occur at intervals as digestion goes on, although it is not for several hours (three to five) that the greater portion of the food reaches the duodenum. During this period the acidity has at first been constantly increasing, although for a time the hydrochloric acid has combined, as it is formed, with the proteids of the food. The combination, however, does not prevent it from contributing to

the total acidity as determined by titration. Then comes a stage where the hydrochloric acid has so much increased that, after combining with all the proteids, some of it remains over as free acid. The lactic acid now rapidly disappears from the stomach because the growth of the bacteria that produce it is checked by the hydrochloric acid; and after a time the total acidity begins to fall, the fully-digested proteids being continually absorbed in the form of peptones, which are only found in traces, if at all, in the chyme. This fall continues till the third or fourth hour, the proportion of free to combined acid continuing, nevertheless, to rise, since nearly all that is now secreted remains free. Easily-diffusible bodies, such as sugars and some of the organic crystalline constituents of meat, *e.g.*, kreatin, will also pass through the gastric mucous membrane into the blood.

The substances which reach the duodenum are: (1) the whole of the fats, with no chemical and little physical change. But the partial digestion in the stomach of the envelopes and protoplasm of the cells of adipose tissue, and of the proteid which keeps the fat of milk in emulsion, prepares the fats for what is to follow in the intestine. (2) All the proteids which have not been carried to the stage of peptone, and perhaps some peptone. (3) All the starch and dextrins—and glycogen, if any be present—which have not been converted into maltose, and possibly a little maltose. (4) Elastin, nuclein, cellulose, and other substances not digestible or digestible only with difficulty in gastric juice. (5) The constituents of the gastric juice itself, including pepsin. The ptyalin of the saliva has been already digested and destroyed.

It must be remembered that all this time, even from the beginning of digestion, a certain amount of pancreatic juice has been finding its way into the duodenum in response to the presence of food in the stomach acting through the reflex mechanism we have described. The secretion of bile, too, always going on, has quickened its pace, and the gall-bladder is getting more and more full as the meal proceeds and gastric digestion begins. When the acid chyme, a grayish liquid, turbid with the débris of animal and vegetable tissues

—with muscular fibres, fat globules, starch granules, and dotted ducts—gushes through the pylorus and strikes the duodenal wall, the muscular fibres of the gall-bladder contract, and a sudden rush of bile takes place from the common duct. By-and-by, as bile and pancreatic juice continue to be poured out, the reaction in the duodenum, as tested by litmus, becomes less acid and even weakly alkaline for a time. But it soon becomes acid again, and the acidity at first increases as the food passes down the gut. In the lower portion of the small intestine the acidity diminishes, and the contents may be neutral or actually alkaline for some distance above the ileo-cæcal valve. To phenolphthalein the reaction is acid throughout the whole intestine. But methyl orange shows an alkaline reaction, all the way from the lower end of the duodenum to the cæcum (Moore and Rockwood). In the upper part of the duodenum the reaction with this indicator is sometimes found acid, but sometimes neutral or alkaline. All this refers to the conditions during full digestion (3 or 4 to 8 or 9 hours after the taking of food). When digestion is over (20 to 24 hours after a meal) the reaction becomes acid to methyl orange, litmus and phenolphthalein throughout the whole intestine* (Pluemer and Stewart).

A consideration of the properties of the indicators mentioned enables us to interpret in some measure these results, which at first sight appear so confusing. Methyl orange, the most stable of the series, is not affected by weak organic acids, but reacts acid to inorganic, and the stronger organic acids like lactic, acetic and butyric acids, and alkaline to salts of the weaker acids, such as sodium carbonate and bicarbonate. Phenolphthalein is very sensitive to acids, even to weak organic acids such as the fatty acids derived from the fat of meat, and to carbonic acid. Litmus is intermediate between methyl orange and phenolphthalein. The chyme as it passes through the pylorus contains free hydrochloric acid, and in addition, during the first stages of digestion of a meal containing carbo-hydrates, free lactic acid. It mingles immediately with the alkaline contents of the duodenum. If these contain a sufficient quantity of bases to combine with the whole of the acids which would affect methyl orange, that indicator will show a neutral or alkaline reaction. Phenolphthalein may at the same time react acid on account of the presence of weaker acids, including carbonic acid, either originally dissolved in the intestinal fluid or liberated by the

* In 18 dogs fed with meat 20 to 24 hours before death this was found to be the case. In 4 of the dogs the gastric contents were almost neutral to litmus and methyl orange, but slightly alkaline to phenolphthalein; in the rest acid to all three indicators.

action of the acids of the chyme on the carbonates. If there is not enough alkali to combine with the whole of the stronger acids of the chyme the reaction will be at first acid to all the indicators, but may soon become alkaline to methyl orange or even to litmus, as pancreatic juice and bile continue to enter the duodenum. As the food progresses along the intestine a certain amount of lactic acid is produced by the action of micro-organisms on the carbo-hydrates, and perhaps also on the proteids. The alkalies of the intestinal secretions are being continually used up, both to neutralize this acid, and to form soaps with the fatty acids set free from the fats by the steapsin and the fat-splitting bacteria. The point may easily be reached, and as a rule is reached, at which enough of the weak acids or of acid salts is present to give an acid reaction with phenolphthalein or litmus, while the reaction is still alkaline to methyl orange. By the time the food has arrived at the lower end of the small intestine the greater part of the fat-splitting may be supposed to be over, and the greater part of the fatty acids absorbed. The acids that remain may be easily neutralized by the alkaline succus entericus, reinforced by the alkalies, especially ammonia produced by the ordinary putrefactive bacteria from proteids; and the reaction, previously alkaline to methyl orange only, may thus become alkaline to litmus as well. Dissolved carbonic acid will still account for the acid reaction to phenolphthalein. Towards the end of intestinal digestion the discharge of pancreatic juice, bile and succus entericus having almost or entirely ceased, the acid-forming bacteria appear again to get the upper hand; and since the reaction is acid to methyl orange as well as to the other indicators, me must assume that strong organic acids, like lactic acid, are present. On the entrance of food into the stomach the inflow of alkaline pancreatic juice, and perhaps of succus entericus, into the intestine begins; and for a considerable time this is not counteracted by the escape of any large quantity of acid chyme through the pylorus. We must accordingly suppose that the conditions for the establishment of an alkaline reaction of the intestinal contents are unfavourable at the end of intestinal digestion, and favourable at the beginning of gastric digestion.

Trypsin, like pepsin, performs its work in part in an acid medium; and although the cause of the acidity and the character of the medium are far from being the same as in the gastric juice, it is obviously an advantage that the chief proteolytic ferment should be able to act upon the proteids in all parts of the intestine and at every stage of intestinal digestion whether the reaction is acid or alkaline. The proteids of the chyme are all carried by the trypsin to the stage of peptone. Much of the peptone is absorbed as it is formed, but some, even in perfectly normal digestion, is further split up into leucin, tyrosin, and similar bodies.

We are not without other examples of digestive juices destined to act in a medium with an opposite reaction to their own. The 'saliva' of *Octopus macropus*, strongly acid though it is, contains a proteolytic ferment which *in vitro* acts, like trypsin, better in an alkaline than in an acid solution. The pepsin of the (in itself) alkaline secretion of the pyloric end of the stomach becomes a constituent of the acid gastric juice; and it may, perhaps, be considered a morphological accident, so to speak, that the oxyntic cells of the cardiac end should mingle their acid products with the (presumedly) alkaline secretion of the chief cells in the lumen of each gland-tube, instead of being massed as a separate organ with a special duct.

In the lower portions of the small intestine bacteria of various kinds are present and active; and it is not unlikely that even throughout its whole length a certain range of action is permitted to them, checked by the acidity of the chyme, though scarcely by the antiseptic properties of the bile. The stomach, with its acid contents, forms during the greater part of gastric digestion a valve or trap to cut off the upper end of the intestine from the bacteria-infested regions of the mouth and pharynx, and to destroy or inhibit the micro-organisms swallowed with the food and saliva. The occasional presence in vomited matter of sarcinæ or regularly arranged groups of micrococci, generally four to a group, shows that under abnormal conditions the gastric contents are not perfectly aseptic; and even from a normal stomach active micro-organisms of various kinds can be obtained. But upon the whole there is no doubt that the acidity of the gastric juice is an important check on bacterial activity during the first part of digestion, and in the upper portion of the alimentary canal.

And, indeed, Koch has shown that the acidity of the gastric juice of a guinea-pig is sufficient to kill the comma bacillus of cholera. Normal guinea-pigs fed with cholera bacilli were unaffected. But if the gastric juice was neutralized by an alkali before the administration of the bacilli the guinea-pigs died. Charrin found, too, that digestion with pepsin and hydrochloric acid causes an appreciable destruction or attenuation of diphtheria toxine. Naturally, bacteria, like the lactic acid bacillus, which form acid products are less affected by the acid gastric juice than the putrefactive bacteria, which, on the whole, form alkalies, and are therefore accustomed to an alkaline medium.

It has been supposed by some that this bactericidal action is the chief function of the stomach, and the question has been asked, why we should attribute any digestive importance to the secretion of that viscus, since the pancreatic juice can do all that the gastric juice does, and some things which it cannot do. Further, it has been shown that a dog may live five years after complete excision of the stomach, comport himself in all respects like a normal dog, and when killed for autopsy show every organ in perfect health (Czerny). Recently, too, the stomach has been excised in man with a successful result. But if this is to be admitted as evidence against the digestive function of the stomach, it is just as good evidence against the bactericidal function, particularly as it has in addition been shown that even putrid flesh has no harmful effect on a dog after excision of the stomach, any more than on a normal dog. And, indeed, the reasoning is fallacious which assumes that what *may* happen under abnormal conditions *must* happen when the conditions are normal. For nothing is impressed more often on the physiological observer than the extraordinary power of adaptation, of making the best of everything, which the animal organism possesses. Doubtless, a dog without a stomach will use to the best advantage the digestive fluids that remain to him; and the pancreatic juice may be adequate to the task of complete digestion. So, too, a man from whom the surgeon has removed a kidney, or a testicle, or a lobe of the thyroid gland, may be in no respect worse off than the man who possesses a pair of these organs. But what do we deduce from this? Not, surely, that the excised thyroid, or testicle, or kidney was useless, or the gastric juice inactive, but that the organism has been able to compensate itself for their loss.

The lower end of the small intestine is not cut off by any bacteria-proof barrier from the large intestine, in which putrefaction is constantly going on. It has been actually shown that small particles such as lycopodium spores, suspended in water, soon reach the stomach when injected into the rectum. So that micro-organisms may be able to work their way above the ileo-cæcal valve, even against the

downward peristaltic movement. But even if this were not the case, a few bacteria or their spores, passing through the stomach with the food, would be enough to set up extensive changes as soon as they reached a part of the alimentary canal where the conditions were favourable to their development. Indeed, from the time when the first micro-organism enters the digestive tube soon after birth, it is never free from bacteria; and their multiplication in one part of it rather than another depends not so much on the number originally present to start the process, as on the conditions which encourage or restrain their increase.

The fats are broken up into their fatty acids and glycerine by the fat-splitting ferment of the pancreatic juice. The acids will form soaps with alkalies wherever they meet them in the intestinal contents, or even in the mucous membrane. A portion of those soluble soaps may be immediately absorbed; the rest may aid in the emulsification of the fats not yet chemically decomposed, and thus greatly hasten the fat-splitting action of the pancreatic juice. The starch and dextrine which have escaped the action of the saliva are changed into maltose by the amylopsin. A little dextrine may be absorbed as such (Bleile).

The succus entericus, as an alkaline liquid, aids in lessening the acidity of the chyme and establishing the reaction favourable to intestinal digestion. It will invert any cane-sugar which may reach the intestine; but it cannot be doubted that cane-sugar may be absorbed by the stomach, being inverted by the hydrochloric acid of the gastric juice or by inverting ferments taken in with the food, or on its way through the gastric walls.

Upon the whole no great amount of water is absorbed in the small intestine, or at least the loss is balanced by the gain, for the intestinal contents are as concentrated in the duodenum as in the ileum. But as soon as they pass beyond the ileo-cæcal valve, water is rapidly absorbed, and the contents thicken into normal fæces, to which the chief contribution of the large intestine is mucin, secreted by the vast number of goblet-cells in its Lieberkühn's crypts.

Bacterial Digestion.—So far we have paid no special attention

to other than the soluble ferments of the digestive tract, although we have incidentally mentioned the action of the lactic acid bacilli on carbohydrates and of the fat-splitting bacteria on fats. It is now necessary to recognise that the presence of bacteria is an absolutely constant feature of digestion; and although their action must in part be looked upon as a necessary evil which the organism has to endure, and against the consequences of which it has to struggle, it is not unlikely that in part it may be ancillary to the processes of aseptic digestion. But bacteria are not essential, as some have supposed. For it has been shown that a young guinea-pig, taken by Cæsarean section from its mother's uterus with elaborate antiseptic precautions, and fed in an aseptic space on sterile milk, grew apparently as fast as one of its sisters brought up in the orthodox microbic way. The alimentary canal remained free from bacteria (Nuttall and Thierfelder).

Among the more important actions of bacteria on the proteid food-products in the intestines may be mentioned the formation of indol, phenol, and skatol, the first having tyrosin for its precursor, and being itself after absorption the precursor of the 'indican' in the urine; the second being to a small extent thrown out with the fæces, but chiefly absorbed and eliminated by the kidneys as an aromatic compound of sulphuric acid; the third passing out mainly in the fæces.

The large intestine is the chosen haunt of the bacteria of the alimentary canal; they swarm in the fæces, and by their influence, especially in the cæcum of herbivora, but also to a small extent in man, even cellulose is broken up, the final products being carbon dioxide and marsh gas. Cellulose-dissolving enzymes of great activity have been found in the hepatic secretion of the snail and the hepato-pancreas of the carp. Filter-paper is rapidly dissolved by the latter. The contents of the large bowel are generally acid from the products of bacterial action, although the wall itself is alkaline.

Fæces.—In addition to mucin, secreted mainly by the large intestine, the fæces consist of indigestible remnants of the food, such as elastic fibres, spiral vessels of plants, and in

general all vegetable structures chiefly composed of cellulose. They are coloured with a pigment, stercobilin, derived from the bile pigments. Stercobilin is identical with 'febrile' urobilin, with the urobilin which forms a common, though not an invariable, constituent of bile itself, and probably with the urobilin of normal urine. No bilirubin or biliverdin occurs in normal fæces, although pathologically they may be present. The dark colour of the fæces with a meat diet is due to hæmatin and sulphide of iron, the latter being formed by the action of the sulphuretted hydrogen which is constantly present in the large intestine on the organic compounds of iron contained in the food or in the secretions of the alimentary canal. A small amount of altered bile acids and their products is also found; and in respect to these, and to the altered pigments, bile is an excretion. And although its important function in digestion, and the fact that the greater part of the bile salts is reabsorbed,* show that in the adult it is very far from being solely a waste product, the equally cogent fact, that the intestine of the new-born child is filled with what is practically concentrated bile (*meconium*), proves that it is just as far from being purely a digestive juice. Skatol and other bodies, formed by putrefactive changes in the proteids of the food, are also present in the fæces, and are responsible for the fæcal odour. Masses of bacteria are invariably present. Of the inorganic substances in fæces the numerous crystals of triple phosphate are the most characteristic. When the diet is too large, or contains too much of a particular kind of food, a considerable quantity of digestible material may be found in the fæces, *e.g.*, muscular fibres and fat. But it should be remembered that under all circumstances the composition of the fæces differs from that of the food. The intestinal contribution is always an important one, although relatively more important with a flesh than with a vegetable diet.

* Stadelmann concludes from an elaborate review of previous work and numerous fresh experiments that a circulation of the bile-acids (*i.e.*, an absorption from and re-excretion into the intestine) is proved; that a circulation of the bile-pigments is probable; but that a circulation of the cholesterin of the bile does not take place at all.

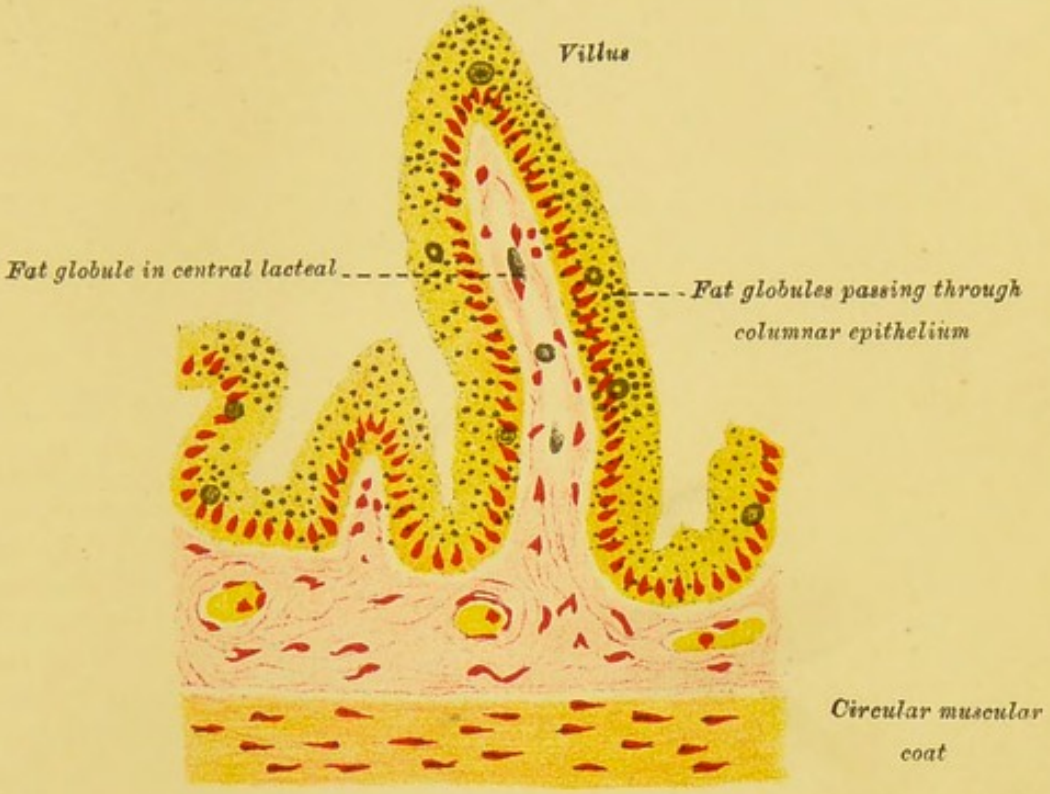
CHAPTER V.

ABSORPTION.

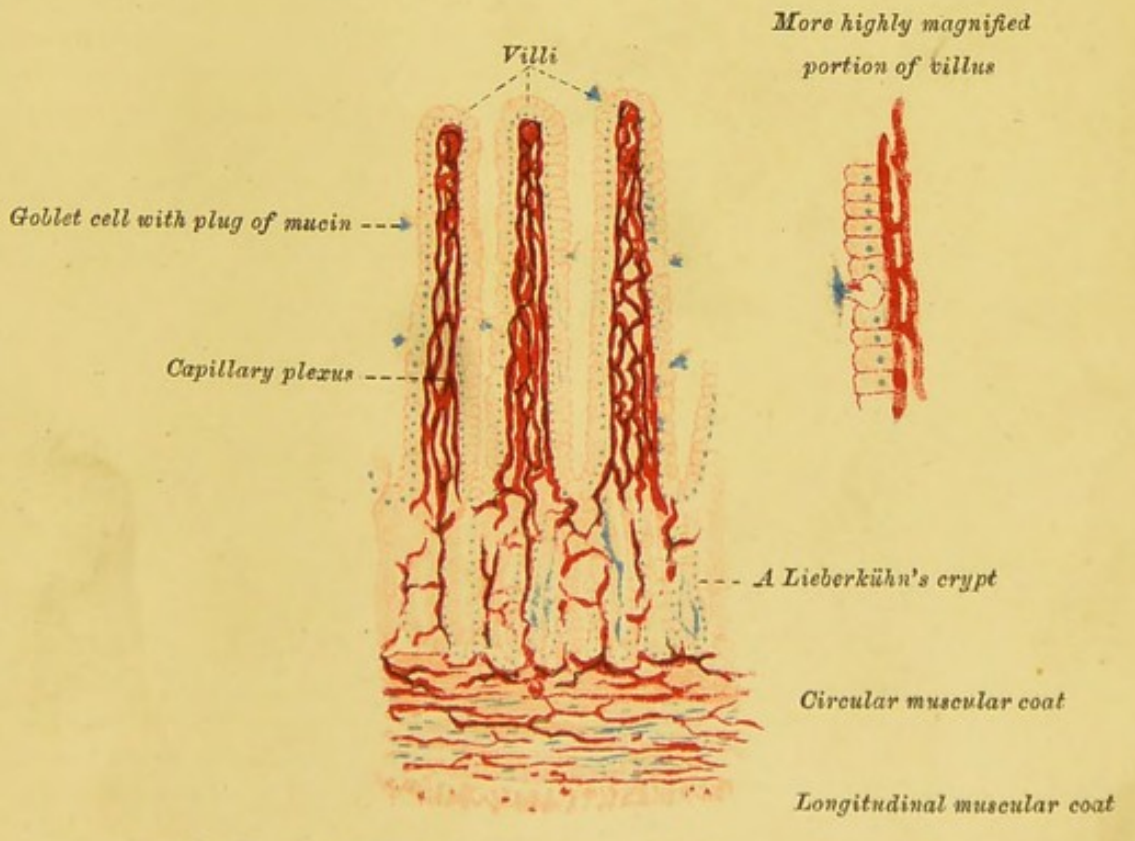
Physical Introduction—Diffusion.—When a solution of a substance is placed in a vessel, and a layer of water carefully run in on the top of it, it is found after a time that the dissolved substance has spread itself through the water, and that the composition of the mixture is uniform throughout. The result is the same when two solutions containing different proportions of the same substance, or containing different substances, are placed in contact. The phenomenon is called *diffusion*. The time required for complete diffusion is comparatively short in the case of a substance like hydrochloric acid or sodium chloride, exceedingly long in the case of albumin or gum. In both it is more rapid at a high temperature than at a low.

Osmosis.—If the solution be separated from water by a membrane absolutely or relatively impermeable to the dissolved substance, but permeable to water, water passes through the membrane into the solution. This phenomenon is called osmosis. *E.g.*, a membrane of ferrocyanide of copper, nearly impermeable to cane-sugar, can be formed in the pores of an unglazed porcelain pot by allowing potassium ferrocyanide and cupric sulphate to come in contact there. If the pot is filled with, say, a 1 per cent. solution of cane-sugar, closed by a suitable stopper, connected to a manometer, and then placed in a vessel of water, water passes into it till the pressure indicated by the manometer rises to a certain height. With a 2 per cent. solution it reaches twice this height, and in general the **osmotic pressure**, as it is called, is in any solution proportional to the molecular concentration* of the solution, or, in other words, to the number of molecules of the dissolved substance in a given volume of the solution. If in this sentence we substitute 'gaseous pressure' for 'osmotic pressure,' and 'gas' for 'solution,' we have a statement of Boyle's law, which asserts that the pressure of a gas is proportional to its density. And, indeed, it has been shown that the osmotic pressure of the dissolved substance is the

* The molecular concentration is strictly defined as the number of grammes of the dissolved substance in a litre of the solution divided by the gramme-molecular weight. The gramme-molecular weight, or gramme-molecule, is the number of grammes corresponding to the molecular weight. Thus, the gramme-molecular weight of sodium chloride (NaCl) is 58·36 grammes, and of cane-sugar ($C_{12}H_{22}O_{11}$), 342 grammes.



1. Section of frog's intestine to show absorption of fat, × 300.
(Stained with picrocarmine and osmic acid.)



2. Section of small intestine. Blood-vessels injected.

(Stained with hæmatoxylin and eosin.)

GEORGE KENNING, COLOR PRINTER.

same as the pressure that would be exerted by a gas, say hydrogen, if all the water were removed, and a molecule of hydrogen substituted for each molecule of the substance, or as would be exerted by the substance itself if, after removal of the solvent, it could be left as a gas filling the same volume. And the osmotic pressure of a solution of one substance is the same as that of a solution of any other substance which contains in a given volume the same number of molecules of the dissolved substance. In other words, the osmotic pressure is not dependent on the nature, but on the molecular concentration, of the substance. The analogy of the laws of osmotic to those of gaseous pressure becomes still more obvious when it is added that the osmotic pressure of a substance with any given molecular concentration is proportional to the absolute temperature; and that when a solution contains more than one dissolved substance, the total osmotic pressure is the sum of the partial osmotic pressures which each substance would exert if it were present alone in the same volume of the solution.

The osmotic pressure of a solution may reach an enormous amount. Thus, a 1 per cent. solution of cane-sugar has a pressure at 0° C. of 493 mm. of mercury. A 10 per cent. solution of cane-sugar would have an osmotic pressure of more than six atmospheres, and a 17 per cent. solution of ammonia a pressure of no less than 224 atmospheres. The osmotic pressure must be due to the kinetic energy of the moving molecules. Where the molecules are hindered from passing a bounding membrane, the pressure exerted by their impacts on the boundary is greater than where the membrane is easily permeable, because in the latter case many of the molecules pass through, carrying with them their kinetic energy. The pressure must be still less when a dissolved substance diffuses freely into water; but however small it may become, it is in the osmotic pressure of the molecules of the dissolved substance that the force which causes diffusion must be sought.

In practice it is inconvenient, and in many cases impossible, to directly measure the osmotic pressure by means of a semi-permeable membrane like ferrocyanide of copper. Recourse is therefore had to indirect methods. Of these, one of the most generally used depends on the fact that the freezing-point of a solution is lower than that of the solvent; for example, salt water freezes at a lower temperature than fresh water. The amount by which the freezing-point is lowered depends on the molecular concentration of the dissolved substance, to which, as we have seen, the osmotic pressure is also proportional. When a gramme-molecule of a substance is dissolved in water, and the volume made up to a litre, the freezing-point is lowered by 1·8° C.; the osmotic pressure is 22·35 atmospheres (16,986 mm. of mercury). It is therefore easy to calculate the osmotic pressure of any solution if we know the amount by which its freezing-point is lowered. A 1 per cent. solution of cane-sugar, for example, would freeze at about – 0·052° C. Its osmotic pressure

$$= \frac{\cdot 052}{1 \cdot 8} \times 16{,}986 = 490 \text{ mm. of mercury.}$$

The osmotic pressure of different solutions may also be compared by observing the effect produced on certain vegetable and animal cells. When a solution with a greater osmotic pressure than the cell-sap (a *hyperisotonic solution*) is left for a time in contact with certain cells in the leaf of *Tradescantia discolor*, *plasmolysis* occurs—that is, the protoplasm loses water and shrinks away from the cell-wall. If the osmotic pressure of the solution is lower than that of the coloured cell-sap (*hypoisotonic* solution), no shrinking of the protoplasm takes place. By using a number of solutions of the same substance but of different strength, two can be found, the stronger of which causes plasmolysis, and the weaker not. Between these lies the solution which is *isotonic* with the cell-sap—that is, has the same molecular concentration and osmotic pressure. The strength of an isotonic solution of some other substance can then be determined in the same way with sections from the same leaf.

Animal cells (red blood-corpuscles) may also be employed, the liberation of hæmoglobin or the swelling of the corpuscles, as measured by the hæmatocrite (p. 35), being taken as evidence that the solution in contact with them is *hypoisotonic* to the contents of the corpuscles. If the corpuscles shrink, the solution is *hyperisotonic* to their contents. But since the cells are much more permeable to certain substances than to others, this method does not always yield trustworthy results.

Electrolytes.—We have said that the osmotic pressure is proportional to the concentration of the solution, but this statement must now be qualified. For certain compounds, including all inorganic salts and many organic substances, the osmotic pressure decreases less rapidly than the theoretical molecular concentration as the solution is diluted. The explanation appears to be that in solution some of the molecules of these bodies are broken up into simpler groups or single atoms, called *ions*. Each ion exerts the same osmotic pressure as the molecule did before. The proportion between the average number of these dissociated molecules and of ordinary molecules is constant for a given concentration of the solution and a given temperature. But as the solution is diluted, the proportion of dissociated molecules becomes greater. The bodies which behave in this way are **electrolytes**—that is, their solutions conduct a current of electricity; bodies which do not exhibit this behaviour do not conduct in solution. And there are many reasons for believing that the dissociation of the electrolytes is the essential thing in electrolytic conduction. We may suppose that in a solution of an electrolyte—sodium chloride, for instance—a certain number of the molecules fall asunder into a *kation* (Na), carrying a charge of positive electricity, and an *anion* (Cl), carrying an equal negative charge. These electrical charges, it must be remembered, are not created by the passage of a current through the solution. We do not know how they arise, but the ions must be supposed to be electrically charged at the moment when the molecule is broken up. And the ions of different substances must each be supposed to carry the same quantity of electricity. But since they are all wandering freely in

the solution, no excess of negative or of positive electricity can accumulate at any part of it—in other words, no difference of potential can exist. When electrodes connected with a voltaic battery are dipped into a solution of an electrolyte, a difference of potential (p. 533), an electrical slope, is established in the liquid, and the positively charged kations are compelled to wander towards the negative pole, the negatively charged anions towards the positive pole. In this way that movement of electricity which is called a current is maintained in the solution. It is clear that the greater the number of ions, and the faster they move in the solution, the greater will be the quantity of electricity carried to the electrodes in a given time, when the difference of potential between the electrodes, or the steepness of the electric slope, remains constant. In other words, the *specific conductivity* of a solution of an electrolyte varies as the number of dissociated molecules in a given volume and the speed of the ions. It increases up to a certain point with the concentration, because the absolute number of dissociated molecules in a given volume increases. The *molecular conductivity*—that is, the conductivity per molecule, or, strictly, the ratio of the specific conductivity to the molecular concentration, increases with the dilution, because the relative number of dissociated molecules, as compared with undissociated, increases. At a certain degree of dilution the molecular conductivity reaches its maximum, for all the molecules are dissociated. The ratio of the molecular conductivity of any given solution to this maximum or limiting value is therefore a measure of the proportion between the number of dissociated and the total number of molecules. The molecular conductivity of the salts dissolved in the liquids of the animal body, for the degree of dilution in which they exist there, is such that we must assume them to be for the most part dissociated.

Absorption of the Food.—In the preceding chapter we have traced the food in its progress along the alimentary canal, and sketched the changes wrought in it by digestion. We have next to consider the manner in which it is absorbed. Then, for a reason which has already been explained, instead of following its fate within the tissues, until it is once more cast out of the body in the form of waste products, it will be best to drop the logical order and pick up the other end of the clue—in other words, to pass from absorption to excretion, from the first step in metabolism to the closing act, and afterwards to return and fill in the interval as best we can.

And here, first of all, it should be remembered that the epithelial surfaces, through which the substances needed by the organism enter it, and waste products leave it, are, physiologically considered, outside the body. The mucous membranes of the alimentary,

respiratory and urinary tracts are in a sense as much external as the fourth great division of the physiological surface, the skin. The two latter surfaces are in the mammal purely excretory. Absorption is the dominant function of the alimentary mucous membrane, but a certain amount of excretion also goes on through it. The pulmonary surface both excretes and absorbs, and that in an equal measure. But it is by no means necessary that the surface through which oxygen is taken in and gaseous waste products given off should be buried deep in the body, and communicate only by a narrow channel with the exterior. In the frog the skin is largely an absorbing as well as an excreting surface; oxygen passes freely in through it, just as carbon dioxide passes freely out. In most fishes, and many other gill-bearing animals, the whole gaseous interchange takes place through surfaces immersed in the surrounding water, and therefore distinctly external. In certain forms it has even been shown that the alimentary canal may serve conspicuously for absorption and excretion of gaseous, as well as liquid and solid substances. Still lower down in the animal scale, the surface of a single tube may perform all the functions of digestion, absorption and excretion. Lower still, and even this tube is wanting, and everything passes in and out through an external surface pierced by no permanent openings.

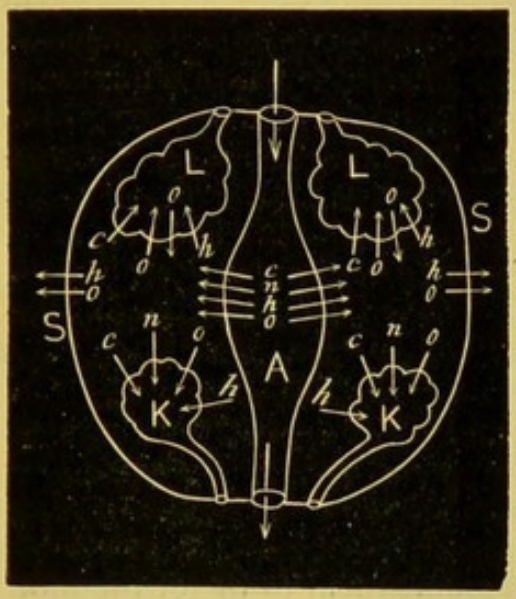


FIG. 111.—DIAGRAM OF ABSORPTION AND EXCRETION.

Carbon *c*, nitrogen *n*, hydrogen *h*, and oxygen *o*. L represents the pulmonary surface; K, the surface of the renal epithelium; A, the alimentary canal; S, the skin.

Indeed, even in man the functions of the various anatomical divisions of the physiological surface are not quite sharply marked off from each other. Though gaseous interchange goes on far more readily through the pulmonary membrane than anywhere else, swallowed oxygen is easily enough absorbed from the alimentary canal and carbon dioxide given off into it; and to a small extent these gases can also pass through the skin. Though water is excreted chiefly by the skin, the pulmonary and the urinary surfaces, and on the whole absorbed chiefly from the digestive tract, there is no surface which in the twenty-four hours pours out so much water as the mucous membrane of the stomach. Under normal conditions, it is true, by far the greater part of this is reabsorbed in the intestine, yet in diarrhœa, whether natural or caused by purgatives, the intestines themselves may, instead of absorbing, contribute largely to the excretion of water. Again, although the solids of the excreta are normally given off in far the greatest quantity in the urine and fæces (only part of the latter is truly an excretion, since

much of the fæces of a mixed diet has never been physiologically inside the body at all), yet salts and traces of urea are constantly found in the sweat, and salts and mucin in the excretions of the respiratory tract. Further, although the solids and liquids of the food are usually taken in by the alimentary mucous surface, it is possible to cause substances of both kinds to pass in through the skin ; and a certain amount of absorption may also take place through the urinary bladder. So that really it may be considered, from a physiological point of view, as more or less an accident that a man should absorb his food by dipping the villi of his intestine into a digested mass, rather than by dipping his fingers into properly prepared solutions, as a plant dips its roots among the liquids and solids of the soil ; or that he should draw air into organs lying well in the interior of his thorax, instead of letting it play over special thin and highly vascular portions of his skin ; or that the surface by which he excretes urea should be buried in his loins, instead of lying free upon his back.

It has been already explained that, although digestion is a necessary preliminary to the absorption of most of the solids of the food, we are not to suppose that all the food must be digested before any of it begins to be absorbed. On the contrary, the two processes go on together. As soon as any peptone has been formed from the proteids, or sugar from the starch, they begin to pass out of the alimentary canal ; and by the time digestion is over, absorption is well advanced.

Even in the mouth it has already begun, and it is continued with far greater rapidity in the stomach. Here peptones, sugar, and diffusible substances like alcohol, and the extractives of meat, which form an important part of most thin soups and of beef-tea, are undoubtedly absorbed. But it is in the small intestine that absorption reaches its height. The mucous membrane of this tube offers an immense surface, multiplied as it is by the valvulæ conniventes, and studded with innumerable villi. Here the whole of the fat, much sugar, proteose and peptone, certain products of the further action of the unformed and formed ferments of the intestine on the food, and certain constituents of the bile are taken in. In the large intestine, as has been already said, water and soluble salts are chiefly absorbed.

What now is the mechanism by which these various products are taken up from the digestive tube, and what paths do they follow on their way to the tissues ?

Theories of Absorption.—Not so very long ago it was supposed by many that the processes of diffusion, osmosis and filtration offered a tolerably complete explanation of physiological absorption. At that time the dominant note of physiology was an eager appeal to chemistry and physics to 'come over and help it'; and as new facts were discovered in these sciences they were applied, with a confidence that was almost naïve, to the problems of the animal organism. The phenomena of the passage of liquids and dissolved solids through animal membranes, upon which the work of Graham had cast so much light, seemed to find their parallel in the absorptive processes of the alimentary canal. And when digestion was more deeply studied, facts appeared which seemed to show that its whole drift was to increase the solubility and diffusibility of the constituents of the food. But as time went on, and more was learnt of the phenomena of absorption and the powers of cells, these crude physical theories broke down, and discarded 'vitalistic' hypotheses began once more to arouse attention. Then came the recent investigations of De Vries, Van't Hoff, and others in the domain of molecular physics, which gave to our notions of osmosis the precision that was wanted before its relation to many physiological processes could be profitably discussed. At the present time it must be admitted that we possess no explanation of absorption which is more than a confession of ignorance, and does not itself need to be explained. Some physiologists, impressed with the vast progress of physics and chemistry, and especially with the strides that have recently been made in the study of osmosis, believe that as our knowledge of these sciences increases, it will become possible to explain on physical principles all the peculiar phenomena which we observe in the passage of substances through the walls of the alimentary canal. Others, taking account of the number and nature of these peculiarities, oppressed with the perennial paradox of vital action, incline to the less sanguine view, that after all physical explanations have been exhausted, the real secret of the cell will still lurk in some ultimate 'vital' property of structure or of function, and still elude our search. Both the optimist and the pessimist, the adherent of the physical and the adherent of the vitalistic hypothesis, admit that the phenomena of absorption are essentially connected with the cells that line the alimentary canal. And the one must confess what the other proclaims, that while the processes carried on in these cells are definite, well ordered, and evidently guided by laws, these laws have as yet denied themselves to the modern physiologist, with chemistry in one hand and physics in the other, as they denied themselves to his predecessor, equipped only with his scalpel, his sharp eyes, and his mother-wit. So that in the present state of our knowledge all we can really say is that, while absorption is certainly aided by physical processes like osmosis, it is at bottom the work of cells with a selective power which we do not understand, and which is probably peculiar to living structures. Thus, dissolved substances pass with equal ease in either direction through an ordinary diffusion membrane, but they pass in general, more readily out of the intestine than into

it. When the cells that line the intestine are injured or destroyed, or subjected to the action of certain poisons, absorption from it is diminished or abolished. And in their normal state they do not take up indiscriminately all kinds of diffusible substances, nor absorb those which they do take up in the direct ratio of their diffusibility, nor do they reject everything which does not diffuse. Albumin, for example, which does not pass through dead animal membranes, is to a certain extent taken up from a loop of intestine without change. Cane-sugar and dextrose are absorbed more rapidly than their velocity of diffusion would indicate, when compared with inorganic salts. And it has been shown that the water, organic and inorganic solids of the serum of an animal are absorbed from a loop of its intestine when the pressure in the capillaries of the intestinal wall is considerably greater than in the cavity of the gut. Since the serum in the intestine and the plasma in the capillaries must be isotonic, and practically identical in chemical composition, the absorption cannot be due to ordinary osmosis or diffusion. Nor can it be due to filtration, since the slope of pressure is from the capillaries to the lumen of the gut (Waymouth Reid). It is therefore extremely difficult to reconcile this experiment with any purely physical theory of absorption.

But if it be true that the action of the columnar epithelium of the intestinal mucous membrane is governed by a secretive and selective power that makes use of purely physical processes, but is not mastered by them, the possibility must be admitted that in the cells of endothelial type which line the serous cavities, the lymphatics, the bloodvessels, the alveoli of the lungs, and the Bowman's capsules of the kidney (p. 397), the element of secretion is less marked, and more overshadowed by the physical factors. And it may very plausibly be urged that changes of considerable physiological complexity can only be wrought on substances that have to pass through a cell of considerable depth, while a mere film of protoplasm suffices for, and indeed favours, mechanical filtration and diffusion. We have already seen (p. 242), in the case of the lungs, that whatever the complete explanation may be of the gaseous exchange which takes place through the alveolar membrane, physical diffusion undoubtedly plays an important part. We shall see, too (p. 407), that in the case of the kidney the endothelium of the Bowman's capsule, although by no means devoid of selective power, does seem to have allotted to it a simpler task than falls to the share of the 'rodded' epithelium. Further, it has been stated that interchange between blood-serum, circulated artificially in the vessels of dogs and rabbits which have been dead for hours, and liquids introduced into the peritoneal cavity, is essentially the same as in the living animal, and can be explained on purely physical principles (Hamburger). Ligation of the thoracic duct has little effect on the fate of liquids injected into serous cavities, since the bloodvessels play the chief part in their absorption, just as strychnia, when injected under the skin—*i.e.*, into the lymph-spaces of areolar tissue—is taken up by the blood and does not appear in the lymph. But even if we admit that substances can

pass, by physical processes alone, from serous cavities into the blood, and from the blood into serous cavities, it is still necessary to inquire whether anything else is concerned in the formation of the lymph; all the more as the recent researches of Asher throw grave doubt on the common view that these sacs are merely expanded lymph spaces, and indicate that the liquid found in them has a different origin from lymph.

Formation of Lymph.—The teaching of Ludwig, that lymph is formed by the filtration and diffusion of the constituents of blood-plasma through the walls of the capillaries into the tissue spaces, was first seriously called in question by Heidenhain, who advanced the theory that it is secreted by the capillary endothelium. One of Heidenhain's strongest arguments in favour of his secretion theory was the existence of substances which, when injected into the blood, increased the flow of lymph without affecting appreciably the arterial pressure. He divided these so-called *lymphagogues* into two classes: (1) substances like peptone, leech-extract, extract of crayfish, egg-albumin, etc., which cause not only an increase in the rate of flow, but an increase in the specific gravity and total solids of the lymph; (2) crystalloid substances, like sugar, salt, etc., which cause an increased flow of lymph more watery than normal. Starling has shown that although the lymphagogues of the second class do not raise the arterial pressure, they do, by attracting water from the tissues and thus causing hydræmic plethora (an excess of blood of low specific gravity), bring about a marked rise of venous, and therefore, what is the important thing for lymph filtration, of capillary pressure. The action of the first class of lymphagogues, which cannot be explained in this way because the pressure in the capillaries is not increased, he attributes to an injurious effect on the capillary endothelium (and especially on the endothelium of the capillaries of the liver, since nearly the whole of the increased lymph-flow comes from that organ), which increases its permeability. Starling's explanation is supported by various facts, but it is not easy to distinguish an increase of permeability produced by lymphagogues from an increase of secretive activity of the endothelial cells. Hamburger, too, has brought forward results which it is difficult to reconcile with a theory of filtration even for the second class of lymphagogues. Further, Heidenhain has shown that some time after injection of a crystalloid substance, like sugar, into the blood, a greater percentage

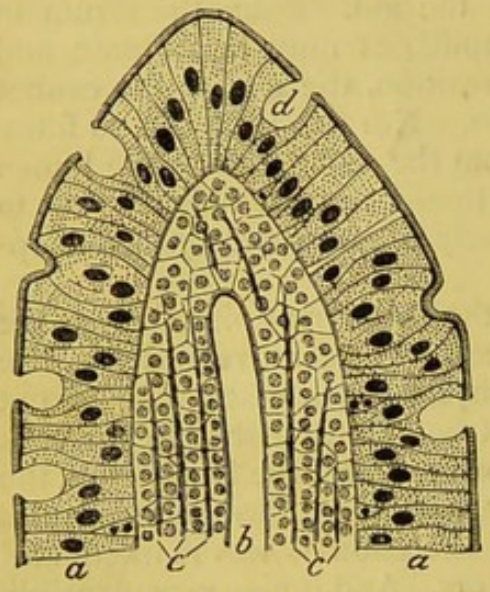


FIG. 112.—VERTICAL SECTION OF A VILLUS (CAT) × 300.

a, layer of columnar epithelium covering the villus—the outer edge of the cells is striated; *b*, central lacteal of villus; *c*, unstriped muscular fibres; *d*, mucin-forming goblet-cell.

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of the substance may be found in the lymph than in the blood. Now, when a mixture of crystalloids and colloids is filtered through a thin membrane, the percentage of crystalloids in the filtrate is never, at most, greater than in the original liquid. And although Cohnstein states that if time enough be allowed, the maximum concentration of sodium chloride in the lymph, after intravenous injection, becomes approximately the same as the maximum in the blood, this fact loses its weight as an argument in favour of the filtration hypothesis when we remember that, according to Asher, all the solids of the lymph are markedly increased when even small quantities of crystalloids are injected into the veins. Lazarus-Barlow found, too, that the maximum outflow of lymph from the thoracic duct does not occur at the time of maximum intravenous pressure, and that in the great majority of his experiments the injection of a concentrated solution of sodium chloride, glucose or urea into a vein was followed, not by an initial diminution in the outflow of lymph (as might have been expected if the exchange of water between the blood and the tissue spaces was regulated solely by differences in osmotic pressure), but by an immediate increase.

So far we may say that while it has been made out that the physical processes of filtration, osmosis and diffusion do play a part in the passage of water and solids through the walls of the capillaries, there is much which they leave unexplained, and which at present, for the want of a more precise term, we must attribute to the secretory activity of the endothelial cells. In addition, the cells of the tissues in general, and particularly of the glands, appear to have a share in the formation of the lymph. Asher and Barbèra have found that defibrinated lymph injected into the carotid artery of a dog produces marked effects on the circulation (Traube-Hering curves, paralysis or in some cases stimulation of the vagus), and that these effects are not produced by defibrinated blood. They conclude that the common doctrine that lymph is simply a diluted blood-plasma is erroneous, and attribute the toxic effects to products of the metabolism of the tissues which have found their way into the lymph. To the lymph-glands they assign the function of transforming these toxic bodies into harmless substances. Lymph, they say, so far from being a mere filtrate or even a secretion from the blood, is formed by the activity of the organs, and may actually be absorbed by the blood from the tissue-spaces. In fact, according to their view the intravenous injection of lymphagogues, both crystalloid and colloid, only causes an increased flow of lymph in so far as it leads to increased glandular secretion. The injection of bile or albumose, for instance, is followed by a greatly increased secretion of bile, and with this increase in the work of the liver is associated the production of a greater quantity of lymph by its cells. While this is doubtless an over-statement of the part played by the organs, we may safely assume that they do make a contribution to the lymph; their waste-products pass into it, and possibly, as Koranyi suggests, by increasing

its molecular concentration cause the passage of water into it from the blood.*

It ought to be remembered in this whole discussion that the epithelium of ordinary glands derives its supplies of material from the lymph. The vicissitudes of blood-pressure affect it only in a secondary and indirect manner. On the other hand, the endothelial cells of the capillaries are in direct contact with the blood. And it is interesting to observe that in this respect the glomeruli of the kidney and the alveoli of the lungs (if the endothelial lining of Bowman's capsule and the alveolar membrane are assumed to be complete) take a middle place between the glands proper and the quasi-glandular capillaries.

Absorption of Fat.—It has been already mentioned that fat is split up in the intestine into glycerine and fatty acids, but it has been a subject of discussion whether it all undergoes this change or only a portion of it. The common view has long been that the greater part of the fat escapes decomposition, and, after emulsification by the soaps formed from the liberated fatty acids, is absorbed as neutral fat by the epithelial cells covering the villi. If an animal is killed during digestion of a fatty meal, these cells are found to contain globules of different sizes, which stain black with osmic acid, are dissolved out by ether, leaving vacuoles in the cell substance, and are therefore fat (Plate III., 1). It has always been difficult to explain how droplets of emulsified fat could get into the interior of the epithelial cells, and yet it certainly passes into them, and not between them. When fat is found in the cement substance between the cells, it has been mechanically squeezed out of them by the shrinking of the villi in preparation. This difficulty is obviated if we suppose that the whole of the fat is split up in the intestine, the products being absorbed in solution, the glycerine as such, and the fatty acids either as soaps or in the free state, or partly free and partly saponified. If this is the true theory—and the evidence of its truth has of late years been continually growing—neutral fat must again be

* Although it is customary to speak of lymph as if it were perfectly homogeneous, there is no experimental ground for supposing that the tissue liquid in contact with the cells of different organs, or even the tissue liquid in contact with one and the same cell at different parts of its periphery, has a uniform composition. There are indeed certain general considerations which show that this cannot be so.

built up in the epithelial cells from the absorbed glycerine and the fatty acids or soaps. Now, it has been shown that when an animal is fed with fatty acids they are not only absorbed, but appear as neutral fats in the chyle of the thoracic duct, having combined with glycerine in the intestinal wall; and the epithelial cells contain globules of fat, just as they do when the animal is fed with neutral fat. Further, it is known that fat-splitting goes on in the alimentary canal to a much greater extent than would be necessary merely for the formation of a quantity of soap sufficient to emulsify the whole of the fat in the food; indeed, at certain stages of digestion most of the fatty material, both in the small and large intestine, has been found to consist of fatty acids. To clinch the matter, it has been proved that fatty substances which are not easily split up and saponified (for example, lanolin, the fat of sheep's wool, a mixture of compounds of fatty acids with cholesterin and allied bodies) are not absorbed even when they are easily emulsified.

Leucocytes have been asserted to be the active agents in the absorption of fat. They have been described as pushing their way between the epithelial cells, fishing, as it were, for fatty particles in the juices of the intestine, and then travelling back to discharge their cargo into the lymph. This view, however, is erroneous. But although the leucocytes do not aid in the absorption of fat from the intestine, they appear to take it up from the epithelial cells, conveying it through the spaces of the network of adenoid tissue that occupies the interior of the villus, to discharge it into the central lacteal, where it mingles with the lymph and forms the so-called molecular basis of the chyle. A part of the fat reaches the lacteal in some other way, without being carried by the leucocytes. The contraction of the smooth muscular fibres of the villus and the peristaltic movements of the intestinal walls alter the capacity of the lacteal chamber, and so alternately fill it from the lymph of the adenoid reticulum, and empty it into the lymphatic vessel with which it is connected. By this kind of pumping action the passage of fat and other substances into the lymphatics is aided. In

the dog no fat is absorbed by the bloodvessels, except perhaps a small quantity in the form of soaps; it nearly all goes into the lacteals, and thence by the general lymph stream through the thoracic duct into the blood. And in man the chyle collected from a lymphatic fistula contained a large proportion of the fat given in the food (Munk). But this bare statement would be misleading if we did not add that the fat taken in can never be entirely recovered in the chyle collected from the thoracic duct. A portion of it disappears, and its fate is unknown. And even after ligature of the thoracic duct a large proportion of a meal of fatty acids is absorbed from the intestine, by what channel is uncertain (Frank).

A dog normally absorbs 9—21 per cent. of the fat in a meal in three to four hours; 21—46 per cent. in seven hours; and 86 per cent. in eighteen hours (Harley). After excision of the pancreas the absorption of fat is hindered, though not abolished. More fat, indeed, can be recovered from the intestine than is given in the food. This at first sight paradoxical result is explained by the well-established fact that a certain amount of fat is normally excreted into the intestine.

Absorption of Water, Salts, and Sugar.—The water, salts, and sugar pass normally into the rootlets of the portal vein, not into the chyle, for no increase in the quantity of these substances flowing through the thoracic duct takes place during digestion, while the sugar in the portal blood is increased after a starchy meal. In man not 1 per cent. of the sugar corresponding to the carbohydrates of the food could be recovered in the chyle escaping from a lymphatic fistula. But when a large amount of a dilute solution of sugar is introduced into the intestine some of it is taken up by the lacteals.

Absorption of Proteids.—The proteids of the food and their digested products also pass directly into the blood-capillaries which feed the portal system. For it has been shown that after ligature of the thoracic duct proteid substances are still absorbed from the intestine, and the urea corresponding to their nitrogen appears in the urine. And

the proteids in the lymph flowing from a lymphatic fistula in a case of elephantiasis in man were not found to be sensibly increased during the digestion of proteid food (Munk).

Although a certain amount of egg-albumin, serum-albumin, alkali-albumin, and other native or slightly altered proteid substances can be absorbed as such by the small, and even by the large, intestine, there can be no doubt that the greater part of the proteids of the food is first changed into proteoses and peptones. But proteose and peptone are absent from the blood, and, indeed, when injected into the blood they are excreted in the urine. When injected in larger amount they pass also into the lymph, from which they gradually reach the blood again, and are eventually, as before, eliminated by the kidneys. The clear inference is that when absorbed from the alimentary canal they must be changed into one or both of the chief proteids of blood and lymph (serum-albumin and serum-globulin) in their passage through its walls. And it has actually been shown that during the digestion of a proteid meal the mucosa of the stomach and intestine contains proteose and peptone, while none is present in the muscular coat or in any other organ. They rapidly disappear from a portion of the mucous membrane kept at a temperature of about 40° C. outside of the body; but not if it has been thrown into boiling water immediately after excision, nor even if it has been heated to 60° C. for a few minutes, and then kept at 40° C. Now, a temperature of 60° C. does not destroy an unorganized ferment, but kills a living cell. The regeneration of the proteose and peptone must therefore presumably take place in cells, and the only available cells in this locality are those which line the intestine, or the leucocytes which wander between them. Accordingly, both have been credited with the power of absorbing and transforming these substances, but the balance of evidence is in favour of the epithelial cells. We cannot, however, as in the case of the fat, single out any particular tract of epithelium as alone engaged in the absorption of proteose and peptone, or, indeed, of the diffusible substances in general. In all likelihood the cells covering the villi are actively concerned, but

there is no valid reason for denying a share to the general lining of the stomach and small intestine, even including the Lieberkühn's crypts, which morphologically form a kind of inverted villi. It is, indeed, true that the crypts do not take part in the absorption of fat, for no granules blackened by osmic acid occur in them during digestion of a fatty meal. But this is a ground for attributing to them other absorptive functions rather than for altogether denying to them a share in absorption, especially as it seems unlikely that the secretion of the comparatively scanty and relatively unimportant succus entericus should engross the whole activity of such an extensive sheet of cells. Even the large intestine, which possesses Lieberkühn's crypts but no villi, is able to absorb not only peptones and sugar, but also undigested proteids; and although these are powers which can be rarely exercised in normal digestion, they form the physiological basis of the important method of treatment by nutrient enemata.

We may add to the proof of the varied powers of the cells of the intestinal wall given by the change which proteoses and peptones undergo in their passage through them the facts, already mentioned, that cane-sugar does not pass into the blood as such unless large quantities are given, but is first converted into dextrose, even in the absence of an inverting ferment, and the remarkable discovery of Munk, that fatty acids given by the mouth appear in the lymph of the thoracic duct as neutral fats, having somewhere or other, in all probability on their way through the epithelium of the gut, been combined with glycerine.

Since, however, the amount of neutral fat recovered from the thoracic duct is not equivalent to more than one-third of the fatty acids given, it has been suggested that this synthesis of fat is only apparent, and that the whole of the fat which appears in the chyle after a meal of fatty acids comes from the fat excreted into the intestine (Frank), which is increased when fatty acids are given by the mouth. But the suggestion is more ingenious than the evidence advanced in its support is convincing.

PRACTICAL EXERCISES ON CHAPTERS IV. AND V.

1. **Saliva.**—*Collection and Microscopic Examination of Saliva.*—Chew a piece of paraffin-wax, or inhale ether or the vapour of strong acetic acid. The flow of saliva is increased. Collect it in a porcelain capsule. Examine a drop under the microscope. It may contain a few flat epithelial scales from the mouth and a few round granular bodies, the salivary corpuscles, the granules in which often show a lively, dancing movement (Brownian motion). Filter the saliva to free it from air-bubbles, and perform the following experiments:

(*a*) Test the reaction with litmus paper. It is usually alkaline. An acid reaction may indicate that bacterial processes are abnormally active in the mouth.

(*b*) Add dilute acetic acid. A precipitate indicates the presence of mucin (p. 296). Filter.

(*c*) Add a drop or two of silver nitrate solution. A precipitate insoluble in nitric acid, soluble in ammonia, proves that chlorides are present.

(*d*) Add to another portion a few drops of dilute ferric chloride, and the same quantity to as much distilled water in a control test-tube. A reddish coloration is obtained, due to the presence of sulphocyanic acid, which is combined with potassium and other bases in the saliva. The colour is discharged by mercuric chloride. Or, a drop of saliva may be allowed to fall from the mouth on a test paper (prepared by soaking filter paper with a dilute starch solution, containing a little iodic acid, and allowing it to dry in the air). The paper is coloured blue by the union of the starch with iodine set free from the iodic acid by the action of the sulphocyanic acid.

(*e*) Take some boiled starch mucilage, and test it for reducing sugar by Trommer's test (p. 23). If no sugar is found, take three test-tubes, label them A, B, and C, and nearly half fill each with the boiled starch. To A add a little saliva,* to B some saliva which has been boiled, to C a little saliva which has been neutralized, and as much 0·4 per cent. hydrochloric acid as has been taken of the mucilage, so as to make the strength of the acid in the mixture 0·2 per cent., or the same as that of the gastric juice. Put the test-tubes into a water-bath at about 40° C. In a few minutes test the contents for reducing sugar. Abundance will be found in A, none in B nor in C. In B the ferment ptyalin has been destroyed by boiling; in C its action has been inhibited by the acid. If the test-tubes have been left long enough in the bath, no blue colour will be given by A on the addition of iodine, but a strong blue colour by B and C; *i.e.*, the starch will have completely disappeared from A.

(*f*) Put some starch in a test-tube, add a little saliva, and hold in the hand or place in a bath at 40° C. On a porcelain slab place several separate drops of dilute iodine solution. With a glass rod

* As it filters slowly, unfiltered saliva may be used for Experiments *e*, *f* and *h*.

add a drop of the mixture in the test-tube to one of the drops of iodine at intervals as digestion goes on. At first only the blue colour given by starch will be seen; a little later a violet colour, due to the presence of erythrodextrin in addition to some unaltered starch. A little later the colour will be reddish, the starch having disappeared, and the erythrodextrin reaction being no longer obscured. Later still no colour reaction will be obtained, the erythrodextrin having undergone further changes, and only sugar (maltose, isomaltose, and perhaps a trace of dextrose) and achroodextrin—a kind of dextrin which gives no colour with iodine—being present.

(*g*) Put a little distilled water in a porcelain capsule, and bring the water to the boil. Now put into the mouth some boiled starch paste, and move it about as in mastication. After half a minute spit

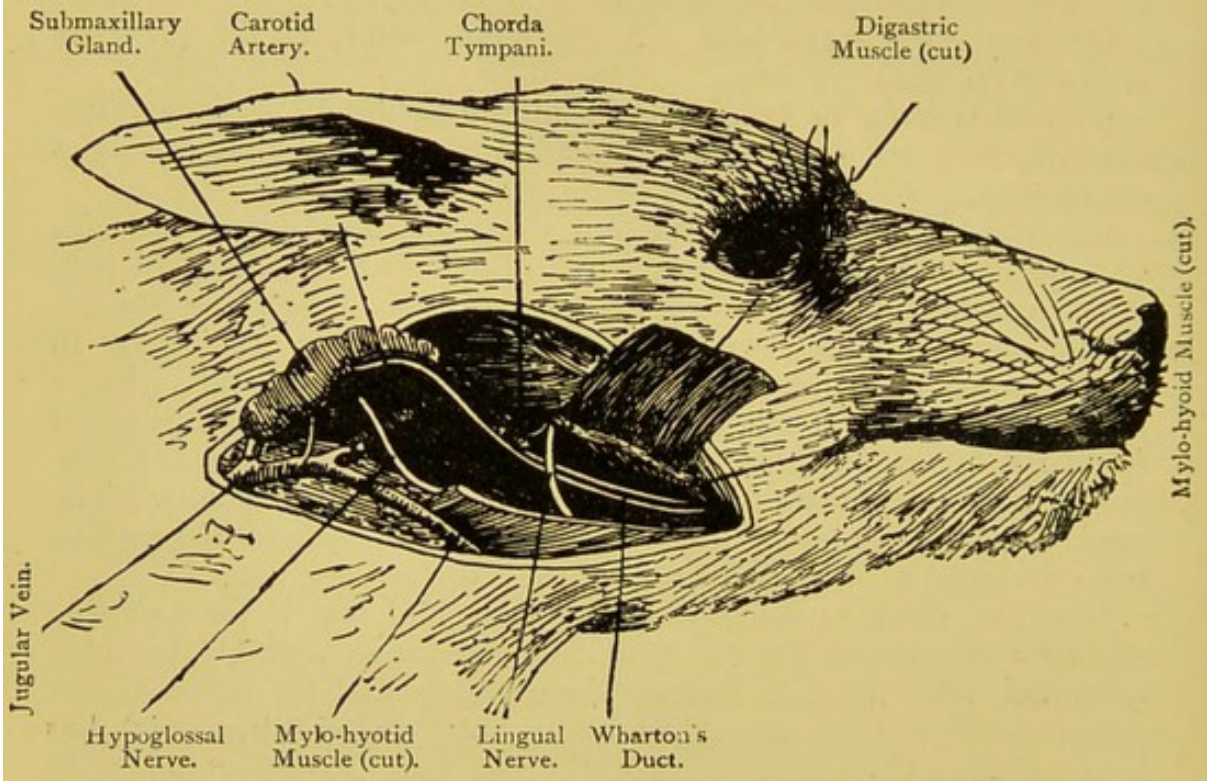


FIG. 113.—DISSECTION FOR STIMULATION OF CHORDA TYMPANI (AFTER BERNARD).

the starch out into the boiling water. Divide the water into two portions. Test one for sugar, and the other for starch. Repeat the experiment, but keep the starch two minutes in the mouth. Report the result.

(*h*) Starch solution to which saliva has been added is placed in a dialyser tube of parchment paper for twenty-four hours. At the end of that time the dialysate (the surrounding water) should be tested for sugar and for starch. Sugar will probably be found, but no starch. If no reaction for sugar is obtained, the dialysate should be concentrated on the water-bath, and again tested.

2. **Stimulation of the Chorda Tympani.**—(1) Having previously studied the anatomy of the mouth and submaxillary region in the dog by dissecting a dead animal (Fig. 113), put a good-sized dog

under morphia. Set up an induction-machine for a tetanizing current (p. 175), and connect it with fine electrodes. Fasten the dog on the holder, give ether if necessary, and insert a cannula in the trachea (p. 177). Then make an incision 3 or 4 inches long, through skin and platysma muscle, along the inner border of the lower jaw beginning about the angle of the mouth, and continuing backwards towards the angle of the jaw. Such branches of the jugular vein as come in the way may be generally pushed aside, but if necessary they may be doubly ligated and divided. Feel for the facial artery, so as to be able to avoid it. Divide the digastric muscle about its anterior third, and clear it carefully from its attachments; or, without dividing it, pull it outwards with a hook. The broad, thin mylo-hyoid muscle will now be seen with its motor nerve lying on it. Divide the muscle about its middle at right angles to its fibres, and raise it carefully. The lingual nerve will be seen emerging from under the ramus of the jaw. It runs transversely towards the middle line, and then, bending on itself, passes forwards parallel to the larger hypoglossal nerve. In its transverse course the lingual will be seen to cross the ducts of the submaxillary and sublingual glands. These structures having been identified, the lingual nerve is to be ligatured before it enters the tongue and cut peripherally to the ligature. Then a glass cannula of suitable size is to be inserted into the submaxillary duct (the larger of the two), just as if it were a bloodvessel (p. 58). A short piece of narrow rubber tubing is carefully slipped on the end of the cannula. The lingual is now to be lifted by means of the ligature, and traced back towards the jaw till its chorda tympani branch is seen coming off and running backwards along the duct. The chordo-lingual nerve (Fig. 107, p. 333) is then to be cut centrally to the origin of the chorda tympani, which can now be easily laid on electrodes by means of the ligature on the lingual. On stimulating the chorda, the flow of saliva through the cannula will be increased. The current need not be very strong. If the flow stops after a short time, it can be again caused by renewed stimulation after a brief rest. A quantity of saliva may thus be collected, and the experiments already made with human saliva repeated.

(2) Expose the vago-sympathetic nerve in the neck on the same side; ligature it; divide below the ligature, and note the effect produced by stimulation of the upper end on the flow of saliva.

(3) Set up another induction-machine, and connect it with electrodes. Stimulate the chorda, and note the rate of flow of the saliva. Then, while the chorda is still being excited, stimulate the vago-sympathetic and observe the effect. If the experiment is successful, finish by stimulating the chorda for a long time. Then harden both submaxillary glands in absolute alcohol, make sections, stain with carmine and compare them.

3. **Effect of Drugs on the Secretion of Saliva.**—(1) Proceed as in 2 (1), but, in addition, insert a cannula into the femoral vein, and while the chorda is being stimulated inject into the vein, in the manner described on p. 177, 10 to 15 milligrammes of sulphate of atropia. This will stop the flow of saliva, and abolish the effect of

stimulation of the chorda. See whether the sympathetic is also inactive, and report the result.

(2) Now empty the cannula in the submaxillary duct by means of a feather, and fill it with a 2 per cent. solution of pilocarpine nitrate by means of a fine pipette. Fill also the short rubber tube attached to the cannula, and close it with a small piece of glass rod or a pair of bulldog forceps. Compress the tube, and so force into the duct a small quantity of the solution. Open the tube. Secretion of saliva will again begin, and stimulation of the chorda will again cause an increase in the flow. But after a few minutes the action of the atropia will reassert itself and the flow will stop. Renewed secretion may be caused by a fresh injection of pilocarpine.

4. **Gastric Juice.**—(*a*) *Preparation of Artificial Gastric Juice.*—Take a portion of the pig's stomach provided, strip off the mucous membrane (except that of the pyloric end), cut it into small pieces with scissors, and put it in a bottle with 100 times its weight of 0·2 per cent. hydrochloric acid. Label and put in a bath at 40° C. for twelve hours. Then filter.

(*b*) Take another portion of the mucous membrane, cut it into pieces, and rub up with clean sand in a mortar. Then put it in a small bottle, cover it with glycerine, label, and set aside for two or three days. The glycerine extracts the pepsin.

(*c*) Take five test-tubes, A, B, C, D, E, and in each put a little washed and boiled fibrin. To A add a few drops of glycerine extract of pig's stomach, and fill up the test-tube with 0·2 per cent. hydrochloric acid. To B add glycerine extract and distilled water; to C glycerine extract and 1 per cent. sodium carbonate; to D 0·2 per cent. hydrochloric acid alone; to E glycerine extract which has been boiled, and 0·2 per cent. hydrochloric acid.

Put up another set of five test-tubes in the same way, except that a few drops of a watery solution of a commercial pepsin are substituted for the glycerine extract. Label the test-tubes A′, B′, C′, D′, E′.

Into another test-tube put a little fibrin, and fill up with the filtered acid extract from (*a*). Label it F. Place all the test-tubes in a tumbler, and set them in a water-bath at 40° C.

After a time the fibrin will have almost completely disappeared in A, A′, and F, but not in the other test-tubes. Filter the contents of A, A′, and F into one dish.

(*d*) Test the filtrate for the products of gastric digestion:

(α) Neutralize a portion carefully with dilute sodium hydrate. A precipitate of acid-albumin may be thrown down. Filter.

(β) To a portion of the filtrate from (α) add excess of sodium hydrate and a drop or two of *very* dilute copper sulphate. A rose colour indicates the presence of proteoses or peptones. The cupric sulphate must be very cautiously added, because an excess gives a violet colour, and thus obscures the rose reaction. If still more cupric sulphate be added, blue cupric hydrate is thrown down, and

nothing can be inferred as to the presence or the nature of proteids in the liquid.

(γ) Heat another portion of the filtrate from (α) to 30° C., and add crystals of ammonium sulphate to saturation. A precipitate of proteoses (albumoses) may be obtained. Filter off.

(δ) Add to the filtrate from (γ) a trace of cupric sulphate and excess of sodium hydrate. A rose colour indicates that peptones are present. More sodium hydrate must be added than is sufficient to break up all the ammonium sulphate, for the biuret reaction requires the presence of free fixed alkali. A strong solution of the sodium hydrate should therefore be used, or the stick caustic soda. The addition of ammonium sulphate will cause the red colour to disappear; so will the addition of an acid. Sodium hydrate will bring it back. Ammonia does not affect the colour.

(*e*) To some milk in a test-tube add a drop or two of rennet extract, and place in a bath at 40° C. In a short time the milk is curdled by the rennin.

5. (1) **To obtain Normal Chyme.**—Inject subcutaneously into a dog, one and a half hours after a meal of meat, 2 mg. of apomorphine. One-half of one of the ordinary tabloids is enough. Collect the vomit.

(2) **To obtain Pure Gastric Juice.**—Put a fasting dog under ether, and fasten on the holder. Clip the hair and shave the skin in the middle line below the sternum. Make a longitudinal incision through the skin and subcutaneous tissue from the xiphoid cartilage downwards for 3 or 4 inches. The linea alba will now be seen as a white mesial streak. Open the abdomen by an incision through it. Pull over the stomach towards the right, stitch it to the abdominal wall, open it, and insert a stomach-cannula (Fig. 114). By mechanically stimulating the mucous membrane of the stomach with a feather, or a smooth glass rod, or by the introduction of pieces of indiarubber, a flow (not very copious) of gastric juice can be caused.

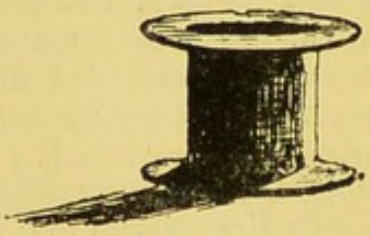


FIG. 114.—STOMACH-CANNULA.

(3) (*a*) Test the reaction to litmus of the chyme obtained in (1), and of the pure juice obtained in (2).

(*b*) Test their proteolytic powers by putting in a bath at 40° C. for two hours two test-tubes containing respectively filtered chyme and fibrin, and gastric juice and fibrin. The fibrin will be digested in both.

(*c*) Add a few drops of the chyme and gastric juice to milk in two test-tubes, and place them in a bath at 40° C. Repeat (*c*) after neutralizing the liquids. Probably neither will curdle milk when neutralized. For the gastric juice of many animals contains no rennin, although the fully-formed ferment or its zymogen may be

present in the gastric mucous membrane. The rennet ferment is active in an acid or neutral, but inactive in an alkaline, medium.

(*d*) Examine a drop of the unfiltered chyme under the microscope. Partially digested fragments of the food will be seen—muscular fibres, or fat cells. Filter, and proceed as in 4 (*d*) (p. 378).

(4) Test the filtrate from the chyme and the gastric juice for lactic acid by Ueffelmann's test, and for hydrochloric acid by Günsburg's reagent.

Ueffelmann's Test for Lactic Acid.—The reagent is a dilute solution of carbolic acid to which dilute ferric chloride has been added till the colour is bluish (say a drop of a 1 per cent. ferric chloride solution to 5 c.c. of a 1 per cent. carbolic acid solution). The blue colour of the mixture is turned yellow by lactic acid, but not by dilute hydrochloric acid.

Günsburg's Reagent for Free Hydrochloric Acid in Gastric Juice is made by dissolving 2 parts of phloroglucinol and 1 part of vanillin in 30 parts by weight of absolute alcohol. A few drops of the reagent are added to a few drops of the filtered gastric juice in a small porcelain capsule, and the whole evaporated to dryness over a small bunsen flame. If free hydrochloric acid is present, a carmine-red residue is left. If all the hydrochloric acid is united to proteids in the stomach contents, the reaction does not succeed. It is also hindered by the presence of leucin.

6. **Pancreatic Juice.**—(*a*) Take a piece of the pancreas of an ox or dog which has been kept twenty-four hours at the temperature of the laboratory, and make a glycerine extract in the same way as in the case of the pig's stomach 4 (*a*). Put in a small bottle, and set aside for a day or two.

(*b*) Put a little boiled fibrin into each of six test-tubes, A, B, C, D, E, F. To A add a few drops of glycerine extract of pancreas, and fill up with 1 per cent. sodium carbonate solution; to B add glycerine extract and distilled water; to C glycerine extract and excess of 0·05 per cent. hydrochloric acid; to D 1 per cent. sodium carbonate alone; to E 1 per cent. sodium carbonate in which a few drops of glycerine extract of pancreas have been previously boiled; to F glycerine extract and excess of 0·2 per cent. hydrochloric acid.*

Set up six test-tubes, A′, B′, C′, D′, E′, F′, in the same way, but substitute a few drops of a solution of commercial pancreatin for the glycerine extract. Put all the test-tubes in a tumbler, and place in a bath at 40° C. The fibrin will be gradually eaten away in A and A′ by the action of the trypsin, but will not swell up or become clear before disappearing, as it does in dilute hydrochloric acid with glycerine extract of stomach. Filter the contents of these test-tubes.

* With hydrochloric acid of different strengths the rapidity of digestion of boiled fibrin by glycerine extract of dog's pancreas (1 volume of extract to 25 of acid) was found about the same for 0·3 and 0·17 per cent. acid; much less for 0·08 per cent., while in 0·04 per cent. acid there was practically no digestion at all. In 0·4 per cent. acid digestion took place more rapidly than in 0·08 per cent., but much less rapidly than in 0·17 per cent. In acid of all strengths digestion was markedly slower than in 1 per cent. sodium carbonate.

Neutralize the filtrate with dilute acid; a precipitate will consist of alkali-albumin. If such a precipitate is obtained, filter it off and test the filtrate for proteoses and peptones as in 4 (*d*), p. 378. Some digestion, and perhaps a considerable amount, may also have taken place in F and F′; less, or none at all in C and C′; and none in the other test-tubes (pp. 306, 354).

(*e*) Add a few drops of the glycerine extract to a test-tube containing starch mucilage, which has been previously found free from reducing sugar. Put in a bath at 40° C. After a short time abundance of reducing sugar will be found, owing to the action of the ferment, amylopsin.

(*d*) *Leucin and Tyrosin.*—If pancreatic digestion of proteids (fibrin, *e.g.*) be allowed to go on for some time, part of the peptone first formed may be broken up into leucin and tyrosin. If the 'digest' be neutralized to separate alkali-albumin, then filtered, and the filtrate concentrated and allowed to stand, a crop of tyrosin crystals will separate out, since tyrosin is only slightly soluble in watery solutions of neutral salts. These crystals having been filtered off, the proteoses (albumoses) and peptones can be precipitated together by alcohol, and afterwards separated, if that is desired, by redissolving the precipitate in water and throwing down the proteoses by saturation with ammonium sulphate. The alcoholic filtrate will contain any leucin that may be present, since that body is moderately soluble in alcohol, as well as traces of tyrosin, which, however, is much less soluble in this medium. On concentration, crystals of both substances will be obtained. Tyrosin crystallizes characteristically from animal liquids in beautiful silky needles united into sheaves, leucin in the form of indistinct fatty-looking balls, often marked with radial striæ and coloured with pigment (Figs. 122 and 123, p. 396).

7. **Bile.**—(*a*) Test the reaction of ox bile. It is alkaline to litmus.

(*b*) Add dilute acetic acid. A precipitate of bile-mucin (really nucleo-albumin) falls down. Some of the bile-pigment is also precipitated. Filter. (Pig's bile contains more of the mucin-like substance than ox bile.)

(*c*) Dilute the filtrate from (*b*). Put a little of it into a porcelain capsule, add a few drops of strong sulphuric acid, and a drop or two of a dilute solution of cane-sugar. A purple colour appearing at once, or after gentle heating, shows the presence of bile-acids (**Pettenkofer's reaction**). Examine the purple liquid in a test-tube with a spectroscope (p. 62). Dilute the liquid if necessary, adding some sulphuric acid to clear up any precipitate caused by the water. Two absorption bands are seen, one to the red side of D, and the other over E.

(*d*) Add yellow nitric acid (containing nitrous acid) to a little bile on a white porcelain-slab. A play of colours, beginning with green and running through blue to yellow and yellowish-brown, indicates the presence of bile-pigment (**Gmelin's reaction.**) The reaction may also be obtained by putting some yellow nitric acid into a test-tube, and then running a little bile from a pipette on to the surface of the acid. The play of colours is seen at the surface of contact.

(*e*) *Cholesterin* (Fig. 115).—*Preparation.*—Extract a powdered gallstone (preferably a white one) with hot alcohol and ether in a test-tube. Heat the test-tube in warm water, *not* in the free flame. Put a drop of the extract on a slide. Flat crystals of cholesterin, often chipped at the corners, separate out. Carefully allow a drop of strong sulphuric acid and a drop of dilute iodine to run under the cover-glass. A play of colours—violet, blue, green, red—is seen. Evaporate a drop of the solution of cholesterin in a small porcelain capsule, add a drop of strong nitric acid, and heat gently over a flame. A yellow stain is left, which becomes red when a drop of ammonia is poured on it while it is still warm.

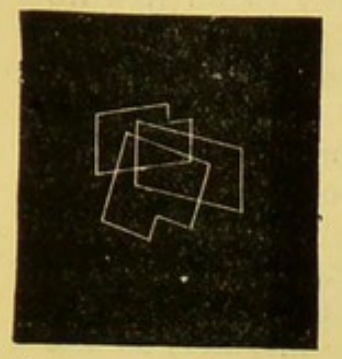


FIG. 115.—CHOLESTERIN CRYSTALS.

(*f*) *To demonstrate the Presence of Iron in the Liver Cells.*—Steep sections of liver in a solution of potassium ferrocyanide, and then in dilute hydrochloric acid. Or a 1·5 per cent. solution of potassium ferrocyanide in 0·5 per cent. hydrochloric acid may be used. (The iron may previously be fixed in the tissue by hardening it in a mixture of alcohol and ammonium sulphide.) The sections become bluish from the formation of prussian blue. A fine-pointed glass rod or a platinum lifter should be used in manipulating them. A steel needle cannot be employed. Mount in glycerine or Farrant's solution, or (after dehydrating with alcohol and clearing in xylol) in xylol-balsam. Blue granules may be seen under the microscope in some of the hepatic cells.

(*g*) To some starch mucilage, shown to be free from sugar, add a little bile, and place in a bath at 40°. After a time test for reducing sugar. Report the result.

8. **Microscopical Examination of Fæces.**—Examine under the microscope the slides provided. Draw, and as far as possible determine the nature of, the objects seen (p. 358).

9. **Absorption of Fat.**—Feed a rat or frog with fatty food; kill the rat in three or four hours, the frog in two or three days. Immediately after killing the rat open the abdomen, carefully draw out a loop of intestine, and look through the thin mesentery. The white lacteals will probably be seen ramifying in the mesentery. They appear white on account of the presence of globules of fat in the chyle with which they are filled. Strip off tiny pieces of the mucous membrane of the small intestine, and steep them in $\frac{1}{2}$ per cent. solution of osmic acid for forty-eight hours. Then tease fragments of the mucous membrane in glycerine, take off the glycerine with blotting-paper, mount in Farrant, and examine under the microscope. Other portions of the mucous membrane may be hardened for a fortnight in a mixture of 2 parts of Müller's fluid and 1 part of a 1 per cent. solution of osmic acid. Sections are then made with a freezing microtome after embedding in gum. No process must be used by which the fat would be dissolved out (Schäfer).

10.* **Time required for Digestion and Absorption of various Food Substances.**—Feed three dogs, A, B and C, which have previously fasted for twenty-four hours, with a meal containing starch (proved to be free from sugar), lard and meat.

(1) After fifteen minutes inject subcutaneously into A 2 c.c. of a 0·1 per cent. solution of apomorphine. Note the time which elapses before the animal vomits. Collect the vomit.

(*a*) Examine a little of it under the microscope, and make out fat globules, muscular fibres and starch granules. The latter can be recognised by their being coloured blue by a drop or two of iodine solution.

(*b*) Filter the chyme, mixing it, if necessary, with a little water, and test it as in 4 (*d*) (p. 378) for the products of digestion of proteids. In addition, test for starch, dextrin, and reducing sugar.

(2) One and a quarter hours after the meal inject apomorphine into dog B, and proceed as in (1).

(3) Two and a half hours after the meal inject apomorphine into dog C, and proceed as in (1). Compare the results from the three specimens of chyme.

11.* **Quantity of Cane-sugar inverted and absorbed in a Given Time.**—Take three dogs, A, B and C, which have fasted for twenty-four hours. The animals should be about the same size. Feed A and B with 100 c.c. of a standard solution of cane-sugar (about a 10 per cent. solution). If the dogs have been kept without water for a day they will more readily take the sugar solution. Or it may be given through a tube passed into the stomach, and in this case a larger quantity of sugar can be given. Feed C with 10 grammes of powdered cane-sugar mixed with lard, the mixture being rolled into little balls.

(1) After a quarter of an hour put A under chloroform or the ACE mixture, and fasten it on a holder. Kill the animal with chloroform, open the abdomen, tie the œsophagus, place double ligatures on the pyloric end of the stomach and the lower end of the small intestine, and divide between them. Cut out the stomach and intestine; wash their contents into separate vessels, and test the reaction with litmus paper. Add water and rub up thoroughly. Filter. Wash the residue repeatedly with small quantities of water, and pass all the washings through the filter. Make up each of the two filtrates to 200 c.c.

(*a*) Test the filtrates from the contents of the stomach and intestines qualitatively for glucose by Trommer's (p. 23) and the phenylhydrazine test (p. 431).

(*b*) If no reducing sugar is present, add to 20 c.c. of each filtrate 1 c.c. of hydrochloric acid, boil for half an hour, and again test for reducing sugar. If it is now found, some cane-sugar is present.

(*c*) If reducing sugar is found, estimate its amount as glucose by Fehling's solution (p. 431) in a measured quantity of the filtrate

* Experiments 10 and 11 are conveniently done in a class by assigning each of the three animals to a separate set of students. The contents of the stomach and intestine are divided into three portions, so that each set has a sample from each dog.

before and after boiling with one-twentieth of its volume of hydrochloric acid.

(*d*) Estimate in the same way the amount (as glucose) of the invert sugar in the standard solution of cane-sugar after inversion, and before inversion if it gives the qualitative test for reducing sugar before it has been boiled with acid.

From the data obtained (and taking 95 parts of cane-sugar as equal to 100 parts of glucose) calculate the amount of cane-sugar absorbed, left unchanged, and inverted, though not absorbed.

(2) One and a half hours after the meal anæsthetize B, and proceed as in (1).

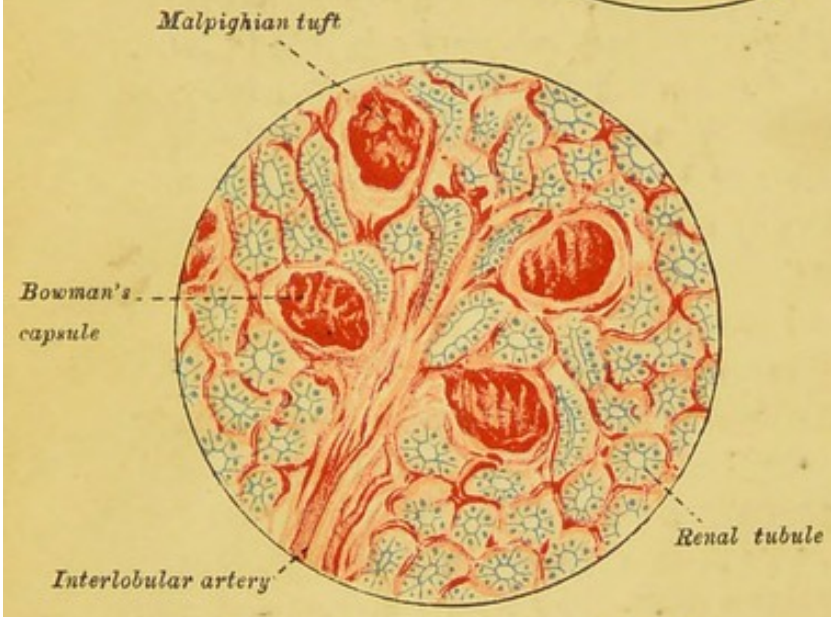
(3) Two hours after the meal proceed in the same way with C. But in addition observe the lacteals in the mesentery, by lifting a loop of intestine gently up immediately after opening the abdomen. If the absorption of the fat has begun, they will be easily visible, as a network of fine milk-white vessels. Also examine the gastric and intestinal contents with the microscope for fat globules. Compare your results on the amount of sugar obtained from the three animals. Probably much more unabsorbed sugar will be found in C than in B, as the lard hinders it from being dissolved.

12. **Auto-digestion of the Stomach.**—In some of the previous experiments the stomach of an animal killed during digestion should be removed from the body after double ligation of œsophagus and duodenum, and placed in a water-bath at 40° C. After several hours the contents should be washed out, and the mucous membrane examined. It may be entirely eaten away in parts.

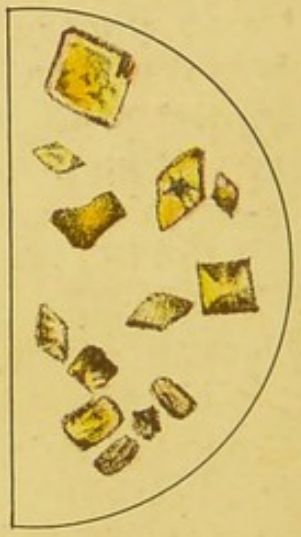
13. **Time required for Food to pass through the Alimentary Canal.**—Feed a dog with bones. Keep in a special cage, and observe how long it takes before the easily-recognised white bone-fæces appear.

3. Crystals of phenyl glucosazone from urine.

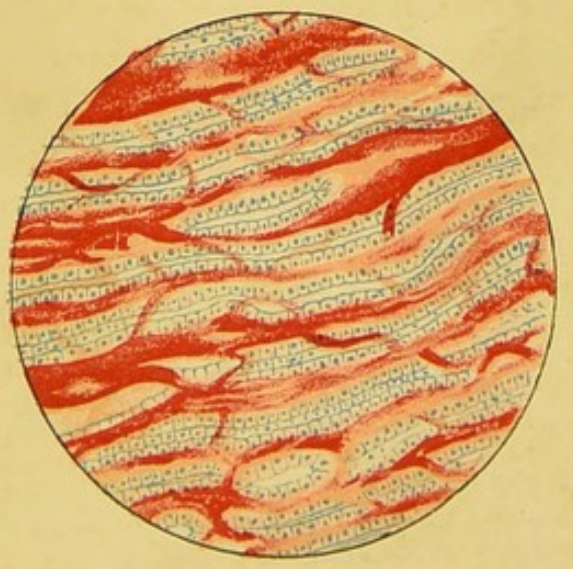
1. Crystals of uric acid from urine.



4. Section of cortex of injected kidney.



2. Crystals of ammonium urate from urine.



5. Section of medulla of injected kidney showing vasa recta and collecting tubules.

GEORGE KENNING, COLOR PRINTE

CHAPTER VI.

EXCRETION.

We have now followed the ingoing tide of gaseous, liquid and solid substances within the physiological surface of the body. There we leave them for the present, and turn to the consideration of the channels of outflow, and the waste products which pass along them. In a body which is neither increasing nor diminishing in mass the outflow must exactly balance the inflow; all that enters the body must sooner or later, in however changed a form, escape from it again. In the expired air, the urine, the secretions of the skin, and the fæces, by far the greater part of the waste products is eliminated. Thus the carbon of the absorbed solids of the food is chiefly given off as carbon dioxide by the lungs; the hydrogen, as water by the kidneys, lungs and skin, along with the unchanged water of the food; the nitrogen, as urea by the kidneys. The fæces in part represent unabsorbed portions of the food. A small and variable contribution to the total excretion is the expectorated matter, and the secretions of the nasal mucous membrane and lachrymal glands. Still smaller and still more variable is the loss in the form of dead epidermic scales, hairs and nails. The discharges from the generative organs are to be considered as excretions with reference to the parent organism, and so is the milk, and even the fœtus itself, with respect to the mother.

Excretion by the lungs and in the fæces has been already dealt with. All that is necessary to be said of the expectoration and the nasal and lachrymal discharges is that the first two generally contain a good deal of mucin, and are produced in small mucous and serous glands, the cells of

which are of the same general type as those of the mucous and serous salivary glands. The lachrymal glands are serous like the parotid; and the tears secreted by them contain some albumin and salts, but little or no mucin. The sexual secretions and milk will be best considered under reproduction (Chap. XIV.), so that there remain only the urine and the secretions of the skin to be treated here.

I. Excretion by the Kidneys.

The Chemistry of the Urine.—Normal urine is a clear yellow liquid of acid reaction, and with an average specific gravity of about 1020, the usual limits being 1015 and 1025, although when water is taken in large quantities, or long withheld, the specific gravity may fall to 1005, or even less, or rise to 1035, or even more. The quantity passed in twenty-four hours is very variable, and is especially dependent on the activity of the sweat-glands, being, as a rule, smaller in summer when the skin sweats much, than in winter when it sweats little. The average quantity for an adult male is 1200 to 1600 c.c. (say, 40 to 50 oz.).*

Composition of Urine.—It is essentially a solution of urea and inorganic salts, the proportion of the latter being about 1·5 per cent., or double the usual amount in physiological liquids. Besides urea, there are other nitrogenous bodies in much smaller quantity, such as uric acid and the allied xanthin bases, hippuric acid, and kreatinin; some of these at least are products of the metabolism of proteids within the tissues. And besides the inorganic salts there are certain organic bodies—indol, phenol, pyrokatechin, skatol—united with sulphuric acid, which are primarily derived from the products of the putrefaction of proteids within the digestive tube. In tabular form the composition of urine,

* The average quantity of urine varies not only with the season, but also with the habits of the person, especially as regards the amount of liquid taken. The average for seventeen healthy (American) students, whose urine was collected for six to eight successive days in winter, was 1166 c.c. The highest average in any one individual for the observation period was 1487 c.c. (for seven days), and the lowest 743 c.c. (for eight days). The greatest quantity passed in any one period of twenty-four hours was 2286 c.c. (by the individual whose average was the highest). The smallest quantity passed in twenty-four hours was 650 c.c. (by the individual whose average was the lowest).

and the total excretion by an average man of 70 kilos, may be given thus:

	Per 1000 grammes.	In 24 hours.	
Water	960	1440 grammes.	
Solids	40	60	
Urea	23	35	
Uric acid and xanthin bases	1·8	0·75	37·75 grammes.
Hippuric acid		0·5	
Kreatinin		1·5	
Sodium	6·5	6	
Potassium		2·5	
Ammonia		0·75	
Calcium and magnesium		0·5	22·25 grammes.
Chlorine	8	7	
Phosphoric acid		3·5	
Sulphuric acid		2	
Mucus, pigment, etc.			

The acidity of urine is not due to free acid, for the tests which reveal the presence of free acid in a mixture, such as the precipitation of sulphur on the addition of sodium hyposulphite, and the change of colour of many organic substances, give a negative result when applied to urine. The acidity is chiefly due to the acid phosphates of sodium and potassium; in a less degree to dissolved carbon dioxide. That a considerable proportion of the phosphoric acid is normally present in the form of acid sodium phosphate (NaH_2PO_4) is shown by the fact that barium chloride usually precipitates only about 40 per cent. of the phosphoric acid, leaving the rest in solution. Now, barium chloride does not cause a precipitate in a dilute solution of acid sodium phosphate, but does precipitate the disodium-hydrogen phosphate (Na_2HPO_4). The acidity is estimated by running into a given quantity of urine a dilute solution of sodium hydrate, which has been previously titrated with a pure acid solution (say, oxalic acid) of known strength, until a neutral reaction is just obtained. From the amount of sodium hydrate required the acidity can be calculated in terms of the standard acid. Normally the acidity of urine is about equal to that of a 0·1 per cent. solution of sulphuric acid. It diminishes distinctly, or even gives place to alkalinity, during digestion when the acid of the gastric juice is being secreted, and varies with the quantity of vegetable food in the diet. The urine of herbivora and vegetarians is alkaline, and is either turbid when passed, or on standing soon becomes turbid from precipitated carbonates and phosphates of earthy bases, while that of carnivora and of fasting herbivora, which are living on their own tissues, is strongly acid and clear. Normal human urine may deposit urates soon after discharge, as they are more soluble in warm than in cold water. They carry down some of the pigment, and therefore usually appear as a pink or brick-red sediment. When urine is allowed to stand after being voided, what is generally described as 'acid fermentation' occurs. The acidity gradually increases, owing apparently to the formation of lactic acid; acid sodium urate is produced from the neutral urate, and comes down in the form of amorphous granules, while the liberated uric acid is deposited often in 'whetstone' crystals, coloured yellow by the pigment

(Fig. 116; Plate IV., 1). Calcium oxalate may also be thrown down as 'envelope,' *a*, *b*, or, less frequently, 'sand-glass' crystals, *c* (Fig. 117). If the urine is allowed to stand for a few days, especially in a warm place, or in a place where urine is decomposing, the reaction becomes ultimately strongly alkaline, owing to the formation of ammonium carbonate from urea by the action of micro-organisms (*Micrococcus ureæ*, *Bacterium ureæ*, and others) which reach it from the air, and

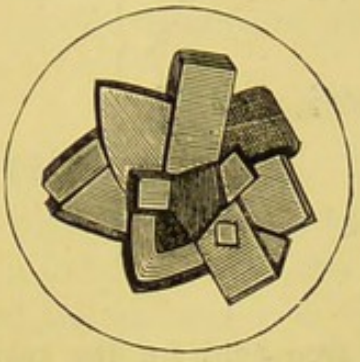


FIG. 116.—URIC ACID.

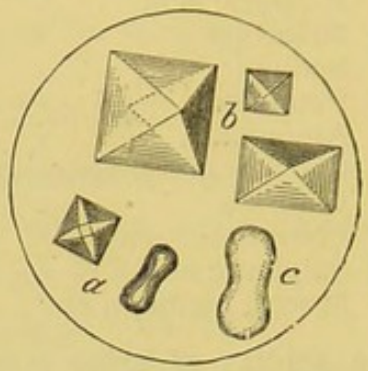


FIG. 117.—CALCIUM OXALATE.

produce a soluble ferment, in whose presence the urea is split up under absorption of water. Thus :

$$\underset{\text{Urea.}}{CON_2H_4} + 2H_2O = \underset{\text{Ammonium carbonate.}}{(NH_4)_2CO_3}.$$

The substances insoluble in alkaline urine are thrown down, the deposit containing *ammonio-magnesic* or *triple phosphate*, formed by the union of ammonia with the magnesium phosphate present in fresh urine, and precipitated as clear crystals of 'knife-rest' or 'coffin-lid' shape (Fig. 118), along with amorphous earthy phosphates, and often acid ammonium urate in the form of dark balls occasionally covered with spines (Plate IV., 2).

FIG. 118.—TRIPLE PHOSPHATE.

It is only in pathological conditions that this alkaline fermentation takes place within the bladder. The reaction of the urine can readily be made alkaline by the administration of alkalies, alkaline carbonates, or the salts of vegetable acids like malic, citric, and tartaric acid, which are broken up in the body and form alkaline carbonates with the alkalies of the blood and lymph. It is not so easy to increase the acidity of the urine, although mineral acids do so up to a certain limit. If the administration of acid be pushed farther, ammonia is split off from the proteids, and is excreted in the urine as the ammonium salt of the acid.

Urea, $CO(NH_2)_2$, is the form in which by far the greater part of the nitrogen is discharged from the body. Its amount is as important a measure of proteid metabolism as the quantity of carbon dioxide given out by the lungs is of the oxidation of carbonaceous material. It is soluble in water and in alcohol, and crystallizes from

its solutions in the form of long colourless needles, or four-sided prisms with pyramidal ends. It can be prepared from urine as described in the Practical Exercises (p. 423.) Urea can also be obtained artificially by heating its isomer, ammonium cyanate (NH_4-O-CN), to 100° C. This reaction is of great historical interest, as it forms the final step in Wöhler's famous synthesis of urea, the first example of a complex product of the activity of living matter being formed from the ordinary materials of the laboratory. Heated in watery solution in a sealed tube to 180° C., urea is entirely split up into carbon dioxide and ammonia, a change which can also be brought about, as already mentioned, by the action of micro-organisms. Nitrous acid, hypochlorous acid, and salts of hypobromous acid carry the decomposition still further, carbon dioxide, nitrogen, and water being the products of their oxidizing action on urea. Thus: $CO.2(NH_2) + 3NaBrO = 3NaBr + 2H_2O + CO_2 + N_2$. This reaction

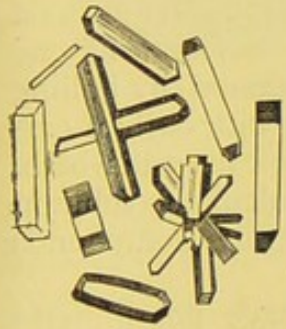


FIG. 119.—KREATIN.

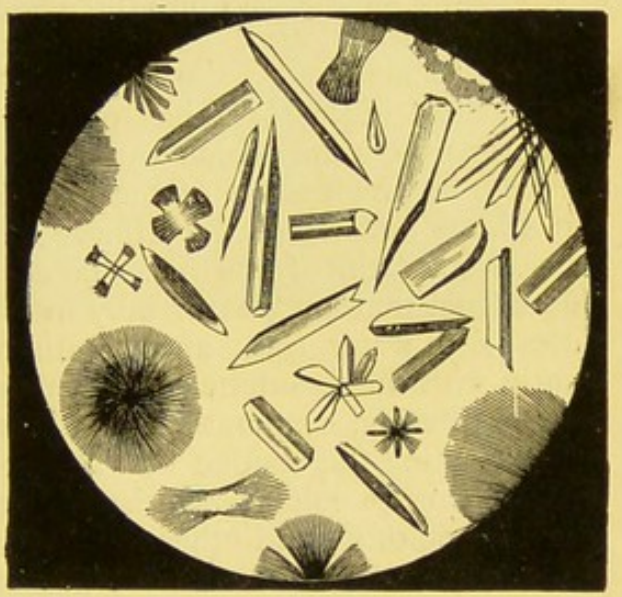


FIG. 120.—KREATININ-ZINC-CHLORIDE.

is the basis of the hypobromite method of estimating the quantity of urea in urine (Practical Exercises, p. 424).

Uric acid ($C_5H_4N_4O_3$) exists in large amount in the urine of birds. The excrement of serpents consists almost entirely of uric acid. In man and mammals the quantity is comparatively small in health, but is increased after a meal, particularly one containing substances rich in nucleo-proteids, *e.g.*, the thymus of the calf.

The xanthin bases are a group of substances allied to uric acid, and including, besides xanthin itself ($C_5H_4N_4O_2$), hypoxanthin ($C_5H_4N_4O$), guanin ($C_5H_5N_5O$), and other bodies. They exist in very small amount in urine, but, like uric acid, are increased in amount by the ingestion of nucleo-proteids.

Hippuric acid ($C_9H_9NO_3$) occurs in considerable quantity in the urine of herbivora; in the urine of carnivora and of man only in traces; in that of birds not at all. Its amount is much more dependent on the presence of particular substances in the food than that of the other organic constituents of urine. Anything which

contains benzoic acid, or substances which can be readily changed into it (such as cinnamic and quinic acids), causes an increase of the hippuric acid in urine. In fact, one of the best ways of obtaining the latter is from the urine of a person to whom benzoic acid is given by the mouth; the sweat may also in this case contain a trace of hippuric acid. Chemically it is a conjugated acid formed by the union of benzoic acid and glycin. Thus:

$$\underset{\text{Benzoic Acid.}}{C_7H_6O_2} + \underset{\text{Glycin.}}{C_2H_5NO_2} = \underset{\text{Hippuric Acid.}}{C_9H_9NO_3} + \underset{\text{Water.}}{H_2O}.$$

Benzoic acid, therefore, meets glycin in the body, and combines with it, as fatty acids meet glycerine and combine with it. But neither free glycin nor free glycerine have been detected in the blood or tissues (p. 428).

Oxalic acid is always present, although in very small amount. Some of it comes from the oxalates of the food, but a portion of it arises in the metabolism of proteids, and under pathological conditions, of carbohydrates. Calcium oxalate crystals are often seen in urinary sediments.

Kreatinin ($C_4H_7N_3O$) has only been found as a constant constituent in the urine of man and a few other mammals. It is possibly the form in which some of the kreatin of muscle leaves the body. But a large portion of the urinary kreatinin is undoubtedly derived from the kreatin of the meat taken as food (p. 445). Its formula differs from that of kreatin only in possessing the elements of one molecule of water less; and kreatinin can be obtained by boiling kreatin with dilute sulphuric acid, then neutralizing with barium carbonate, filtering, evaporating the filtrate to dryness on the water-bath, and extracting the residue with alcohol. From its alcoholic solution it crystallizes in colourless prisms. It forms crystalline compounds with zinc chloride and other salts (p. 428).

Pigments of Urine.—The pigments of urine have not hitherto been exhaustively studied; but we already know that normal urine contains several, and pathological urines probably additional, pigmentary substances. The best-known pigments in normal urine are *urochrome*, the yellow substance which gives the liquid its ordinary colour; *uroerythrin*, the pink pigment which often colours the deposits of urates that separate even from healthy urine; and *urobilin*, sometimes termed *normal urobilin*, to distinguish it from the so-called *febrile* urobilin, which, as has been already mentioned, is identical with the fæcal pigment stercobilin, and occurs not only in many febrile conditions, but also in cases with no fever, such as functional derangements of the liver, dyspepsia, chronic bronchitis, and valvular diseases of the heart. Normal and febrile urobilin are said to show certain spectroscopic differences, but are probably one and the same substance, and represent simply the portion of the stercobilin which is not excreted with the fæces, but absorbed from the intestine into the blood. The urobilin in normal urine only exists in small amount in the fully-formed condition, most of it being present as a *chromogen* or mother substance, which by oxidation, as on standing exposed to the air, is converted into urobilin.

The pigments of the blood and bile and some of their derivatives are of common occurrence in the urine in disease. *Hæmatoporphyrin* has not only been found in some pathological conditions, but appears to be constantly present in minute traces in normal urine. In paroxysmal hæmoglobinuria, *methæmoglobin*, mixed with some oxyhæmoglobin, is found in the urine in large amount; and it is worthy of note that it is not formed in the urine after secretion, but is already present as such when it reaches the bladder.

Ferments.—The urine contains traces of proteolytic and amylolytic ferments (Fig. 121). These may be easily separated from it by putting a little fibrin, which has the power of fixing enzymes, into the urine.

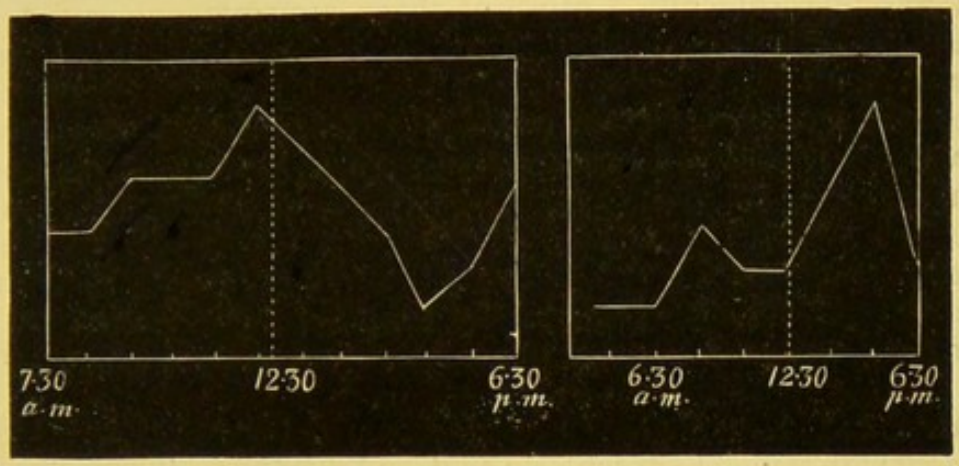


FIG. 121.—PEPSIN IN URINE. DIASTATIC FERMENT IN URINE. AT DIFFERENT TIMES OF THE DAY (HOFFMANN).

Of the inorganic constituents of urine the most important and most easily estimated are the chlorine, phosphoric acid, and sulphuric acid.

Chlorine.—Much the greater part of the chlorine is united with sodium, a smaller amount with potassium. The chlorides of the urine are undoubtedly to a great extent derived directly from the chlorides of the food, and have not the same metabolic significance as the organic, and even as some of the other inorganic constituents. But it is noteworthy that in certain diseased conditions the chlorine may disappear entirely from the urine, or be greatly diminished, *e.g.*, in pneumonia, and in general in cases in which much material tends to pass out from the blood in the form of effusions (p. 421).

Phosphoric Acid.—The phosphoric acid of the urine is chiefly derived from the phosphates of the food, but must partly come from the waste products of tissues rich in phosphorus-containing substances, such as lecithin and nuclein. The phosphoric acid is united partly with alkalies, especially as acid sodium phosphate, and partly with earthy bases, as phosphates of calcium and magnesium. The earthy phosphates are precipitated by the addition of an alkali to urine, or in the alkaline fermentation. In some pathological urines

they come down when the carbon dioxide is driven off by heating; a precipitate of this sort differs from heat-coagulated albumin in being readily soluble in acids (p. 422).

Sulphuric Acid.—This is only to a slight extent derived from ready-formed sulphates in the food. The greater part of it is formed by oxidation of the sulphur of proteids. About nine-tenths of the sulphuric acid of normal urine are united to alkalies; the other tenth is combined, in the form of ethereal sulphates, with aromatic bodies derived from the putrefaction of proteids in the intestine. Such are potassium-phenyl-sulphate ($C_6H_5KSO_4$), potassium-kresyl-sulphate ($C_7H_7KSO_4$), potassium-indoxyl-sulphate ($C_8H_6NKSO_4$), potassium-skatoxyl-sulphate ($C_9H_8NKSO_4$), and two double sulphates of potassium and pyrocatechin. Most of those aromatic compounds are present in greater amount in the urine of the horse than in the normal urine of man; but in disease the quantity in the latter may be much increased; and to a certain extent it must be looked upon as an index of the intensity of putrefactive processes in the intestine and of absorption from it. Munk made the curious observation that in the urine of a starving dog the phenol-forming substances are absent, while in the urine of a starving man they are present in abnormally large amount. The indigo-forming substances ('indican'), on the other hand, are in hunger excreted in considerable quantity by the dog, and not at all by man (p. 423).

Phenol and kresol can easily be obtained from horse's urine by mixing it with strong hydrochloric acid, and distilling. These aromatic bodies pass over in the distillate. Pyrocatechin remains behind, and can be extracted by ether; it gives a green colour with ferric chloride, which becomes violet on the addition of sodium carbonate.

A small amount of **phosphorus** and of **sulphur** may appear in the urine in less oxidized forms than phosphoric and sulphuric acids. Such sulphur compounds are potassium sulphocyanide, which is probably, in part at least, derived from that of the saliva; and ethyl sulphide, a substance with a penetrating odour, which appears to be a constant constituent of dogs' urine (Abel).

Thiosulphuric acid ($H_2S_2O_3$) occurs almost constantly in cat's urine, often in dog's. It is not free, but combined with bases.

Carbonates of sodium, ammonium, calcium and magnesium occur in alkaline urine. Their source is the carbonates and the vegetable organic acids of the food. In acid urine a certain amount of carbon dioxide is present, although not firmly united with bases, so that most of it can be pumped out.

The Urine in Disease.—Although, strictly speaking, a truly pathological urine has no place in physiology, the line which separates the urine of health from that of disease is often narrow, sometimes invisible; while the study of abnormal constituents is not only of great importance in practical medicine, but throws light upon the physiological processes

taking place in the kidney, and upon the general problems of metabolism. Even in health the quantity of the urine, its specific gravity, its acidity, may vary within wide limits. A hot day may increase the secretion of sweat, and correspondingly diminish the secretion of urine, and the deficiency of water may lead to a deposit of brick-red urates. A meal rich in fruit or vegetables may render the urine alkaline, and its alkalinity may determine a precipitate of earthy phosphates. But neither the scanty acid urine, with its sediment of urates, nor the alkaline urine with its sediment of phosphates, comes under the heading of pathological urines; the deviation from the normal does not amount to disease. The maximum deviation from the line of health is the total suppression of the urine. If this lasts long, a train of symptoms, of which convulsions may be one of the most prominent, and which are grouped under the name of uræmia, appears. At length the patient becomes comatose, and death closes the scene. Suppression of urine may be the consequence of many pathological conditions, but there is one case on record which, in the human subject, in effect, though not in intention, belongs to experimental physiology. A surgeon diagnosed a floating kidney in a woman. With a natural impatience of loose odds and ends of this sort, he offered to remove it, and in an evil hour the patient consented. The surgeon, a perfectly skilful man, who acted for the best, and to whom no blame whatever attached, carried the kidney to a well-known pathologist for examination. The latter, to the horror of the operator, suggested, from the appearance of the organ, that it was the only kidney the woman possessed. This turned out to be the fact. Not a drop of urine was passed. Apart from this ominous symptom, all went well for seven or eight days; but then uræmic troubles came on, and the patient died on the eleventh or thirteenth day after the operation. The autopsy showed that her only kidney had been taken away.

In disease the urine may contain abnormal constituents, or ordinary constituents in abnormal amounts. Of the normal constituents which may be altered in quantity, the most important are the water, the inorganic salts, the urea, the uric acid, and the aromatic substances.

Water. — A marked and persistent diminution in the quantity of urine, that is to say, practically in the water, with or without an increase in the specific gravity, is suggestive of disorganization of the renal epithelium. In some infective diseases the kidney is liable to be secondarily involved, its secreting cells being perhaps crippled in the attempt to eliminate the bacterial poisons. In the form of parenchymatous or tubal nephritis which so frequently complicates scarlet fever, the quantity of urine has in some cases fallen to 50 or 60 c.c. in the twenty-four hours.

In interstitial nephritis, on the other hand, where the structural changes in the tubules are for a long time at least comparatively circumscribed, the quantity of urine is often increased, seldom diminished. In these cases the increase in the blood-pressure, associated with hypertrophy of the heart, may be considered responsible for the exaggerated renal secretion. In diabetes mellitus the quantity of urine is greatly increased, perhaps in some cases because more urea is excreted than normal and urea acts as a diuretic, perhaps also because the elimination of sugar draws with it an increased excretion of water to hold it in solution. Although a specific gravity as low as 1002 has been seen in healthy persons (after copious potations), the persistence of a density below 1010 should suggest hydruria. On the other hand, while the specific gravity has been occasionally observed to mount in health to at least 1036, its persistence at 1025 to 1030 or anything above this, especially if the urine is pale and *apparently* dilute, should suggest diabetes mellitus.

Inorganic Salts.—The changes in the quantity of the inorganic constituents of the urine in disease are not, in the present state of our knowledge, of as much importance as the changes in the organic constituents. The chlorides may totally disappear from the urine in pneumonia, and their reappearance after the crisis is, so far as it goes, a favourable symptom. In most cases in which the quantity of the urine is markedly lessened, all the inorganic substances are diminished in amount.

Urea.—The quantity of urea is, as a rule, increased in

fever, either absolutely or in proportion to the amount of nitrogen in the food. In the interstitial varieties of kidney disease the urea is usually not diminished, but when the stress of the change falls on the tubules (parenchymatous nephritis), it is distinctly decreased—it may be even to one-twentieth of the normal.

Uric acid is diminished in the urine in gout (perhaps to one-ninth of the normal), not only during the paroxysms, but in the intervals. It accumulates in the blood and tissues, and, as sodium urate, may form concretions in the joints, the cartilage of the ear, and other situations. Watson relates the case of a gentleman who used to avail himself of his resources in this respect by scoring the points at cards on the table with his chalky knuckles. In leukæmia the quantity of uric acid and xanthin bases in the urine is greatly increased.

The **aromatic bodies**, of which indoxyl may be taken as the type, are increased when the conditions of disease favour the growth of bacteria in the intestine, *e.g.*, in cholera, acute peritonitis, carcinoma of the stomach. A marked increase in the amount of the 'paired' sulphuric acid in the urine is to be taken as an indication that the bacteria are gaining the upper hand in the intestinal tract; a marked diminution is usually a sign that the battle has begun to turn in favour of the organism (Practical Exercises, p. 423).

Sugar, proteids, the pigments of bile and blood, or their derivatives, are the most important abnormal substances found in solution in the urine. Toxalbumins produced by bacterial action have also been demonstrated in the urine in certain diseases, as in erysipelas (Brieger and Wassermann). Red blood-corpuscles and leucocytes (pus corpuscles, white blood-corpuscles, mucus corpuscles) are the chief organized deposits; but spermatozoa may occasionally be found, as well as pathogenic bacteria, *e.g.*, the typhoid bacillus; and in disease of the kidney casts of the renal tubules are not uncommon. These tube-casts may be composed chiefly of red blood-corpuscles, or of leucocytes, or of the epithelium of the tubules, sometimes fattily degenerated, or of structureless proteid, or of amyloid substance. Abnormal crystalline substances, such as leucin, tyrosin, and cystin, may be on rare occasions found in urinary sediments; but generally the unorganized deposits of pathological urine consist of bodies actually present in, or obtainable from, the normal secretion, but present in excess, either absolutely, or relatively to the solvent power of the urine.

Sugar.—In diabetes mellitus, although the quantity of urine is usually much increased, its specific gravity is above the normal; and this is due chiefly to the presence of sugar (glucose), which generally amounts to 1 to 5 per cent., but may in extreme cases reach 10 or even 15 per cent., more than half a kilogramme being sometimes given off in twenty-four hours.

The name of the tests for glucose is legion. They are mostly founded on its reducing action in alkaline solution. Hydrated oxide of bismuth (Boettcher), salts of gold, platinum and silver, indigo (Mulder), and a host of other substances, are reduced by glucose, and may be used to show its presence. The reduction of cupric salts (Trommer) and the formation of crystals of phenyl-glucosazone (Plate IV., 3) are perhaps the best established tests. (See Practical Exercises, p. 431.)

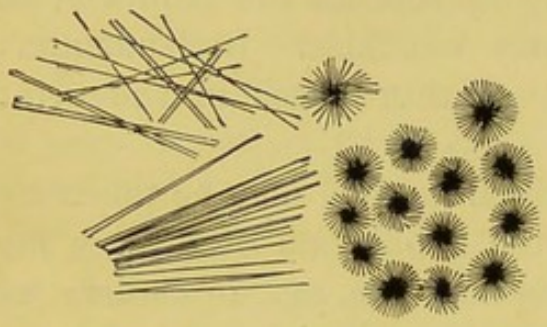


FIG. 122.—LEUCIN CRYSTALS.

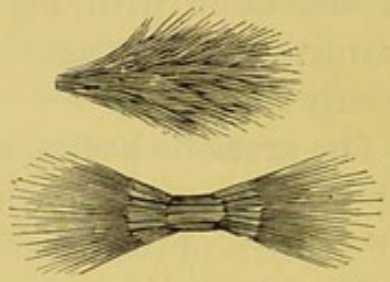


FIG. 123.—TYROSIN CRYSTALS.

Proteids.—Serum-albumin and serum-globulin are the proteids most commonly found in pathological urine. Both are coagulated by heating the urine, slightly acidulated, if it is not already acid, or by the addition of strong nitric acid in the cold. Proteoses (albumoses) are also occasionally present, *e.g.*, in the disease called 'osteomalacia,' and in conditions associated with the formation and especially with the decomposition of pus. They may be recognised by the tests given in the Practical Exercises (p. 429). It is doubtful whether the presence of true peptone has as yet been satisfactorily made out.

The pigments of blood and bile may be detected by the characters described in treating of these substances; the spectrum of oxyhæmoglobin, or methæmoglobin, or any of the other derivatives of hæmoglobin, with the formation of hæmin crystals, would afford proof of the presence of the former, and Gmelin's test of the latter. The red blood-corpuscles, seen with the microscope, are the most decisive evidence of the presence of blood, as leucocytes in abundance are of the presence of pus. It should be remembered that pus in the urine of women has sometimes no significance except as showing that there has been an admixture of leucorrheal discharge from the vagina. (See Practical Exercises, pp. 62, 66, 381.)

The Secretion of the Urine.—We have now to consider the mechanism by which the urine is formed in the kidney

from the materials brought to it by the blood. And here the same questions arise as have already been discussed in the case of the salivary and other digestive glands: (1) Are the urinary constituents, or any of them, present as such in the blood? (2) If they do exist in the blood, can they be shown to be separated from it by processes mainly physical or mainly vital—in other words, by ordinary filtration, diffusion and osmosis, or by the selective action of living cells? In the case of the digestive juices it has been seen that some constituents are already present in the blood, but that physical laws alone, so far as we at present understand them, cannot explain the proportions in which they occur in the secretions, nor the conditions under which they are separated; while other constituents—and these the more specific and important—are manufactured in the gland-cells.

In the kidneys the conditions seem at first sight favourable to physical separation, as opposed to physiological secretion. Urine has been described as essentially a solution of urea and salts, and both are ready formed in the blood. The arrangement of the bloodvessels, too, suggests an apparatus for filtering under pressure.

Bloodvessels and Secreting Tubules of Kidney.—The renal artery splits up at the hilus into several branches, which pass in between the Malpighian pyramids, and form at the boundary of the cortex and medulla vascular arches, from which spring, on the one side, interlobular arteries running up into the cortex between the pyramids of Ferrein, and, on the other, vasa recta running down into the boundary layer of the medulla (Fig. 124). The interlobular arteries give off at intervals afferent vessels; each of these soon breaks up into a glomerulus or tuft of vascular loops, which gather themselves up again into a single efferent vessel of somewhat smaller calibre than the afferent. The glomerulus is fitted into a cup or capsule (of Bowman), which is closely reflected over it, except where the afferent and efferent vessels pass through, and forms the beginning of a urinary tubule. If we suppose the tuft pushed into the blind end of the tubule so as to indent it, it will be easily understood that the single layer of flattened epithelium reflected on the glomerulus is continuous with that lining the capsule, which in its turn is continuous with the epithelial layer of the rest of the urinary tubule. This has been divided by histologists into a number of parts which it is unnecessary to enumerate here, further than to say that the urinary tubule proper begins in the cortex in Bowman's capsule and the proximal convoluted tubule

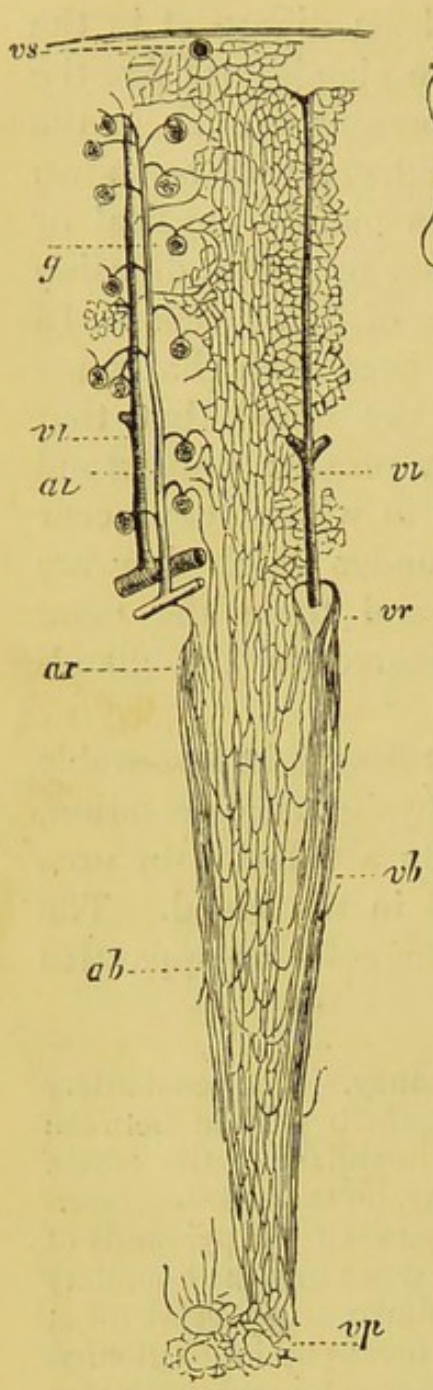


FIG. 124. — DIAGRAM OF BLOODVESSELS OF KIDNEY (KLEIN, after LUDWIG).

ai, interlobular artery; *vi*, interlobular vein; *g*, glomerulus, to which an afferent artery is seen coming from the interlobular artery and from which an efferent artery proceeds to break up into a capillary network surrounding the renal tubules; *vs*, vena stellata; *ar*, arteriæ rectæ; *vb*, leash of venæ rectæ; *vp*, vascular network round ducts at apex of a papilla.

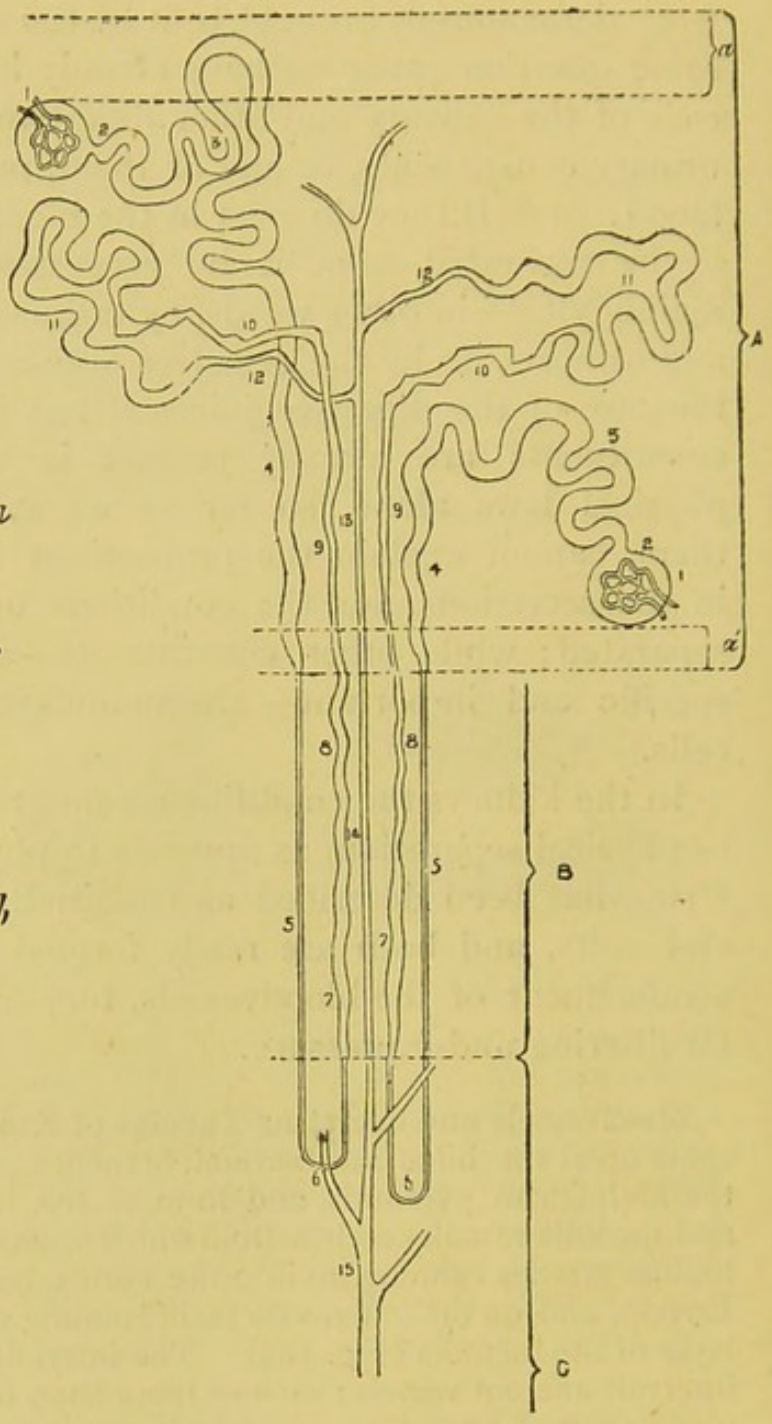


FIG. 125.—DIAGRAM OF RENAL TUBULE (KLEIN).

A, cortex; *a*, layer of cortex immediately under capsule containing no Malpighian corpuscles; *a'*, inner layer of cortex devoid of Malpighian corpuscles; B, boundary layer; C, papillary zone of medulla; 1, Bowman's capsule; 2, neck of capsule; 3, proximal convoluted tubule; 4, spiral tubule; 5, descending part of Henle's loop-tubule; 6, the loop; 7, 8, and 9, ascending limb of loop-tubule; 10, irregular tubule; 11, distal convoluted tubule; 12, junctional tubule; 13, collecting tubule, in a medullary ray or pyramid of Ferrein; 14, collecting tubule in the boundary layer; 15, large collecting tubule ending in a duct of Bellini.

(with its continuation, the spiral tubule), and ends in the cortex with the distal convoluted tubule, the connection between the two being made by a long loop (Henle's) with a descending and an ascending limb (Fig. 125).

The distal convoluted tube joins by means of the short connecting tubule one of the straight tubules which form the pyramids of Ferrein or medullary rays in the cortex, and which run down into the medulla, always uniting into larger and larger tubes as

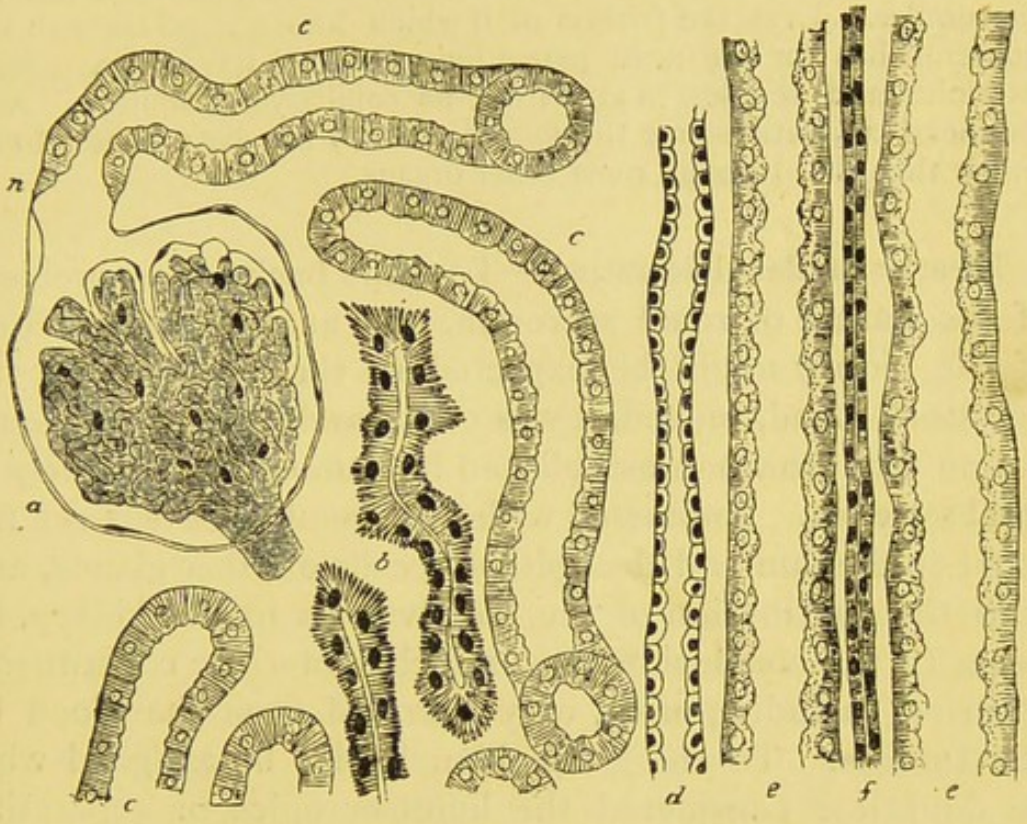


FIG. 126.—FROM A VERTICAL SECTION OF DOG'S KIDNEY TO SHOW THE STRUCTURE OF DIFFERENT PORTIONS OF THE RENAL TUBULE (KLEIN).

a, Bowman's capsule enclosing glomerulus, the capillaries of which are arranged in lobules separated by a little connective tissue. The capsule and glomerulus together constitute a Malpighian body or corpuscle; *n*, neck of capsule; *c*, *c*, convoluted tubules, cut in various directions; *b*, irregular or zigzag tubule; *d*, *e*, and *f* are straight tubules, which take part in the formation of a medullary ray or pyramid of Ferrein; *d*, collecting tubule; *e*, *e*, spiral tubule; *f*, narrow part of ascending limb of Henle's loop-tubule: *c* and *e* are lined with rodded epithelium.

they go, until at length they open as ducts of Bellini on the apex of a papilla. The two convoluted tubules and the ascending limb of Henle's loop are lined by similar epithelial cells with granular contents and a striated or 'rodded' appearance (Fig. 126). We shall see directly that this morphological agreement is the index of a functional likeness. The blood-supply of the tubules, especially of the convoluted portions, is exceedingly rich, the efferent vessels of the glomeruli breaking up around them

into a close-meshed network of capillaries, from which the blood is collected into interlobular veins running parallel to the interlobular arteries between the pyramids of Ferrein. The straight tubules of the medulla are also surrounded by capillaries given off from straight arteries (arteriæ rectæ) running down into it partly from the arterial arches and partly from efferent vessels of the glomeruli nearest the boundary layer, the blood passing away by straight veins (venæ rectæ) which join the larger veins accompanying the arterial arches. The greater part of the blood going through the kidney has to pass through two sets of capillaries, one in the glomeruli, the other around the tubules. Even the portion of it which does not go through the glomeruli has for the most part a long route to traverse in narrow arterioles and venules to and from its capillary distribution. And the mean circulation-time through the kidney has been found to be longer than that through most other organs.

Theories of Renal Secretion.—To come back to our problem of the nature of renal secretion, the anatomical structure of the kidney might be expected to throw light upon the question. And, indeed, it was on a purely histological foundation that Bowman established his famous **'vital' theory of renal secretion.** Impressed with the resemblance between the renal epithelium and the epithelial cells of other glands, and with the distribution of the bloodvessels in the kidney, he came to the conclusion that the characteristic constituents of urine, including urea, were secreted from the blood by the tubules. To the Malpighian bodies he assigned what he doubtless considered the humbler office of separating water from the blood for the solution of the all-important solids. To Ludwig, on the other hand, with his whole attention fastened on the **mechanical factors** by which the flow of urine could be influenced, the tubules seemed of secondary importance, while the glomeruli appeared a complete apparatus for filtering urine from the blood into Bowman's capsule. He saw that the efferent vessel was smaller than the afferent; that it was therefore easier for blood to come to the glomerulus than to get away from it, and that the pressure in the capillaries of the tuft must be higher than in ordinary capillaries, because the resistance beyond them in the comparatively narrow efferent vessel, and especially in the second plexus, is greater than the resistance beyond a single capillary network. And experimental

investigation soon showed him that the rate at which urine was formed could be greatly influenced by changes in the blood-pressure.

On such considerations, Ludwig founded the 'mechanical' theory of urinary excretion, which, although in a much modified form, still divides with the vital theory the allegiance of physiologists. It is impossible here to enter in detail into a controversy that has extended over half a century and produced an extensive literature. The result of the discussion has been, in our opinion, to establish in its essential principles the 'vital' theory of Bowman, or at least to show that no purely mechanical theory as yet constructed will account for all the facts.

Ludwig supposed that the urine, qualitatively complete in all its constituents, was simply filtered through the glomeruli; but as the proportion of salts, and especially of urea, is very far from being the same in urine as in blood, he further assumed that the liquid which passes into Bowman's capsule is exceeding dilute, and that absorption of water, and perhaps of other constituents, takes place in its passage along the renal tubules. The great length of these tubules, as compared with those of most other glands, might seem to indicate a long sojourn of the urine in them, and the probability of important changes being caused in its passage along them. But if we consider the immense length (60 to 70 cm.) of the seminal tubules and of their gigantic ducts (epididymis 6 metres), where, of course, absorption of water on a large scale is out of the question, it will be granted that little can be built upon the mere length of the renal tubules. On the other hand, the salivary glands, where there are no glomeruli, secrete as much water as the kidneys are supposed to filter; and the pancreas, whose capillaries form the first of a double set, and therefore in this respect correspond to the renal glomeruli, secretes less water than the liver, whose capillaries correspond to the low-pressure plexus around the convoluted tubules of the kidney. So that deductions drawn from the anatomical relations of the bloodvessels are not in this case of much value, unless supported by physiological results.

Tried by the latter test, the mechanical theory breaks down for the kidney, as it does for other glands.

In the first place, the absence from urine of the proteids and sugar of the blood under normal circumstances—if infinitesimal quantities of these substances, as some have asserted, are really to be found in healthy urine, it makes no difference to the argument—and the elimination by the kidney of egg-albumin, peptone, and other bodies when injected into the veins, show a selective power inexplicable except by reference to the vital activity of cells. Urea and sugar, both highly diffusible substances, circulate side by side in the bloodvessels of the kidney. "The one is taken and the other left." The urea is a waste-product of no further use in the economy. The sugar is a valuable food-substance. The kidney selects with unerring certainty the urea, of which only 4 parts in 10,000 are present in the blood, but rejects the sugar, of which there is five times as much.

Egg-albumin injected into the blood passes through the renal circulation side by side with the serum-albumin of the plasma. Both are indiffusible through membranes, and to the chemist the differences between them may appear superficial and minute. But the kidney does not hesitate for an instant. A large part of the egg-albumin is promptly excreted as a foreign substance; the serum-albumin passes on untouched.

Not only does the kidney exercise a power of qualitative selection; it also takes cognizance of the quantitative composition of the blood. So long as there is less sugar in the plasma than about 3 parts in 1,000, it is refused passage into the renal tubules. But when this limit is passed, and the proportion of sugar in the blood becomes excessive, the kidney begins to excrete sugar, and continues to do so till the balance is redressed.

The advocates of the theory of filtration, driven from one position to another, have made their firmest stand on the excretion of the inorganic constituents of the urine. But even here the theory has at length become untenable; and there is little more reason to believe that the copious flow of

urine which follows the absorption of a large quantity of water is due to a mere process of filtration than there is to believe that filtration, and not selective secretion, is the cause of the gush of saliva which precedes vomiting, or the sudden outburst of sweat on sudden and severe exertion. It is true that the direct introduction of water into the blood, or its attraction from the lymph spaces when the osmotic pressure of the blood is increased by the injection of substances like urea, sugar and sodium chloride, may cause a condition of *hydræmic plethora*, and that this plethora may sometimes be associated with an increase of pressure in the capillaries in general, and therefore in the vessels of the Malpighian tuft. It may also be admitted that such an increase of pressure might be accompanied by an increased filtration of water and salts into the Bowman's capsule. But who will believe that the addition of a tumbler of water, absorbed from the alimentary canal, to $5\frac{1}{2}$ litres of blood circulating in a system of vessels whose capacity can and does vary within wide limits, should cause in the capillaries of the kidney an increase of pressure exactly proportional to the increase in the elimination of water in the urine, lasting for the same time and disappearing at the moment when the normal composition of the blood is restored? Nor is it easier to explain on any filtration hypothesis how it is that in a starving animal, the quantity of inorganic substances eliminated in the urine drops almost to zero, while the proportional amount in the blood and tissues is little, if at all, affected. Such facts suggest that the secreting cells of the kidney are stimulated by the contact of blood or lymph in which the normal constituents are present in too small or in too great amount, and that the strength of the stimulus is proportional to the degree of deficiency or excess.

As to the nature of the mechanism thus set in motion, and the series of events that take place as the constituents of the urine journey from the interior of the bloodvessels to the lumen of the tubules, we know no more than in the case of other glands. This alone is clear, that the separation of the urine from the blood implies the performance of a large

amount of work by the kidney. For the osmotic pressure of urine is several times as great as that of the plasma of the blood. Blood-plasma freezes at −0·55° to −0·65° C. (on the average, say, −0·6° C.). The osmotic pressure corresponding to −0·6° C. is 5,662 millimetres of mercury (p. 361), or, in round numbers, 75 metres of water. Human urine has been found to freeze at −1·38 to −2·11° C. (say, on the average, −1·8° C.), and for highly concentrated urines the depression of the freezing-point may be considerably greater. The osmotic pressure corresponding to −1·8° C. is 16,986 millimetres of mercury or 225 metres of water. This exceeds the osmotic pressure of the plasma by 150 metres of water. In separating a kilogramme of urine from the blood the kidney accordingly does work approximately equivalent to raising a weight of a kilogramme to the height of 150 metres, *i.e.*, 150 kilogramme-metres. It is evident that the excess of the blood-pressure in the glomeruli over the pressure of the urine in the tubules, which, even if we neglect the latter altogether, since there is only slight resistance to the flow of urine towards the bladder, cannot at most be greater than 100 millimetres of mercury, or 1·35 metres of water, will account for only an insignificant part of this work. The rest must be done at the expense of the energy of the food-materials taken up by, and transformed in, the cells concerned with the secretion of the urine. But we do not know in what way these cells, by applying this energy, perform the remarkable feat of permanently maintaining a difference of fifteen atmospheres in the osmotic pressure of the liquids in contact with their attached and free surfaces.

But, secondly, there is positive proof that the 'rodded' epithelium of the tubules, which no one supposes to be abandoned more to mere physical influences than the epithelium of the salivary glands, plays a part in the secretion of some of the urinary constituents. For Bowman saw crystals of uric acid in the epithelium of the convoluted tubules of birds. Heidenhain found that urate of soda and indigo-carmine injected into the blood of a rabbit are excreted by the epithelium of the convoluted tubules and the ascending part of Henle's loop. And Nussbaum's experi-

ments, although not perhaps quite conclusive, have made it probable that in the frog urea is actually separated by the epithelium of the tubules.

The **experiments of Heidenhain and Nussbaum** deserve more detailed description. The former injected indigo-carmine into the blood of rabbits and after a variable time killed them, cut out the kidneys, and flushed them with alcohol. His results were as follows: (1) When the spinal cord was cut before the injection in order to reduce the blood-pressure, the blue granules were found in the 'rodded' epithelium of the convoluted tubules and the ascending limb of Henle's loop, and in the lumen of the tubules, but nowhere else. The renal cortex was coloured blue. (2) When the spinal cord was not cut, the pigment was found in the medulla and pelvis of the kidney, as well as in the cortex, but always in the lumen of the tubules, and not in the epithelium, except in the situations mentioned. (3) If a portion of the cortex of the kidney had been cauterized with nitrate of silver before injection of the pigment, the spinal cord being left intact, a wedge of the renal substance, corresponding to this area, remained coloured only in the cortex, although the rest was blue in the medulla also. The rodded epithelium was filled with blue granules as before (Fig. 127).

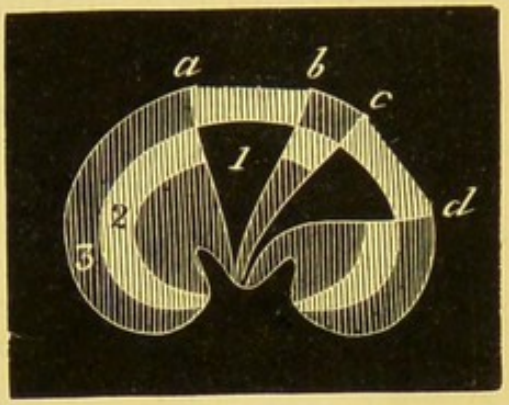


FIG. 127.—DIAGRAM OF DISTRIBUTION OF PIGMENT IN KIDNEY AFTER INJECTION INTO BLOOD.

The cortex between *a* and *b* and between *c* and *d* was cauterized before the injection. In the black wedge-shaped portions 1 there was no pigment. In the zones shaded like 2 there was some pigment, but not so much as in the areas shaded like 3.

(1) shows that the epithelium is capable of excreting some substances at least. (2) appears to show that when the blood-pressure is normal water is poured out from some part of the tubule, and washes the pigment separated by the 'rodded' epithelium down towards the papillæ. (3) suggests that it is through the glomeruli that most of the water passes. For cauterization has not destroyed the power of the epithelium to excrete pigment, and therefore, presumably,

would not have destroyed its power to excrete water if it possessed this power in any great degree; and the glomeruli and their capsules are the only other part of the renal mechanism which can have been affected. The fact that in birds and serpents, whose urine is solid or semi-solid, the glomeruli are smaller than in mammals is corroborative evidence that the glomeruli have to do with the excretion of water.

An attempt has recently been made by Sobieránski, on the strength of a reinvestigation of the microscopical appearances presented by the kidney after injection of pigments into the blood, to revive Ludwig's theory that absorption takes place from the tubules. He asserts that, although pigment granules are found in the rodded epithelium, they are always near the lumen of the tubule, never near the basement membrane. From this he concludes that the pigment is not passed through the cells from the blood, but absorbed by them from the tubules after excretion by the glomeruli. It cannot, however, be admitted that his observations are decisive.

Nussbaum's experiments were founded on the anatomical fact that the kidney of batrachians, and, indeed, that of fishes and ophidia as well, has a double blood-supply. The renal artery gives off afferent vessels to the glomeruli, and the *vena advehens* or renal portal vein breaks up, like the portal vein in the liver, into a plexus of capillaries surrounding the tubules, with which plexus the efferent arterioles of the glomeruli communicate. By tying the renal arteries in the frog, Nussbaum thought he could at will stop the circulation in the glomeruli, and he found that after this was done, sugar, peptones and egg-albumin, injected into the blood, no longer passed into the urine, although they readily did so when the arteries were not tied. Urea, however, was still eliminated by the kidneys after ligature of the renal arteries, and water along with it. He concluded that the Malpighian corpuscles have the power of excreting water, sugar, peptone, and albumin, while the epithelium of the tubules excretes urea as well as water.

Adami has since shown that the circulation in the glomeruli is not wholly stopped by Nussbaum's operation, for there is a certain amount of anastomosis between the arteries of the generative organs and the renal arteries. He therefore

suggests that the water secreted during the elimination of urea after ligature of the renal arteries may really come through the Malpighian tufts. At the same time, this objection does not touch the conclusion of Nussbaum, that the glomeruli are alone concerned in the separation of the other bodies mentioned. For his operation, whether it completely cut off the circulation in the tufts or not, interfered with it so much as to stop the excretion of these substances, while leaving the epithelium of the tubules as able to continue that function, if it possessed it, as it was before. Adami himself has shown that hæmoglobin when free in the blood-plasma is excreted by the glomeruli, even when the renal artery has been ligatured, and that menisci of this substance may be coagulated within the lumen of the Bowman's capsules by plunging the kidney into boiling water. In the dog, too, hæmoglobin is excreted by the glomeruli, and may be washed out of the capsule by the increased quantity of water secreted when sodium nitrate is administered. This shows that a diuretic may act upon the glomerular epithelium, which is thus brought into line with the 'rodded' epithelium of the tubules.

What, then, is the significance of the peculiar arrangement of the glomerular bloodvessels, if the epithelium of the capsules has secretive powers like that of ordinary glands? It is difficult to believe that these unique vascular tufts have not a near and important relation to the renal function; but it is by no means clear what that relation is. The secretion of water, and even its rapid secretion, is not at all bound up with any set arrangement of bloodvessels. Gland-cells all over the body secrete water under the most varied conditions of blood-pressure, although a comparatively high pressure is upon the whole favourable to a copious outflow.

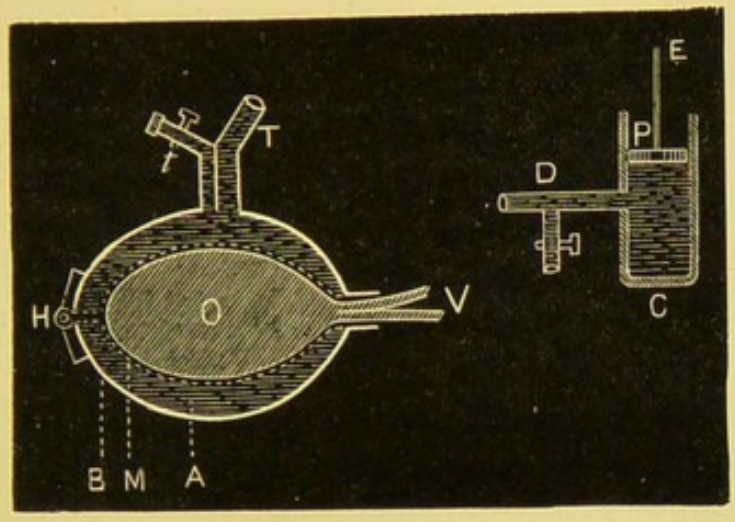
But the kidney has, as we now know, other functions than mere excretion (p. 483). And it may be that the simplest part of the latter process, the elimination of water and salts, is largely thrown upon the Malpighian corpuscles, as a physiologically cheaper machine than the epithelium of the tubules, which is left free for more complex labours. These may include not only the separation of nitrogenous metabolites, but perhaps the building up of urea, or of less completely metabolized substances which precede it, into higher combinations, and the consequent regulation of the quantity of urea finally excreted, and the ultimate proteid waste which this expresses. The epithelium of the glomerulus, being a less highly organized and less delicately selective mechanism than that of the convoluted tubules, may more

easily respond to increase of blood-pressure by increased secretion. At the same time, placed as it is at the last flood-gate of the circulation, where the escape of anything valuable means probably its total loss, the glomerular epithelium may be endowed with a general power of resistance to transudation, which renders a comparatively high blood-pressure a necessary condition of its acting at all. And as a matter of fact, water ceases to be secreted by the kidney long before the blood-pressure in the glomeruli can have fallen below that which suffices for the highest activity of the liver. Perhaps, however, the high minimum pressure required (30 to 40 mm. of mercury in the dog) is merely the necessary consequence of the long and difficult path which most of the blood going through the kidney has to take, and that a sufficient blood-flow cannot be kept up with less. It may be, too, that the comparatively small surface of the glomeruli, restricted in order to leave room for the more highly organized parts of the renal mechanism, entails the more intense and concentrated activity, which the high blood-pressure renders possible, and the simplicity of work and organization renders harmless.

An obvious result, and perhaps an important one, of the peculiar arrangement of the bloodvessels of the kidney is that the more highly organized parts of the renal tubules are shielded from an excessive blood-pressure by the interposition of the glomeruli as a block. This may be either because the epithelium of the tubules would not perform its proper work so well under a high blood-pressure, or because there would be a danger of substances which ought to be retained being cast out into the urine. In this connection it is interesting to note that the specific constituents of urine are separated by epithelium surrounded by capillaries of the second order, and therefore with a smaller blood-pressure than exists in the capillaries of most glands, while the same is true of bile, another proteid-free secretion.

The maximum secretory pressure in the kidney, as shown by a manometer tied into the divided ureter, is about 60 mm. of mercury in the dog, or less than half that of saliva. If the escape of the urine is opposed by a greater pressure than this, or if the ureter is tied, the kidney becomes œdematous. Whether the œdema is due to reabsorption of urine or to the pouring out of lymph owing to the pressure of the dilated tubules on the veins has not been definitely settled. It has been already pointed out that there is no necessary relation between the blood-pressure in the capillaries of a gland and its secretory pressure; and, so far as this goes, water might just as well be secreted at a pressure of 60 mm. of mercury from the low-pressure blood of the second set of renal capillaries as from the high-pressure blood of the glomeruli.

The Influence of the Circulation on the Secretion of Urine.—Although the activity of no organ in the body is governed more by the indirect effects of nervous action than that of the kidney, no proof has yet been given of the existence of secretory fibres for it comparable to those of the salivary glands. All the changes in the rate of renal secretion which



B, metal box in two halves opening on the hinge H; M, thin membrane; A, space filled with oil; O, organ enclosed in oncometer; V, vessels of organ; *t*, tube for filling instrument with oil; T, tube connected with D, which opens into cylinder C; C is also filled with oil; P, piston attached by E to a writing lever.

FIG. 128.—DIAGRAM OF ORGAN-PLETHYSMOGRAPH OR ONCOMETER.

follow the section or stimulation of nerves can be explained as the consequences of the rise or fall of local or general blood-pressure, and of the corresponding variations in the velocity of the blood in the renal vessels.

The best way to study variations in the calibre of the renal vessels is the plethysmographic method, and the oncometer of Roy is a plethysmograph adapted to the kidney. It consists of a metal capsule lined with a loose membrane, between which and the metal there is a space filled with oil. The two halves of the capsule open and shut on a hinge; and the kidney, when introduced into it, is surrounded on all sides by the membrane, the vessels and ureter passing out through an opening. The oil-space is connected with a cylinder also filled with oil, above which a piston, attached to a lever, moves. The lever registers on a drum the changes in the volume of the kidney, *i.e.*, practically the changes in the quantity of blood in it, and therefore in the calibre of its vessels. A still better oncometer is that of Schäfer, in which air is employed instead of oil.

Nerves of the Kidney.—Both vaso-constrictor and vaso-dilator fibres for the renal vessels, but most clearly the former, have been shown to leave the cord (in the dog) by the anterior roots of the sixth thoracic to second lumbar nerves, and especially of the last three thoracic. They run in the splanchnics, and then through the renal plexus—around the renal artery—into the kidney. The vaso-constrictors predominate, so that the general effect of stimulation of

the nerve-roots, the splanchnics, or the renal nerves is shrinking of the kidney, with diminution or cessation of the secretion of urine. But slow rhythmical stimulation of the roots causes increase of volume, the dilators being by this method excited in preference to the constrictors.

Section of the renal nerves is followed by relaxation of the small arteries in the kidney, and consequent swelling of the organ. The flow of urine is greatly increased, and sometimes albumin appears in it, the excessive pressure in the capillaries (particularly in those of the glomeruli) being supposed to favour the escape of substances to which the renal epithelium refuses a passage under normal conditions.

The recent investigations of Berkely have shown that the renal nerves, entering at the hilum, branch repeatedly, so as to form a wide-meshed plexus around the arteries, and accompany them even to their finest ramifications in the cortex. No nerve-fibres have as yet been seen on the veins in the kidney-substance or on the straight arteries. Coming off from the nerves surrounding the arteries are fine fibres which are distributed to the convoluted tubules, and are perhaps secretory nerves. Some of them terminate in globular ends, others in fine threads that pass through the membrana propria.

It is often assumed that the renal nerves affect chiefly the afferent arterioles of the glomeruli; but there seems to be no experimental ground for this view, which is merely a doctrinaire deduction from Ludwig's filtration theory. For if that theory, or any modification of it which postulates a close connection between the blood-pressure in the glomerular capillaries and the rate of secretion of urine, be accepted, it is evidently an advantage that there should be no similar influence on the efferent arterioles, since constriction of both would not necessarily cause any fall, nor dilatation of both any rise, of intra-glomerular pressure. Heidenhain's suggestion, that the velocity of the blood-flow, and not the pressure in the glomeruli, is the determining factor in urinary secretion, does not require any arbitrary restriction of the tract influenced by the renal vaso-motor nerves. If both afferent and efferent vessels were constricted, the blood-

flow would be diminished; if both were relaxed, it would be increased; if only the vas afferens were affected, the changes would be in the same sense, although less marked, since the total alteration of resistance would be less.

An experiment which is sometimes quoted as a decisive test of the relative importance of changes in the rate of flow,

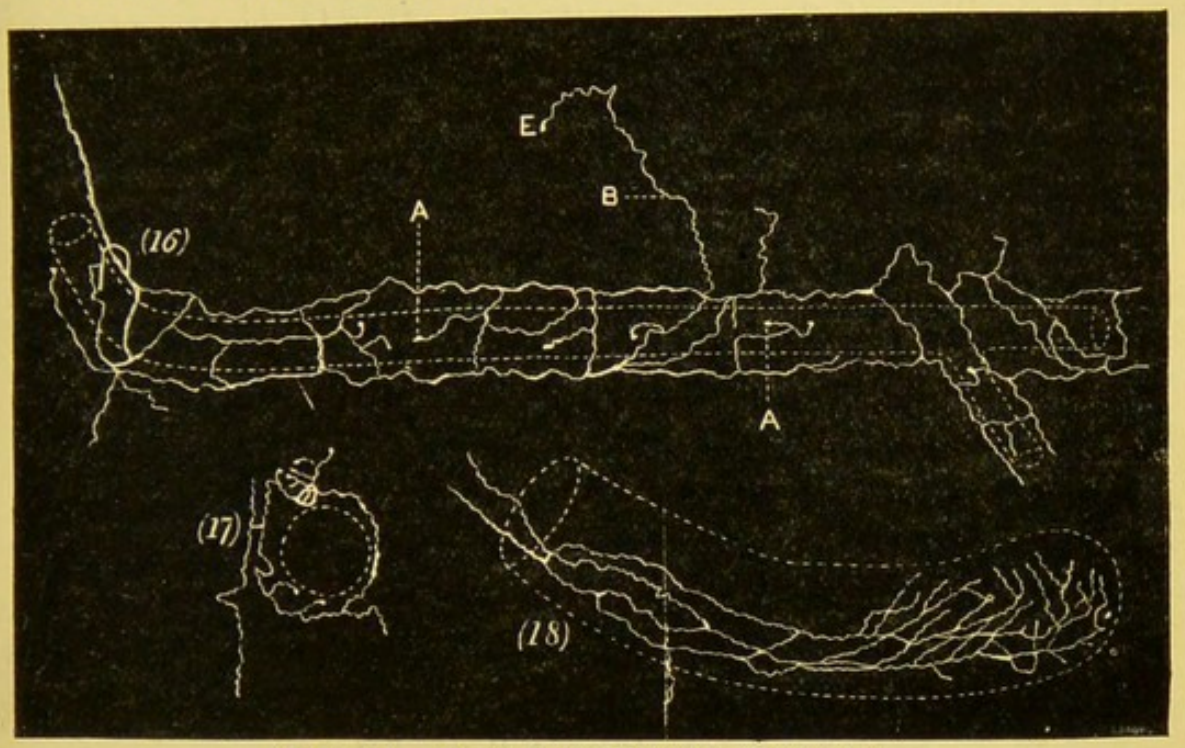


FIG. 129.—NERVES OF KIDNEY (BERKELY)

(16) medium-sized artery with its nerve-plexus; A, terminal knobs; B, aberrant branch ending in terminal knob E; the dotted lines outline the artery. (17) Nerve-fibres surrounding a Bowman's capsule, which is indicated by a dotted line; some of the endings are close to the membrane; (18) convoluted tubule shown in outline with fine nerve-fibres on it, which seem to enter the basement membrane.

and in the pressure of the blood within the glomeruli, is that of tying the renal vein. This undoubtedly does not lower the intra-glomerular pressure—on the contrary, it must increase it—but the secretion of urine stops. If the venous outflow from the kidney is only partially interfered with, the flow of urine is immediately diminished, but the administration of a diuretic like potassium nitrate causes an increase. It is suggested that in these experiments the secretion stops or slackens because an active circulation, and not a high blood-pressure, is its necessary condition. The conclusion is probably correct, but the experiment does not prove it. For few glands can go on performing their function after the circulation has ceased. The kidney must be able to feed

itself in order to continue its work; and it might be urged that if the blood in the glomeruli could be kept at the normal standard of arterial blood, secretion might still go on after ligature of the renal vein.

According to Ludwig, indeed, the flow of urine stops, in spite of continued filtration through the glomeruli, because the swelling of the veins in the boundary layer compresses the tubules, and may even obliterate their lumen. There is no conclusive experimental evidence, however, and no *à priori* probability, that the obstruction so produced is sufficiently sudden or sufficiently complete to cause instant and total cessation of the flow. It is even less justifiable to conclude from the experiment that the liquid part of the urine is, at any rate, not separated by the epithelium of the tubules, since the blood-pressure in the capillaries around the tubules must rise very greatly after ligature of the vein, and yet secretion is stopped. It might equally well be argued that the renal epithelium normally secretes water under a *low* blood-pressure, but is disorganized under the excessive and entirely unaccustomed pressure which follows the closure of the vein. But the whole discussion is an illustration—and this is the reason we have gone into it so fully—of the complexity, the many-sidedness of physiological phenomena, even when reduced by well-planned experiments to their simplest terms, and the unconscious bias which theory sometimes gives to even the most acute and original minds in interpreting the results of observation.

It is not only through nerves directly governing the calibre of the vessels of the kidney that the rate of urinary secretion can be affected. Any change in the general blood-pressure, if not counteracted by, still more if conspiring with, simultaneous local changes in the renal vessels, may be followed by an increased or diminished flow of urine; and the law which explains all such variations, or at least serves to sum them up, is that in general *an increase in the rate of the blood-flow through the kidney is followed by an increase in the rate of secretion.* It will be remarked that this is the converse of the great law, of which we have already seen so many illustrations, that *functional activity increases blood-flow.* It is

probable that this law holds for the kidney as well as for other organs, but that the influence of activity on blood-supply is subordinated to that of blood-supply on activity, while in most tissues, as in the muscles, the opposite is the case. It is evident that an increase in the blood-flow would favour the secretory activity of the renal cells, since the average concentration of the blood presented to them as regards those constituents which they select would remain relatively high in its circuit through the kidney. The 'stimulus' to secretion would, therefore, be relatively intense.

Destruction of the medulla oblongata (*i.e.*, of the vaso-motor centre), or section of the cord below it, diminishes the secretion of urine, because the arterial pressure is lowered so much as to over-compensate the dilatation of the renal vessels, which the operation also brings about. If the blood-pressure falls below 40 mm. of mercury, the secretion is abolished. Stimulation of the medulla or cord also lessens the flow of urine by constricting the arterioles of the kidney so much as to over-compensate the rise of general blood-pressure, caused by the constriction of small vessels throughout the body.

If the renal nerves have been cut, stimulation of the medulla oblongata increases the urinary secretion, because now the rise of general blood-pressure is no longer counter-balanced by constriction of the renal vessels. Puncture of a certain part of the floor of the fourth ventricle may produce a copious flow of urine, perhaps by destroying the portion of the vaso-motor centre governing the renal nerves, while the rest remains uninjured and keeps up the general blood-pressure, but possibly by stimulating a secretory 'centre.'

Section of the splanchnic nerves causes a fall of arterial pressure, which is, however (in animals like the dog, in which compensation soon takes place), more than balanced by the simultaneous dilatation of the renal vessels, and therefore for some time the flow of urine is increased, but not so much as when the renal nerves alone are cut. In the rabbit there is no increase. On the other hand, stimulation of the splanchnics stops the urinary secretion, because the

general rise of pressure is not enough to make up for the constriction of the renal vessels.

Diuretics are substances that increase the flow of urine. Some of them act mainly by increasing the general blood-pressure, others mainly by a direct influence on the secreting mechanism. Digitalis is a representative of the first class; urea and caffein belong to the second. The action of digitalis is to strengthen the beat of the heart, which is at the same time somewhat slowed, and to constrict the arterioles. Both effects contribute to the increase of pressure. It is possible that in addition this drug directly stimulates the renal epithelium. Caffein, when injected into the blood, affects the pressure but little. It causes dilatation of the renal vessels after a passing constriction, and an increase in the flow of urine after a temporary diminution. The vascular dilatation is not the chief reason for the diuretic effect, for the latter is still obtained when the vaso-motor mechanism has been paralyzed by chloral hydrate, and even after the secretion of urine has been stopped by the fall of pressure consequent on section of the spinal cord. Caffein, therefore, acts directly on the renal epithelium. The action of urea, potassium nitrate, and the saline diuretics is probably also a direct action on the secreting structures, although some have supposed that their primary effect is to cause vaso-dilatation in the kidney, and a consequent local increase in the capillary pressure.

Summary.—Our knowledge of renal secretion may be thus summed up: *The water and salts of the urine are chiefly separated by the glomeruli; the process is not a mere physical filtration, but a true secretion. Substances like sugar, peptone, egg-albumin, and hæmoglobin when injected into the blood are excreted by the glomeruli: so probably is the sugar of diabetes. Urea, uric acid, and presumably the other organic constituents of normal urine, with a portion of the water and salts, are excreted by the physiological activity of the 'rodded' epithelium of the renal tubules. The rate of secretion of urine rises and falls with the pressure, and still more with the velocity, of the blood in the renal vessels. No secretory nerves for the kidney have been definitely found; the effects of section or stimulation of nerves on the secretion can all be explained by the changes produced in the renal blood-flow. Some diuretics act by increasing the blood-flow, others directly on the epithelium of the tubules.*

Micturition.—The urine, like the bile, is being constantly formed; although secretion varies in its rate from time to time, it never ceases. Trickling along the collecting tubules, the urine reaches the pelvis of the kidney, from which it is

propelled along the ureters by peristaltic contractions of their walls, and drops from their valve-like orifices into the bladder. When this becomes distended, rhythmical peristaltic contractions are set up in it, and notice is given of its condition by a characteristic sensation, which is perhaps aided by the squeezing of a few drops of urine past the tonically contracted circular fibres that form a sphincter round the neck of the bladder, and into the first part of the urethra. The desire to empty the bladder can be resisted for a time, as can the desire to empty the bowel. If it is yielded to, the smooth muscular fibres in the wall of the viscus are thrown into contraction. This is aided by an expulsive effort of the abdominal muscles. The sphincter vesicæ is relaxed; and the urine is forced along the urethra, its passage being facilitated by discontinuous contractions of the ejaculator urinæ muscle, which also serve to squeeze the last drops of urine from the urethral canal at the completion of the act.

Regurgitation into the ureters is to a great extent prevented by their compression between the mucous and muscular coats of the bladder, where they run for more than half an inch before opening at the posterior angle of the trigone. But it has been shown that a certain amount of back flow can take place. Small bodies like diatoms suspended in water and pigments dissolved in it have been found in the pelvis of the kidney, the renal tubules, and even the circulation after being injected into the bladder.

The pressure in the bladder of a man may be made as high as 10 cm. of mercury during the act of micturition; about half this amount is due to the contraction of the vesical walls alone, the rest to the contraction of the abdominal muscles.

Although the whole performance seems to us to be completely voluntary, there are facts which show that it is at bottom a reflex series of co-ordinated movements, that can be started by impulses passing to a centre in the spinal cord from above or from below—from the brain or from the bladder. In dogs, with the spinal cord divided at the upper level of the lumbar region, micturition takes place regularly when the bladder is full, and can be excited by such slight

stimuli as sponging of the skin round the anus (Goltz). Here, of course, the act is entirely reflex; and the centre is situated at the level of the fifth lumbar nerves. The efferent nerves of the bladder, like those of the rectum, come partly from the cord directly through the sacral nerves, and partly through the lumbar sympathetic chain (second to sixth ganglia). The sacral fibres are connected with nerve cells in the hypogastric plexus, and the sympathetic, partly at least, in the inferior mesenteric ganglia. This anatomical coincidence acquires interest in view of the striking physiological similarity between the processes of micturition and defæcation, a similarity which is emphasized by the fact that the latter is almost invariably accompanied by the former. An important difference, however, is that the will can far more readily set in motion the machinery of micturition than that of defæcation; a man can generally empty his bladder when he likes, but he cannot empty his bowels when he likes.

Sometimes in disease, and especially in disease of the spinal cord, the mechanism of micturition breaks down; the bladder is no longer emptied; it remains distended with urine, which dribbles away through the urethra as fast as it escapes from the ureters. To this condition the term *incontinence of urine* is properly applied.

Reflex emptying of the bladder, without an act of will or during unconsciousness, is not true incontinence. The involuntary micturition of children during sleep, for example, is a perfectly normal reflex act, although more easily excited and less easily controlled than in adults.

II. Excretion by the Skin.

Besides permitting of the trifling gaseous interchange already referred to (p. 258), the skin plays an important part in the elimination of water by the sweat-glands.

Sweat is a clear colourless liquid of low specific gravity (1003 to 1006), consisting chiefly of water with small

quantities of salts, neutral fats, volatile fatty acids, and the merest traces of proteids and urea. It is acid to litmus except in profuse sweating, when it may become neutral or even alkaline. It is secreted by simple gland-tubes, which form coils lined with a single layer of columnar epithelium, in the subcutaneous tissue, with long ducts running up to the surface through the true skin and epidermis. Unless collected from the parts of the skin on which there are no hairs, such as the palm, it is apt to be mixed with *sebum*, a secretion formed by the breaking down of the cells of the sebaceous glands, which open into the hair follicles, and consisting chiefly of glycerin and cholesterin fats, soaps, and salts.

Although it is only occasionally that sweat collects in visible amount on the skin, water is always being given off in the form of vapour. This invisible perspiration leaves behind it on the skin, or in the glands, the whole of the non-volatile constituents, which may be to some extent reabsorbed; and since even the visible perspiration is in large part evaporated from the very mouths of the glands in which it is formed, the sweat can hardly be considered a vehicle of solid excretion, even to the small extent indicated by its chemical composition.

The total quantity of water excreted by the skin, and the relative proportions of *visible and invisible perspiration*, vary greatly. A dry and warm atmosphere increases, and a moist and cold atmosphere diminishes the total, and, within limits, the invisible perspiration. Visible sweat—given the condition of rapid heat-production in the body as in muscular labour—is more readily deposited on freely exposed surfaces when the air is moist than when it is dry. The air in contact with surfaces covered by clothing is never far from being saturated with watery vapour. Here, accordingly, a comparatively slight increase in the activity of the sweat-glands suffices to produce more water than can be at once evaporated; and the excess appears as sweat on the skin, to be absorbed by the clothing without evaporation, or to be evaporated slowly, as the pressure of the aqueous vapour gradually diminishes in consequence of diffusion.

The *quantity of sweat* given off by a man in twenty-four hours varies so much that it would not be profitable to quote here the numerical results obtained under different conditions of temperature and humidity of the air. It is enough to say that the excretion of water from the skin is of the same order of magnitude as that from the kidneys: a man loses upon the whole as much water in sweat as in urine. But it is to be carefully noted that these two channels of outflow are complementary to each other; when the loss of water by the skin is increased, the loss by the kidneys is diminished, and *vice versâ*.

The Influence of Nerves on the Secretion of Sweat.—The sweat-glands are governed directly by the nervous system; and though an actively perspiring skin is, in health, a flushed skin, the vascular dilatation is a condition, and not the chief cause of the secretion. Stimulation of the peripheral end of the sciatic nerve causes a copious secretion of sweat on the pad and toes of the corresponding leg of a young cat, and this although the vessels are generally constricted by excitation of the vaso-motor nerves. Not only so, but when the circulation in the foot is entirely cut off by compression of the crural artery or by amputation of the limb, stimulation of the sciatic still calls forth some secretion. As in the case of the salivary glands, injection of atropia abolishes the secretory power of the sciatic, while leaving its vaso-motor influence untouched; and pilocarpin increases the flow of sweat by direct stimulation of the endings of the secretory nerves in the glands.

That the sweating caused by a high external temperature is normally brought about by nervous influence, and not by direct action on the secreting cells, is shown by the following experiments. One sciatic nerve is divided in a cat, and the animal is put into a hot-air chamber. No sweat appears on the foot whose nerve has been cut, but the other feet are bathed in perspiration. Similarly, a venous condition of the blood (in dyspnœa) causes sweating in the feet whose nerves have not been divided, but none in the other foot; and stimulation of the central end of the cut sciatic has the same effect. All this points to the existence of a reflex

mechanism ; and it is certain that dyspnœa acts by direct stimulation of the centre or centres. The vaso-motor centre is at the same time stimulated, and the bloodvessels constricted, as in the cold sweat of the death agony. Fear may also cause a cold sweat, impulses passing from the cerebral cortex to the vaso-motor and sweat centres.

It is probable that a general sweat-centre exists in the medulla oblongata, but its position has not been exactly determined nor even its existence definitely proved. On the other hand, it is known that in the cat there are at least two spinal centres, one for the fore-limbs in the lower part of the cervical cord, and another for the hind-limbs where the dorsal portion of the cord passes into the lumbar. That this latter centre does not exist or is comparatively inactive in man is indicated by the following case. A man fell from a window and fractured his backbone at the fifth dorsal vertebra. The lower half of the body was paralyzed for a time, but recovered. Ultimately, however, the paralysis returned ; and shortly before his death (twenty-one years after the accident) it was noticed that a copious perspiration broke out several times on the upper part of the body, while the lower portion remained perfectly dry. If there is any spinal centre in man, it appears to lie above the fifth spinal segment. For it was seen in a professional diver who fractured his neck at that level, and lived three months after the accident, that sweat frequently appeared on the parts of the body above the lesion, but never below. At the autopsy the whole thickness of the cord, except perhaps a small portion of the anterior columns, was found destroyed.

The secretory fibres for the fore-limbs (in the cat) leave the cord in the anterior roots of the fourth to ninth thoracic nerves. They pass by white rami communicantes to the sympathetic chain, in which they reach the ganglion stellatum, where they are all connected with nerve-cells. Then, as non-medullated fibres, they gain the brachial plexus by the grey rami, and run in the median and ulnar to the pads of the feet. The fibres for the hind-limbs leave the cord in the anterior roots of the twelfth thoracic to the third or fourth lumbar nerves; pass by the white rami to the sympathetic ganglia, in which they form connections with ganglion cells; then, as non-medullated fibres, run along the grey rami, and are distributed to the foot in the sciatic.

The evidence of the direct secretory action of nerves on the sweat glands is singularly striking and complete, in contrast to what we know of the kidney. In the latter, blood-flow is the important factor; increased blood-flow entails increased secretion. In the former, the nervous impulse to secretion is the spring which sets the machinery in motion ; vascular dilatation aids secretion, but does not generally cause

it. It would, however, be easy to lay too much stress on this distinction, for in the horse the mere dilatation of the blood-vessels of the head after section of the cervical sympathetic has been found to be accompanied by increased secretion of sweat, and urinary secretion can certainly be affected by the direct action of various substances on the secretory mechanism, independently of vascular changes. But the broad difference stands out clearly enough, and the reason of it lies, perhaps, in the essentially different purpose of the two secretions. The water of the urine is in the main a vehicle for the removal of its solids; the solids of the sweat are accidental impurities, so to speak, in the water. The kidney eliminates substances which it is vital to the organism to get rid of; the sweat-glands pour out water, not because it is in itself hurtful, not because it cannot pass out by other channels, but because the evaporation of water is one of the most important means by which the temperature of the body is controlled. In short, urine is a true excretion, sweat a heat-regulating secretion. No hurtful effects are produced when elimination by the skin is entirely prevented by varnishing it, provided that the increased loss of heat is compensated. A rabbit with a varnished skin dies of cold, as a rabbit with a closely-clipped or shaven skin does; suppression of the secretory function of the skin has nothing to do with death in the first case any more than in the second.

PRACTICAL EXERCISES ON CHAPTER VI.

Urine.

For most of the experiments human urine is employed—in the quantitative work the mixed urine of the twenty-four hours. Urine may also be obtained from animals. In rabbits pressure on the abdomen will empty the bladder. Dogs may be taught to micturate at a set time or place, or kept in a cage arranged for the collection of urine. Or a catheter may be used (p. 526).

1. **Specific Gravity.**—Pour the urine into a glass cylinder, and remove froth, if necessary, with filter-paper. Place a urinometer (Fig. 130) in the urine, and see that it does not come in contact with the side of the vessel. Read off on the graduated stem the

division which corresponds with the bottom of the meniscus. This gives the specific gravity.

2. **Reaction.**—Test with litmus-paper. Generally the litmus is reddened, but occasionally in health the urine first passed in the morning is alkaline. Sometimes urine has an amphicroic reaction, *i.e.*, affects both red and blue litmus paper. This is the case when there is such a relation between the bases and acids that both acid and 'neutral' (dibasic) phosphates are present in certain proportions. The acid phosphate reddens blue litmus, and the 'neutral' phosphate turns red litmus blue.

3. **Chlorides**—(*a*) *Qualitative Test.*—Add a drop of nitric acid and a drop or two of silver nitrate solution. The nitric acid is added to prevent precipitation of silver phosphate. A white precipitate soluble in ammonia shows the presence of chlorides. The precipitate *appears* to be incompletely soluble in ammonia, since the ammonia brings down a small precipitate of earthy phosphates.

(*b*) *Quantitative Estimation.*—The *quantitative estimation of the chlorine in urine* without previous evaporation and incineration is best made by one of the modifications of *Volhard's method.* It depends upon the complete precipitation of the chlorine combined with the alkaline metals, and also of sulphocyanic acid, by silver from a solution containing nitric acid in excess; and avoids the error introduced into simpler methods, like Mohr's, by the union of some of the silver with other substances than chlorine. A given quantity of a standard solution of silver nitrate (more than sufficient to combine with all the chlorine) is added to a given volume of urine. The excess of silver is now estimated by means of a standard solution of ammonium sulphocyanide. A solution of the double sulphate of iron and ammonium (known as iron-ammonia-alum) is taken as the indicator, since a ferric salt does not give the usual red colour with a sulphocyanide so long as any silver in the solution is uncombined with sulphocyanic acid.

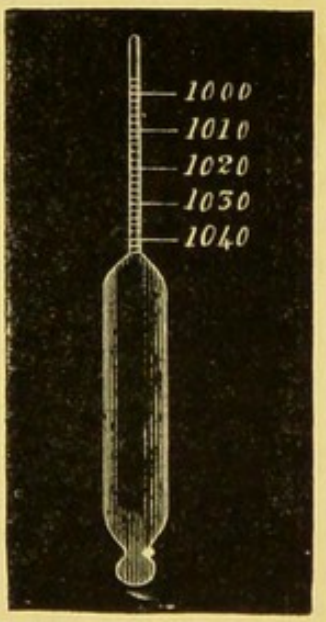


FIG. 130.—URINOMETER.

To carry out the method, put 10 c.c. of urine, which must be free from albumin, in a stoppered flask, with a mark corresponding to 100 c.c., or a graduated cylinder. Add 50 c.c. of water, 4 c.c. of pure nitric acid (specific gravity 1·2), and 15 c.c. of the standard silver solution (of which 1 c.c. corresponds to ·01 gramme NaCl, or ·00607 gramme Cl); shake well, fill with water to the mark, and again shake. After the precipitate has settled, filter it off. Take 50 c.c. of the filtrate, add 5 c.c. of a concentrated solution of iron-ammonia-alum, and run in from a burette the standard solution of ammonium sulphocyanide until a weak but permanent red coloration appears. 2 c.c. of the sulphocyanide solution correspond exactly to 1 c.c. of the silver solution, so as just to allow of the end reaction with the iron solution being seen, and no more.

Suppose x cc. of the sulphocyanide solution are required, then the chlorine in 10 cc. of urine evidently corresponds to $(15 - x)$ 0·01 gramme NaCl.

4. **Phosphates.**—(1) *Qualitative Tests.*—(*a*) Render the urine alkaline with ammonia. A precipitate of earthy phosphates (calcium and magnesium phosphates) falls down. Filter. To the filtrate add magnesia mixture (a mixture of sulphate or chloride of magnesium, ammonium chloride and ammonia); a precipitate shows the presence of alkaline phosphates (sodium, potassium, or ammonium phosphates). The precipitate is ammonio-magnesic or triple phosphate. (*b*) Add to urine half its volume of nitric acid and a little molybdate of ammonium, and heat. A yellow precipitate of ammonium phosphomolybdate shows that phosphates are present. This test is given both by alkaline and earthy phosphates.

(2) *Quantitative Estimation.*—The *quantitative estimation of phosphoric acid in urine* is best done volumetrically, by titration with a standard solution of uranium nitrate, using ferrocyanide of potassium as the indicator. Uranium nitrate gives with phosphates, in a solution containing free acetic acid, a precipitate with a constant proportion of phosphoric acid. As soon as there is more uranium in the solution than is required to combine with all the phosphoric acid, a brown colour is given with potassium ferrocyanide, due to the formation of uranium ferrocyanide. In carrying out the method, 5 c.c. of a mixture of acetic acid and sodium acetate (there are 10 grammes of sodium acetate and 10 grammes of glacial acetic acid in 100 c.c. of the mixture) are added to 50 c.c. of urine, which is then heated in a beaker on the water-bath to about 80° C. The standard uranium solution (which contains 35·5 grammes of uranium nitrate in the litre, and 1 c.c. of which corresponds to 0·005 gramme P_2O_5) is now run in from a burette, until a drop of the urine gives, with a drop of potassium ferrocyanide solution, on a porcelain slab, a brown colour. Uranium acetate may be used instead of uranium nitrate, but the latter keeps best.

5. **Sulphates**—(1) *Qualitative Test.*—Add to urine a drop of hydrochloric acid and then a few drops of barium chloride. A white precipitate comes down, showing that inorganic sulphates are present. The hydrochloric acid prevents precipitation of the phosphates.

(2) *Quantitative Estimation of the Sulphuric Acid united with Inorganic Bases.*—Acidulate 100 c.c. of albumin-free urine with acetic acid, add excess of barium chloride, and heat on the water-bath till the precipitate has settled; filter through an ash-free filter, wash the precipitate with water, with dilute hydrochloric acid, then again with water. Dry, incinerate in a platinum or porcelain dish, and weigh. From the weight of barium sulphate the inorganic sulphuric acid is easily calculated (SO_4 in 1 gramme of barium sulphate = 0·41187 gramme).

(3) *Quantitative Estimation of the Sulphuric Acid united with Aromatic Bodies* (aromatic or organic sulphuric acid).—Add to the filtrate and the washings from (2) a little hydrochloric acid, and heat

in order to break up the aromatic sulphates. The elements of water are thus taken up by these salts; and the sulphuric acid is able to unite with the barium. Filter through an ash-free filter. Add a few drops of barium chloride to the first portion of the filtrate which comes through. If there is no precipitate, enough barium chloride to combine with all the sulphuric acid is present, and the filtration can be proceeded with. But if there is any precipitate, more barium chloride must be added, and the liquid passed again through the filter. Treat the precipitate on the filter as in (2). Its weight after incineration gives the quantity of barium sulphate corresponding to the sulphuric acid of the aromatic compounds.

6. **Indoxyl** can be oxidized into indigo, and so estimated.

A qualitative test is the following: Ten c.c. of horse's urine is mixed with 10 c.c. of strong hydrochloric acid, and a dilute solution of sodium hypochlorite added drop by drop; a bluish colour appears if, as is generally the case, indoxyl is present, indigo ($C_{16}H_{10}N_2O_2$) being formed by the oxidizing action of the hypochlorite on the indoxyl, the compound of which with sulphuric acid has been broken up by the hydrochloric acid. The number of drops of the hypochlorite required to give the maximum change of colour is determined. Then the experiment may be repeated by dropping this quantity of hypochlorite into 10 c.c. of the hydrochloric acid, and adding 10 c.c. of the urine. The urine must be free from albumin. If too much hypochlorite be added, the indigo is itself oxidized. In performing the test in human urine, which contains a smaller quantity of the indigo-forming substance, the urine should first be concentrated on the water-bath. If the faint blue liquid be shaken up with a few drops of chloroform, the latter takes up the colour, which is thus rendered more evident. The **skatoxyl** of urine can also be oxidized to indigo, but it is present in far smaller amount. The average quantity of indigo obtained from a litre of horse's urine is about 150 milligrammes; from a litre of human urine, not a twentieth of that quantity.

7. **Urea**—(1) *Preparation.* — Urea can be obtained from dog's urine by evaporating it to a syrup, extracting with absolute alcohol, evaporating most of the alcohol, and allowing the mass to crystallize. Or human urine may be concentrated to a small bulk, cooled to 0°, and mixed with excess of strong pure nitric acid. A mass of rhombic or six-sided tabular crystals of nitrate of urea separates. From the nitrate, after purification, urea itself is obtained by addition of barium carbonate till carbon dioxide ceases to be given off. What remains is a mixture of urea and barium nitrate, from the dry residue of which urea can be dissolved out by alcohol (Hoppe-Seyler).

(2) *Decomposition of Urea.*—Heated dry in a test-tube, it gives off ammonia. The residue contains biuret, which, when dissolved in water, gives a rose colour with a trace of cupric sulphate and excess of sodium hydrate (or of the hydrates of certain other metals of the alkalies and alkaline earths, p. 20). Some proteids—peptones and albumoses—in the presence of the same reagents, give a similar colour, the so-called biuret reaction.

(3) *Quantitative Estimation—The Hypobromite Method.*—The urea is split up by sodium hypobromite (p. 389), and the carbon dioxide being absorbed by the excess of sodium hydrate used in preparing the hypobromite, the nitrogen is collected over water in an inverted burette. It is easy to calculate the weight of urea corresponding to a given volume of nitrogen measured at a given temperature and pressure. The nitrogen of urea is $\frac{28}{60}$, or $\frac{7}{15}$ of the whole molecular weight. Now, 1 c.c. of N weighs, at 760 millimetres of mercury and 0° C., ·00125 gramme. Therefore, 1 c.c. of N corresponds to $\cdot00125 \times \frac{15}{7} = \cdot00268$ gramme urea. Suppose, now, that 1 c.c. of urine was found to yield 10 c.c. of N measured at 17° C. and 750 millimetres barometric pressure. Since a gas expands $\frac{1}{273}$ part of its volume at 0° for every degree above 0°, we must correct the apparent volume of the nitrogen by multiplying by $\frac{273}{290}$. Since the volume of a gas is inversely proportional to the pressure, we must further multiply by $\frac{750}{760}$. Thus we get $10 \times \frac{273}{290} \times \frac{750}{760} = \frac{204750}{22040} = 9{\cdot}29$ c.c. as the volume of the nitrogen reduced to 0° C. and 760 millimetres of mercury. Multiplying this by ·00268, we get ·0249 gramme urea for 1 c.c. urine, which for the daily yield of 1,200 c.c. would correspond to 29·88 grammes urea.

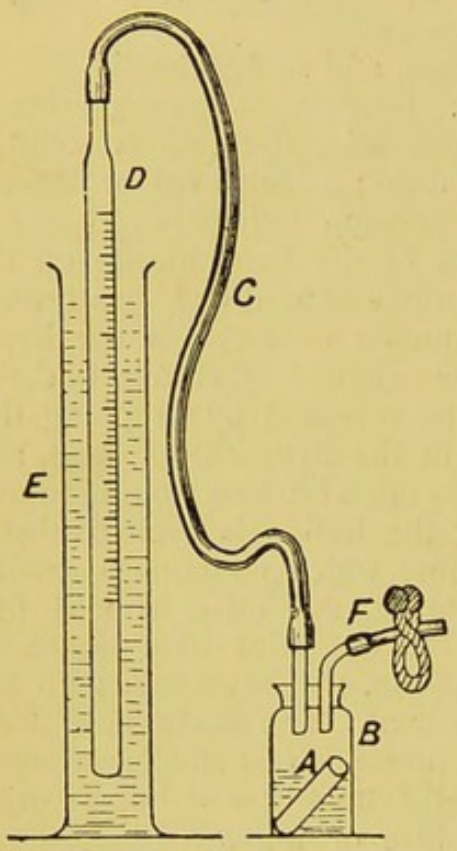


FIG. 131.—HYPOBROMITE METHOD OF ESTIMATING UREA.

A, glass thimble; B, bottle, through the rubber cork of which pass two short glass tubes, one connected by the rubber tube C with a burette D, and the other armed with a short piece of rubber tube F. F is provided with a pinchcock. The burette is supported on a stand, and immersed in water contained in the glass cylinder E.

As a matter of fact, however, it has been found that there is always a deficiency of nitrogen, that is, a given quantity of urea yields less than the estimated amount of gas. A gramme of urea in urine, instead of giving off 373 c.c. of nitrogen, gives only 354 c.c. at 0° C. and 760 millimetres pressure. We must therefore take 1 c.c. of N as corresponding to ·00282 gramme, instead of ·00268 gramme urea. But it is affectation to make this correction if, as is constantly done in hospitals, the temperature is not taken into account.

A convenient apparatus for clinical use is shown in Fig. 131. In B, place 10 c.c. of a solution made by adding bromine to ten times its volume of 40 per cent. sodium hydrate solution. Mix 5 c.c. of urine with 5 c.c. of water. Put 5 c.c. of the mixture into the thimble A, which is then set in the small bottle B. The cork is now carefully fixed in B, and the tube F being open, the level of

the water in the burette is read off. The pinchcock having been closed, the bottle B is now tilted so that the urine in the thimble is gradually mixed with the hypobromite solution, and the nitrogen given off is added to the air in the burette and its connections. The level of the water in the burette is therefore depressed. When gas ceases to be given off, and a short time has been allowed for the whole to cool, the tube is raised till the level of the water is once more the same inside and out. The level is again read off; the difference of the two readings gives the volume of nitrogen at the temperature of the air and the barometric pressure. In order that the temperature of the water may be the same as that of the air, the cylinder should be filled a considerable time before the observations are begun.

8. **Estimation of the Total Nitrogen.**—It is sometimes more important to determine the total nitrogen of the urine than the urea alone; and this is conveniently done by Kjeldahl's method (or some modification of it), which can also be applied to the estimation of the nitrogen in the fæces, or in any of the solids or liquids of the body. It depends on the oxidation of the nitrogenous matter in such a way that the nitrogen is all represented as ammonia. The ammonia is then distilled over, collected and estimated, and from its amount the nitrogen is easily calculated. In urine the method can be carried out by adding to a measured quantity of it (say 5 c.c.) four times its volume of strong sulphuric acid, and boiling in a long-necked flask (capacity 200 c.c.), after the addition of a globule of mercury (about 0·1 c.c.), which hastens oxidation and obviates bumping. A part of the mercuric sulphate formed remains in solution; the rest forms a crystalline deposit. The heating should continue for half an hour, or until the liquid is decolourized. This completes the process of oxidation; and the next step is to liberate the ammonia from the substances with which it is united in the solution, and to distil it over. Dilute the liquid with water, after cooling, up to about 150 c.c., and pour into a larger long-necked flask. Add enough of a solution of sodium hydrate (specific gravity about 1·25) to render the liquid alkaline, avoiding excess, as this favours bumping. The proper quantity can be found by determining beforehand how much of the alkali is needed to neutralize the acid used for oxidation, and this amount should be added. Bumping may further be prevented by the addition of a little granulated zinc. Shake the flask two or three times. Add also about 12 c.c. of a concentrated solution of potassium sulphide (1 part to 1½ parts water), which favours the setting free of the ammonia from the amido-compounds of mercury that have been formed during oxidation. Commercial 'liver of sulphur' will do quite well. Immediately connect the distilling-flask with the worm, as shown in Fig. 132, and distil the ammonia over into 50 c.c. of standard (decinormal) sulphuric acid contained in a flask into which a glass tube connected with the lower end of the worm dips. Heat the distilling flask at first gently, then strongly, and boil for three-quarters of an hour, or until about two-thirds of the liquid has passed over. Then lift the tube out of the standard acid, and continue the

distillation for two or three minutes longer. The ammonia is now all united with the standard acid, a certain amount of which is left over. By determining this amount we arrive at the quantity combined with ammonia, and therefore at the quantity of ammonia. Fill a burette with a decinormal solution of potassium or sodium hydrate.* Add a little methyl orange solution to the standard sulphuric acid, to serve as indicator. Then run in the potassium or sodium hydrate till the pink tinge gives place to a permanent but just recognisable yellow. Let x be the number of c.c. run in. Since 1 c.c. of any decinormal solution is equivalent to 1 c.c. of any other, x represents also the number of c.c. of the standard sulphuric

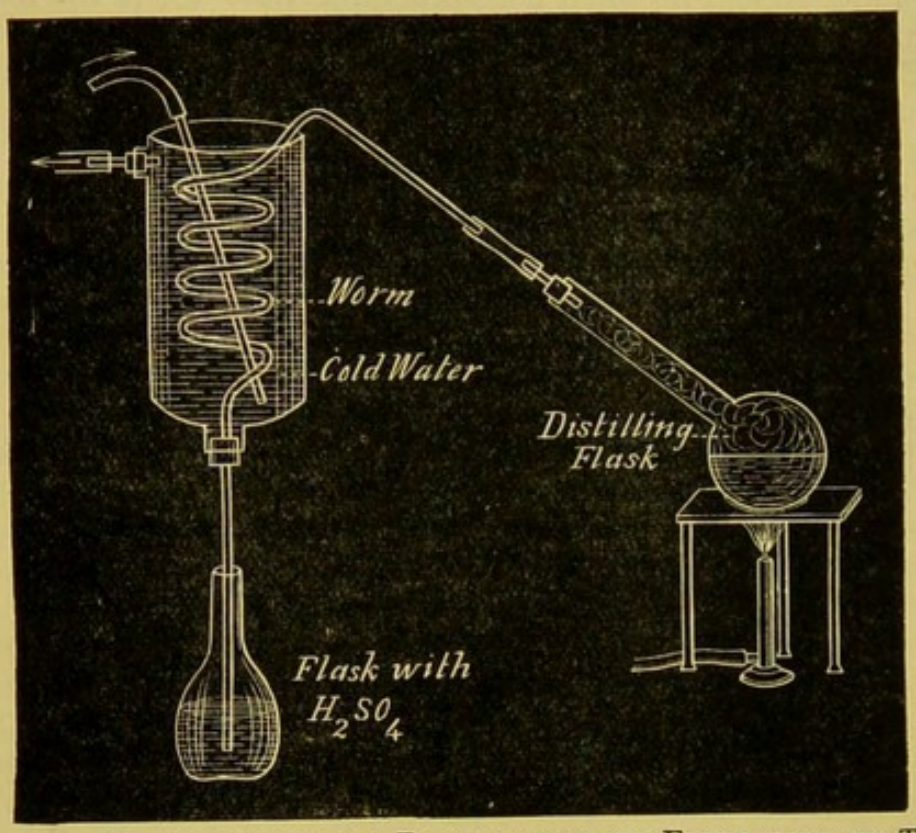


FIG. 132.—ARRANGEMENT FOR DISTILLATION IN ESTIMATION OF TOTAL NITROGEN.

acid left uncombined with ammonia ; and $50 - x$, the quantity combined with ammonia. Then, 1 c.c. of decinormal sodium or potassium hydrate being equivalent to 1 c.c. of decinormal ammonium hydrate, and 1 c.c. of decinormal ammonium hydrate containing ·0014 gramme nitrogen, we get $(50 - x) \times ·0014$ as the quantity of nitrogen in 5 c.c. of urine.

9. **Uric Acid**—(1) *Preparation.*—Uric acid can be prepared in a pure form from serpents' excrement, by dissolving it in dilute sodium hydrate, and filtering. The filtrate contains sodium urate, which is

* A normal solution of a substance contains in a litre a number of grammes of the substance equal to the number which expresses its equivalent weight—a decinormal solution one-tenth of this amount, a centinormal one-hundredth, etc. Thus, a normal solution of potassium hydrate contains 56 grammes of KOH, and a decinormal solution 5·6 grammes in 1000 c.c.

precipitated by a current of carbon dioxide. The uric acid is set free by boiling the precipitate with dilute hydrochloric acid, and is deposited as a colourless crystalline powder on cooling.

(2) *Qualitative Test for Uric Acid—Murexide Test.*—A small quantity of uric acid or one of its salts is heated with a little dilute nitric acid. The colour of the residue left by evaporation becomes yellow, and then red, and on the addition of ammonia changes to deep purple-red. Potassium or sodium hydrate changes the yellow to violet. The purple-red substance is murexide or ammonium purpurate, which is also formed by the action of nitric acid and ammonia on theobromine (dimethylxanthin), the alkaloid of cocoa, and theine or caffeine (trimethylxanthin), the alkaloid of tea and coffee.

(3) *Quantitative Estimation—(a) by Precipitation and Weighing.*—Uric acid is precipitated like grains of cayenne pepper on the sides and bottom of the vessel in which urine, strongly acidulated with pure hydrochloric acid, is allowed to stand for forty-eight hours. By collecting the crystals from a measured quantity of urine (say 200 c.c. with 10 c.c. hydrochloric acid added) on a small weighed filter, washing the precipitate on the filter with as small a quantity of water as possible (not more than 30 c.c.), drying at 110° C., and weighing, an estimate may be made of the amount of uric acid present (Heintz). Notwithstanding that the pigment carried down with the uric acid is added to the weight of the latter, this method gives results somewhat too small, as a portion of the uric acid is left in solution. A better method is the following:

(*b*) *Hopkins's Method of Estimation of Uric Acid.*—Add about 25 grammes of ammonium chloride to 100 c.c. of urine in a beaker. Stir well to dissolve all the salt. Then add 2 c.c. of strong ammonia. Let the mixture stand till the precipitate of ammonium urate which is formed has entirely settled to the bottom and the liquid above it is clear. Then filter through a small filter-paper. Wash the precipitate on the filter twice with saturated solution of ammonium chloride from a wash-bottle. Then wash the precipitate into a porcelain capsule with hot water from a wash-bottle with a fine jet, unfolding the filter-paper over the capsule so as to get it all off. For this purpose not more than 20 to 30 c.c. of water should generally be necessary; but if much more has been used the excess should be got rid of by evaporation on a water bath. Pour about 1 c.c. of strong hydrochloric acid into the capsule, heat to boiling, and then allow the capsule to stand in the cold till the uric acid crystallizes out. The time required for this is 2 to 12 hours, being shorter the lower the temperature. The crystals are filtered off through a small weighed filter, the filtrate being received in a graduated cylinder and measured. The crystals are then washed on the filter with cold distilled water, till the washings come through the filter free from chlorides, as tested by silver nitrate (p. 421). The filter with the crystals is dried in the oven and weighed. To the weight of the uric acid thus obtained 1 milligramme must be added for each 15 c.c. of the filtrate (the mother liquor) collected in the graduated cylinder.

Or, instead of being estimated by weighing, the uric acid crystals may, after having been washed with the cold distilled water as described, till free from chlorides, be washed again with hot water off the filter (which need not in this case be a weighed one) into a capsule. The capsule is filled up with distilled water, 1 c.c. of 10 per cent. sodium carbonate solution added, and the contents heated to boiling to dissolve the uric acid. The solution is allowed to cool, and then emptied into an Erlenmeyer's flask with a mark roughly corresponding to 100 c.c. The solution is made up to 100 c.c. with distilled water. A burette is filled with standard potassium permanganate solution (a twentieth-normal solution made by dissolving 1·581 grammes of the permanganate in a litre of water). 20 c.c. of strong sulphuric acid are poured into the flask, which is then shaken. The permanganate is now run in with constant shaking of the flask. At first the pink colour produced where the drops of permanganate fall into the liquid disappears at once without spreading through the liquid. When a certain amount has been run in, however, the whole liquid becomes pink, although the colour soon disappears. This indicates that enough of the permanganate has been added. Each c.c. of the permanganate used is equivalent to 0·00375 gramme uric acid. One milligramme must be added, as before, to the result for each 15 c.c. of the mother liquor from which the uric acid crystals were deposited.

10. **Kreatinin.**—*Qualitatively*, kreatinin may be recognised in very small amounts by *Weyl's test.* A few drops of a dilute solution of sodium nitro-prusside are added to urine, and then dilute sodium hydrate drop by drop. A ruby-red colour appears, which soon turns yellow. If the urine is now strongly acidified with acetic acid and heated, it becomes first greenish and then blue. Enough acid must be added to more than neutralize the alkali.

Kreatinin forms crystalline compounds with various acids and salts. One of the best known of these is kreatinin-zinc-chloride, formed on the addition of zinc chloride to an alcoholic or watery solution of kreatinin, often in the shape of beautiful thick-set rosettes of needles. Neubauer has made this reaction the basis of a method for the *quantitative* estimation of kreatinin (Fig 120, p. 389).

11. **Hippuric Acid.**—From horse's or cow's urine hippuric acid is prepared by evaporating to a small bulk, and adding strong hydrochloric acid. The crystalline precipitate is washed with cold water, then dissolved in hot water, and filtered hot. Hippuric acid separates out from the filtrate in the cold in the form of long four-sided prisms with pyramidal ends. Heated dry in a test-tube, the crystals melt, and benzoic acid and oily drops of benzonitrile, a substance with a smell like that of oil of bitter almonds, are formed.

ABNORMAL SUBSTANCES IN URINE.

12. **Proteids.**—(1) *Qualitative Tests.*—(*a*) Boil and add a few drops of nitric acid. A precipitate on boiling, increased or not affected by the acid, shows the presence of coagulable proteids

(serum-albumin or globulin). A precipitate of earthy phosphates sometimes forms on boiling. It is distinguished from a precipitate of proteids by dissolving on the addition of acid.

(*b*) *Heller's Test.*—Put some nitric acid in a test-tube. Pour carefully on to the surface of the acid a little urine. A white ring at the junction of the liquids indicates the presence of albumin, globulin (or albumose?). When this test is performed with undiluted urine, uric acid may be precipitated and cause a brown colour at the junction. A similar ring may be found in the absence of proteids when the test is made on the urine of a patient who has been taking copaiba.

(*c*) Filter some urine, and add to the filtrate its own volume of acetic acid. A precipitate may indicate mucin or nucleo-albumin. If any is formed, filter it off, and add to the filtrate a few drops of potassium ferrocyanide. A white precipitate shows the presence of proteids.

(*d*) *Test for Globulin in Urine.*—Serum-globulin probably never occurs in urine apart from serum-albumin. It may be detected by Kauder's test. Make the urine alkaline with ammonia, let it stand for an hour and filter. Half saturate the filtrate with ammonium sulphate, *i.e.*, add to it an equal volume of a saturated solution of ammonium sulphate. Serum-globulin is precipitated, serum-albumin is not.

(*e*) *Test for Albumose in Urine* (*Albumosuria*).—Coagulable proteids are removed by boiling the urine (acidulated if necessary), and filtering off the precipitate if any. The filtrate is neutralized. If a further precipitate falls down it is filtered off, the clear filtrate is heated in a beaker placed in a boiling water-bath, and there saturated with crystals of ammonium sulphate. A precipitate indicates that albumoses (proteoses) are present. A slight precipitate might possibly be due to the formation of ammonium urate. A further test may be performed on the original urine if it is free from coagulable proteids, or on the filtrate after their removal. Add a few drops of pure nitric acid. If albumoses are present, a precipitate is thrown down which disappears on heating, and reappears on cooling the test-tube at the cold-water tap.

(*f*) *Test for Peptone in Urine* (*Peptonuria*).—Place some of the urine in a beaker on a boiling water-bath for thirty minutes, and saturate with ammonium sulphate crystals. Then boil over a small flame or in an air-bath for half an hour. All the proteids, including peptones, are precipitated. But the peptones can still be redissolved by water, the others not. Filter hot. Wash the precipitate on the filter with a boiling saturated solution of ammonium sulphate. Then extract the residue with cold water, filter, and test the filtrate by the biuret test (addition of very dilute cupric sulphate and excess of sodium hydrate). A rose colour indicates the presence of peptone (p. 379, (δ)), but if the reaction is only a faint one, it may be due to urobilin (Stokvis).

(2) *Quantitative Estimation of Coagulable Proteids* (*Serum-Albumin and Globulin*)—(*a*) *Gravimetric Method.*—Heat 50 to 100 c.c. of the urine to boiling, adding a dilute solution (2 per cent.) of

acetic acid by drops as long as the precipitate seems to be increased. Filter through a weighed filter. Wash the precipitate on the filter with hot water, then with hot alcohol, and finally with ether. Dry in an air-bath at 110° C., and weigh between watch-glasses of known weight.

(*b*) *Method of Roberts and Stolnikow (modified by Brandberg).*—This method is founded on the fact that the time taken for the white ring to appear in Heller's test depends on the proportion of coagulable proteid present. It has been found that when 1 part of albumin is contained in 30,000 parts of an albuminous solution (0·0033 per cent.), the ring appears in two and a half to three minutes. The amount of dilution of the urine which is necessary to delay the formation of the ring for this length of time is what has to be determined. To do this, proceed as follows: Dilute a portion of the urine (say 5 c.c.) ten times; that is, add to it nine times its volume of distilled water (45 c.c.) from a burette. Place some pure nitric acid in a test-tube with a pipette, taking care not to wet the sides of the test-tube with the acid. Now run on to the surface of the nitric acid some of the diluted urine, and note the interval that elapses before formation of the white ring. If it is more than three minutes, the diluted urine contains less than 1 part in 30,000, and the undiluted urine less than 1 part in 3,000 (*i.e.*, less than ·033 per cent.) of coagulable proteid, and the experiment must be repeated with urine diluted to a smaller extent. If the ring appears after a shorter interval than three minutes, the diluted urine contains more than 1 part in 30,000 (the original urine more than ·033 per cent.), and must be further diluted. Fill a burette with the diluted urine. Run 1 c.c. of it into a test-tube and add 9 c.c. of distilled water. Repeat the test with this second dilution. If the ring appears at a longer interval than three minutes, the twice-diluted urine contains less than 1 part of albumin in 30,000, and the original undiluted urine less than 1 part in 300, *i.e.*, less than 0·33 per cent. So far, then, we have found, let us suppose, that the proportion of albumin in the original urine lies between 0·033 and 0·33 per cent. Now run 1 c.c. of the urine of the first dilution (the urine diluted ten times) into a test-tube, and add 4 c.c. of distilled water, *i.e.*, dilute again five times. If this gives the white ring in Heller's test in three minutes, the original urine will contain 1 part of albumin in $\frac{30,000}{10 \times 5}$, *i.e.*, in 600 parts, or 0·16 per cent. If the interval is longer or shorter than three minutes, the urine of the first dilution (1 to 10) must be diluted less or more than five times until the interval amounts to about three minutes. The total dilution corresponding to a percentage of 0·0033 of albumin is thus known, and the percentage in the undiluted urine can be easily calculated.

13. **Sugar**—(1) *Qualitative Tests*—(*a*) *Trommer's Test.*—See p. 23. It is to be remarked that some substances present in small amount in normal urine reduce cupric sulphate, *e.g.*, uric acid (present as urates) and kreatinin, but although a normal urine may thus de-

colourize the copper solution, it rarely causes so much reduction that a yellow or red *precipitate* is formed, as is the case in diabetic urine. Glycuronic acid, which is said to occur even in normal urine in very slight traces, and which appears in considerable amount after the administration of chloroform, chloral, nitro-toluol and other substances, also reduces cupric salts, as does alcapton or homogentisinic acid, a substance found in rare cases in disease. If less than 0·5 per cent. of sugar is present in the urine, no precipitate of cuprous oxide will be formed till the urine is cooled. The test may also be performed with Fehling's solution.

(*b*) *Phenyl-hydrazine Test.*—This test depends upon the fact that phenyl-hydrazine forms with sugars such as glucose, maltose, isomaltose, etc., but not with cane-sugar, characteristic crystalline substances (phenyl-glucosazone, phenyl-maltosazone, etc.) which can be recognised under the microscope, and are distinguished from each other by melting at different temperatures. Phenyl-glucosazone ($C_{18}H_{22}N_4O_4$) melts at 205° C. To perform the test for glucose in the urine, proceed thus: Put 5 c.c. of urine in a test-tube, add 1 decigramme of hydrochlorate of phenyl-hydrazine and 2 decigrammes of sodium acetate. Heat the test-tube in a boiling water-bath for half an hour. Then cool at the tap and examine the deposit under the microscope for the yellow osazone crystals (Plate IV., 3). Sometimes the osazone precipitate is amorphous. Lest this should be the case the precipitate, if no crystals can be seen, must be dissolved in hot alcohol. The solution is then diluted with water and the alcohol boiled off, when the osazone, if any be present, will crystallize out. Very minute traces of sugar can be detected in this way (as little as 0·1 per cent. in urine). Often in normal urine yellow crystals are deposited during the first fifteen minutes' heating. They must not be mistaken for glucosazone. They probably consist of a compound of glycuronic acid and phenyl-hydrazine. They are changed as the heating goes on into an amorphous brownish-yellow precipitate (Abel).

(*c*) *The Yeast Test* is an important confirmatory test for distinguishing the fermentable sugars from other reducing substances, but it is not very delicate, and will with difficulty detect sugar when less than 0·5 per cent. is present. It can be performed thus: A little yeast (the tablets of compressed yeast do very well) is added to a test-tube half filled with urine. The test-tube is then filled up with mercury, closed with the thumb, and inverted over a dish containing mercury. The dish may be placed on the top of a water-bath whose temperature is about 40° C. After twenty-four hours the sugar will have been broken up into alcohol and carbon dioxide. The latter will have collected above the mercury in the test-tube, and the former will be present in the urine. The tests for sugar will either be negative or will be less distinct than before. A control test-tube containing water and yeast should also be set up, as impurities in the yeast sometimes yield a small amount of carbon dioxide.

(2) *Quantitative Estimation of Sugar in Urine.*—(*a*) *Volumetrically*, the sugar can be estimated by titration with Fehling's solution. As this does not keep well, two solutions containing its ingredients

should be kept separately and mixed when required. *Solution I.:* Dissolve 34·64 grammes pure cupric sulphate in distilled water, and make up the volume to 500 c.c. *Solution II.:* Dissolve 173 grammes Rochelle salt in 400 c.c. of water, add to this 51·6 grammes sodium hydrate, and make up the volume with water to 500 c.c. Keep in well-stoppered bottles in the dark. For use, mix together equal volumes of the two solutions. Ten c.c. of this mixture is reduced by 0·05 gramme dextrose. To estimate the sugar in urine, put 10 c.c. of the mixture into a porcelain capsule or glass flask, and dilute it four or five times with distilled water. Dilute some of the urine, say ten or twenty times, according to the quantity of sugar indicated by a rough determination. Run the diluted urine from a burette into the Fehling's solution, bringing it to the boil each time urine is added, until, on allowing the precipitate to settle, the blue colour is seen to have entirely disappeared from the supernatant liquid. The observation of the colour must be made while the liquid is still hot.

Suppose that 10 c.c. of Fehling's solution is decolourized by 20 c.c. of the ten-times diluted urine. Then 2 c.c. of the original urine contains 0·05 gramme dextrose. If the urine of the twenty-four hours (from which this sample is assumed to have been taken) amounts to 4,000 c.c., the patient will have passed $0{\cdot}05 \times 2{,}000 = 100$ grammes sugar, in twenty-four hours.

(*b*) The *polarimeter* affords a rapid and, with practice, a delicate means of estimating the quantity of sugar in pure and colourless solutions, but diabetic urine must in general be first decolourized by adding lead acetate and filtering off the precipitate. What is measured is the amount by which the plane of polarization of a ray of polarized light of given wave-length (say sodium light) is rotated when it passes through a layer of the urine or other optically active solution of known thickness. Let a be the observed angle of rotation, l the length in decimetres of the tube containing the solution, w the number of grammes of the optically active substance per c.c. of solution, and $(a)_D$ the specific rotation of the substance for light of the wave-length of the part of the spectrum corresponding to the D line (*i.e.*, the amount of rotation expressed in degrees which is produced by a layer of the substance 1 decimetre thick, when the solution contains 1 gramme of it per c.c.). Then $(a)_D = \pm\frac{a}{wl}$. In this equation a and l are known from direct measurement; $(a)_D$ has been determined once for all for most of the important active substances, and therefore w is easily calculated. For dextrose $(a)_D$ may be taken as 52·6°. It varies somewhat with the concentration, but for most investigations on the urine these variations may be neglected.

It is not possible to describe here the numerous forms of polarimeter that are in use. Among the best are those constructed on what is called the 'half-shadow' system. A half-shadow polarimeter consists, like other polarimeters, of a fixed Nicol's prism (the polarizer), and a nicol capable of rotation (the analyzer). In addition,

there is an arrangement which rotates by a definite angle the plane of polarization in one half of the field, but not in the other, *e.g.*, a small nicol occupying only half of the field. In the zero position of the analyzer, both halves of the field are equally dark. The solution to be investigated is placed in a tube of known length, the ends of which are closed by glass discs secured by brass screw caps. The glass discs must be slid on, so as to exclude all air. The tube having been introduced between the polarizer and analyzer, the sharp vertical line which indicates the division between the two half-fields is focussed with the eye-piece, and then the analyzer is rotated till the two halves are again equally shadowed. The angle of rotation, *a*, is read off on the graduated arc, which is provided with a vernier.

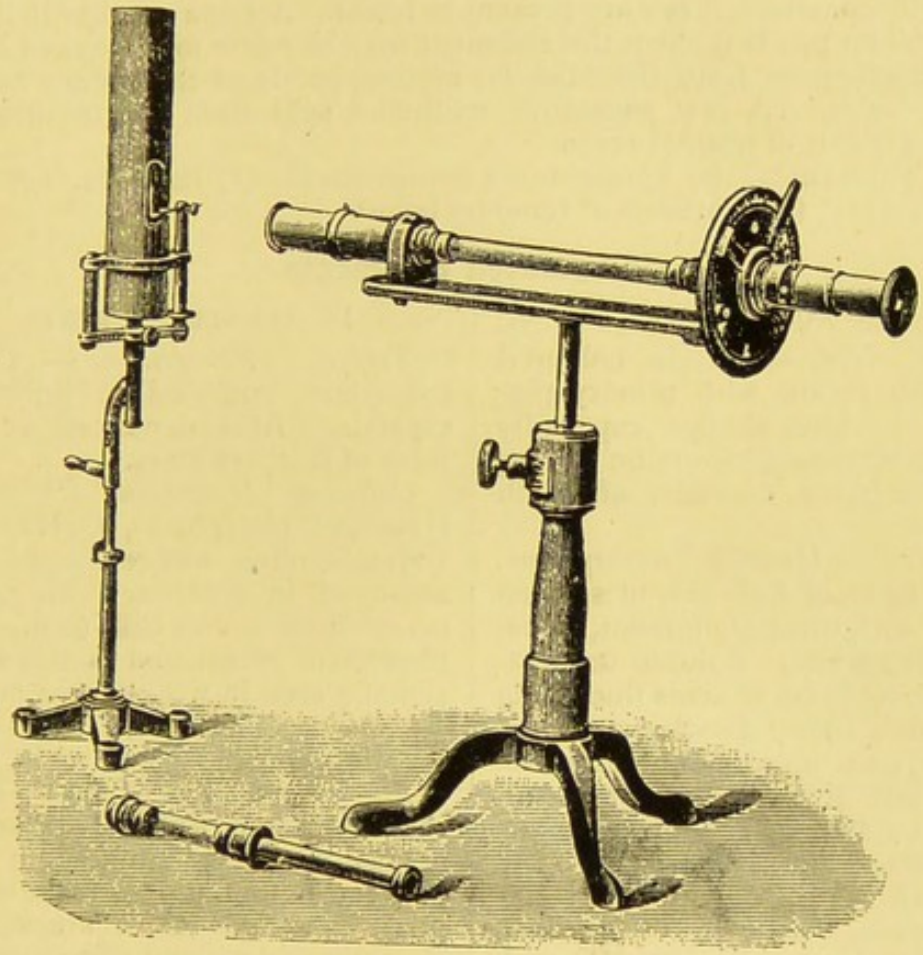


FIG. 133.—MITSCHERLICH'S POLARIMETER.
(Half-Shadow Instrument.) (Simple Form.)

Acetone.—Put 250 to 500 c.c. of the urine suspected to contain acetone into a litre flask. Add a few c.c. of phosphoric acid ; connect the flask with a worm (see Fig. 132) and distil over the urine into a small flask. For qualitative tests it is best to collect only the first 20 to 30 c.c., as most of the acetone is contained in this. Test the distillate for acetone by

Lieben's Test.—To a few cc. of the distillate in a test-tube add a few drops of solution of iodine in potassium iodide and then sodium or potassium hydrate. A precipitate of yellow iodoform crystals is thrown down if acetone be present.

Systematic Examination of Urine.—In examining urine, it is convenient to adopt a regular plan, so as to avoid the risk of overlooking

anything of importance. The following simple scheme may serve as an example ; but no routine should be slavishly followed, the object being to get at the important facts with the minimum of labour :

1. Anything peculiar in colour or smell? If colour suggests blood, examine with spectroscope, hæmin test, guaiacum test (pp. 62, 64, 66) ; if it suggests bile, test for bile-pigments by Gmelin's test (p. 381).

2. Reaction.

3 Sediment or not? Sediment may be procured by letting the urine stand in a conical glass, or in a few minutes by the centrifuge. If the appearance of the sediment suggests anything more than a little mucus, examine with microscope. The sediment may contain organized or unorganized deposits.

Organized Sediments.—(*a*) Red blood-corpuscles (considerably altered if they have come from the upper part of the urinary tract).

(*b*) Leucocytes. A few are present in health. A large number indicate pus. When pus is present the sediment may be white to the naked eye.

(*c*) Epithelium from the bladder, ureters, pelvis of the kidney or the renal tubules. A few squamous epithelial cells from the urethra are always present in normal urine.

(*d*) Tube casts. (*e*) Spermatozoa (occasional). (*f*) Bacteria. (*g*) Parasites (rare). (*h*) Portions of tumours (rare).

Unorganized Sediments.

IN ACID URINE.

Uric Acid.—Crystals coloured brownish yellow with urinary pigment. Various shapes, especially oval 'whetstones,' rhombic tables, and elongated crystals, often in bundles.

Urates. — Usually amorphous, in the form of fine granules, often tinged with urinary pigment, sometimes brick-red. Soluble on heating. On addition of acids (including acetic acid) they dissolve and uric acid crystals appear in their place. Acid urate of sodium and of ammonium occasionally found in the crystalline form (rosettes of needles).

Calcium Oxalate.—Octahedral, 'envelope' crystals, not coloured. Insoluble in acetic acid.

Cystin. — Hexagonal plates. Rare.

Leucin and Tyrosin. — (Figs. 122, 123.) Rare. Also found in alkaline urine, but rarely.

Triple Phosphate. — Sometimes found in weakly acid urine.

IN ALKALINE URINE.

Triple Phosphate. — Clear, colourless, coffin-lid or knife-rest crystals. Also deposited in the form of feathery stars.

Calcium Hydrogen Phosphate ('stellar' phosphate), $CaHPO_4$.—Crystals often wedge-shaped and arranged in rosettes. May also occur in a dumb-bell form. (A phosphate of calcium is also occasionally seen in weakly acid urine.)

Calcium Phosphate, $Ca_3(PO_4)_2$. —Amorphous.

Magnesium Phosphate. — Long rhombic tablets, which are dissolved at the edges by ammonium carbonate solution, unlike triple phosphate. All the above are soluble in acetic acid without effervescence.

Calcium Carbonate. — Small spherical or dumb-bell-shaped bodies soluble in acetic acid with effervescence.

Ammonium Urate.—Dark balls, often covered with spines. Soluble in acetic or hydrochloric acid, with formation of uric acid crystals.

4. Specific gravity.

5. Quantity of urine in twenty-four hours. If quantity abnormally large and specific gravity high, test for sugar.

6. Inorganic constituents not generally of clinical importance, but in special diseases they should be examined—*e.g.*, chlorides in pneumonia.

7. Normal organic constituents. Sometimes quantitative estimation of urea or total nitrogen in fever, and in diabetes and Bright's disease.

8. Chemical examination for abnormal organic constituents, especially albumin and sugar.

Albumin.—(1) Heat some of the urine in a test-tube to boiling. A precipitate insoluble on addition of a few drops of acetic acid consists of coagulable proteid. A precipitate soluble in acetic acid consists of earthy phosphates.

(2) Heller's test. Put some strong nitric acid in a test-tube and run on to it some urine. A white ring indicates proteid.

A quantitative estimation may be made by the method of Roberts and Stolnikow (p. 430).

Sugar.—(1) Trommer's test. (Fehling's solution may be used.) If the result is indecisive:

(2) Phenyl-hydrazine test (p. 431).

(3) In case of doubt confirm by yeast test.

A quantitative estimation may be made with Fehling's solution or the polarimeter.

CHAPTER VII.

METABOLISM, NUTRITION AND DIETETICS.

We return now to the products of digestion as they are absorbed from the alimentary canal, and, still assuming a typical diet containing proteids, carbo-hydrates and fats, we have to ask, What is the fate of each of these classes of proximate principles in the body? what does each contribute to the ensemble of vital activity? It will be best, first of all, to give to these questions what roughly qualitative answer is possible, then to look at metabolism in its quantitative relations, and lastly to focus our information upon some of the practical problems of dietetics.

1. **Metabolism of Proteids.**—The two chief proteids of the blood-plasma, serum-globulin and serum-albumin, must, as has been already pointed out, be recruited from proteids absorbed from the intestine and for the most part altered in their passage through the epithelium which lines it. What at bottom the reason and the mechanism of this alteration are, we do not know; but we do know that it is imperative that peptone, and particularly albumose, should not appear in quantity in the blood, for when injected they cause profound changes in that liquid, one expression of which is the loss of its power of coagulation, and are rapidly excreted by the kidneys, or separated out into the lymph. It is not definitely known whether the peptones formed in digestion yield, under the influence of the epithelial cells, both the chief proteids of the blood in the proportions in which they exist in the plasma, or only one of them, which is afterwards

and elsewhere partially changed into the other. But there is some evidence that serum-albumin is more directly related to the proteids of the food than serum-globulin. And it is said that during starvation the albumin is relatively diminished, and the globulin relatively increased. However this may be, it cannot be doubted that the conversion of peptones, directly or indirectly, into the proteids of the blood-plasma forms the first recognisable step in the transformation of the greater part of the digested proteids.

Living and Dead Proteids.—Now and again a living proteid molecule in the whirl of flying atoms which we call a muscle-fibre, or a gland-cell, or a nerve-cell, falls to pieces. Now and again a molecule of proteid, hitherto dead, coming within the grasp of the molecular forces of the living substance, is caught up by it, takes on its peculiar motions, acquires its special powers, and is, as we phrase it, made alive. But it is not any difference in the kind of proteid which determines whether a given molecule shall become a part of one tissue rather than of another. For it is from the serum-albumin and serum-globulin of the blood that all the proteid material required to repair the waste of the body must ultimately be derived; and a particle of serum-albumin may chance to take its place in a liver-cell and help to form bile, while an exactly similar particle may become a constituent of an endothelial scale of a capillary and assist in forming lymph, or of a muscular fibre of the heart and help to drive on the blood, or of a spermatozoon and aid in transferring the peculiarities of the father to the offspring. Indeed, although there are differences of detail, the broad lines of nutrition are the same for all tissues; and just as a tomb and a lighthouse, a palace and a church, may be, and have been built with the same kind of material, or even in succession with the very same stones, so every organ builds up its own characteristic structure from the common quarry of the blood.

In the case of the more highly developed tissues at least, no mere change of food will radically alter structure. A cell may be fed with different kinds of food, it may be over-fed, it may be ill-fed, it may be starved; but its essential peculiarities remain as long as it continues to live. But in proportion as the advance of physiology has emphasized the dominant position of organization, it has taken away the hope of our ever being able to understand in what it is that the difference between the living and the dead cell, between living and dead proteid, or protoplasm, really consists.

The speculation of Pflüger, that the nitrogen of living proteid exists in the form of cyanogen radicals, whilst in dead proteid it is in the form of amides, and that the cause of the characteristic instability of the living substance—its prodigious power of dissociation and reconstruction—is the great intramolecular movement of the atoms of the cyanogen radicals, is very interesting and ingenious, but it remains, and is likely to remain, a speculation. And the same

is true of the suggestion of Loew and Bokorny, that the endowments of living protoplasm depend on the presence of the unstable aldehyde group H – C = O. Nor do the known differences of chemical composition in dead organs give any insight into the peculiarities of organization and function which mark off one living tissue from another. For so far as they do not depend upon differences in the dead plasma which interpenetrates the living substance, they only show that the latter does not split up quite in the same way at death in all the tissues, while the general similarity in the elementary composition of excitable structures leaves us free to imagine as great or as small a similarity as we please in the grouping of the atoms in the living combinations. Be this as it may, the living proteid molecule, whatever function it may have been fulfilling in the organized elements of the body, has certainly a much greater tendency to fall to pieces than the dead proteid molecule. And it falls to pieces in a fairly definite way, the ultimate products, under the influence of oxygen,* being carbon dioxide, water, and comparatively simple nitrogen-containing substances, which after further changes appear in the urine as urea, uric acid, and ammonia. We have no definite information as to the production of water from the hydrogen of the tissues, except what can be theoretically deduced from the statistics of nutrition (p. 472). A few words will be said a little farther on about the production of carbon dioxide from proteids; we have now to consider the seat and manner of formation of the nitrogenous metabolites. And since in man and the other mammals urea contains by far the greater part of the excreted nitrogen, it will be well to take it first.

Formation of Urea.—The starting-point of all inquiries into the formation of urea is the fact that it occurs in the blood in small amount (4 to 6 parts per 10,000 in man; 3 to 12 parts per 10,000 in the dog), the largest quantity being found when the food contains most proteid, and at the height of digestion. Evidently, then, *some*, at least, of the urea excreted in the urine may be simply separated by the kidney from the blood; and analysis shows that this is actually the case, for the blood of the renal vein is poorer in urea than that of the renal artery, containing only one-third to one-half as much. If we knew the exact quantity of blood passing through the kidneys of an animal in twenty-four hours, and

* It is a remarkable fact that this combustion of proteids, as well as of the other constituents of the tissues and the food, takes place at a temperature so low as that of the body. Some have supposed that this is due to the action of ozone derived from a portion of the oxygen taken in; others that it is due to the presence in the organs of oxidizing ferments. As a matter of fact, extracts of various tissues contain substances, with the properties of globulins or nucleo-proteids, which act as 'oxygen-carriers' and cause rapid oxidation of such bodies as the guaiaconic acid of guaiacum, salicylic aldehyde, glucose, etc., on which atmospheric oxygen has either no action or a feeble and tardy one. The activity of these oxygen-carriers is destroyed by boiling.

the average difference in the percentage of urea in the blood coming to and leaving them, we should at once be able to decide whether the whole of the urea in the urine reaches the kidneys ready made, or whether a portion of it is formed by the renal tissue. Although data of this kind are as yet inexact and incomplete, it is not difficult to see that all, or most of the urea, may be simply separated by the kidney.

If we take the weight of the kidneys of a dog of 35 kilos at 160 grammes ($\frac{1}{210}$th of the body-weight is the mean result of a great number of observations in man), and the average quantity of blood in them at rather less than one-fourth of their weight, or 35 grammes, and consider that this quantity of blood passes through them in the average time required to complete the circulation from renal artery to renal vein, or, say, ten seconds, we get about 300 kilos of blood as the flow through the kidneys in twenty-four hours. At ·3 per 1,000, the urea in 300 kilos of blood would amount to 90 grammes. Now, Voit found that a dog of 35 kilos body-weight, on the minimum proteid diet (450 to 500 grammes lean meat per day) which sufficed to maintain its weight, excreted 35 to 40 grammes urea in the twenty-four hours. If, then, the renal epithelium separated somewhat less than half of the 90 grammes urea offered to it in the circulating blood, the whole excretion in the urine could be accounted for, and the blood of the renal vein would still contain more than half as much urea as that of the renal artery. So that the whole of the urea in the urine *may* be simply separated by the kidney from the ready-made urea of the blood.

Another line of evidence leads us to the same conclusion: that the kidney is, at all events, not an important seat of urea-formation. When both renal arteries are tied, or both kidneys extirpated, in a dog, urea accumulates in the blood and tissues; and, upon the whole, as much urea seems to be formed during the first twenty-four hours of the short period of life which remains to the animal as would under normal circumstances have been excreted in the urine.

Where, then, is urea chiefly formed? We should naturally look first to the muscles, which contain three-fourths of the proteids of the body; but we should look there in vain for any great store of urea—only a trace is normally present. *The liver* contains a relatively large amount, and there is very strong evidence that it is the manufactory in which the greater part of the nitrogenous relics of broken-down proteids reach the final stage of urea. This evidence may be summed up as follows:

(1) An excised 'surviving' liver forms urea from ammonium

carbonate mixed with the blood passed through its vessels, while no urea is formed when blood containing ammonium carbonate is sent through the kidney or through muscles. Other salts of ammonium, such as the lactate and the carbamate, undergo a like transformation in the liver. It is difficult, in the light of this experiment, to resist the conclusion that the increase in the excretion of urea in man, when salts of ammonia are taken by the mouth, is due to a similar action of the hepatic cells.

(2) If blood from a dog killed during digestion is perfused through an excised liver, some urea is formed, which cannot be simply washed out of the liver-cells, because when the blood of a fasting animal is treated in the same way there is no apparent formation of urea (v. Schroeder). This suggests that during digestion certain substances which the liver is capable of changing into urea enter the blood in such amount that a surplus remains for a time unaltered. These substances may come directly from the intestine; or they may be products of general metabolism, which is increased while digestion is going on; or they may arise both in the intestine and in the tissues. Leucin—which, as we have seen, is constantly, or, at least, very frequently, present in the intestine during digestion—can certainly be changed into urea in the body. So can other amido-acids of the fatty series, like glycocoll or glycin, and asparaginic acid, and it has been shown by perfusion experiments that this change takes place in the liver. Further, the blood of the portal vein during digestion contains several times as much ammonia as the arterial blood, and the excess disappears in the liver.

(3) Uric acid—which in birds is the chief end-product of proteid metabolism, as urea is in mammals—is formed in the goose largely, and almost exclusively, in the liver. This has been most clearly shown by the experiments of Minkowski, who took advantage of the communication between the portal and renal-portal veins (p. 328) to extirpate the liver in geese. When the portal is ligatured the blood from the alimentary canal can still pass by the roundabout road of the kidney to the inferior cava, and the animals survive

for six to twenty hours. While in the normal goose 50 to 60 per cent. of the total nitrogen is eliminated as uric acid in the urine, and only 9 to 18 per cent. as ammonia, in the operated goose uric acid represents only 3 to 6 per cent. of the total nitrogen, and ammonia 50 to 60 per cent. A quantity of lactic acid equivalent to the ammonia appears in the urine of the operated animal, none at all in the urine of the normal bird. The small amount of urea in the normal urine of the goose is not affected by extirpation of the liver. And while urea, when injected into the blood, is in the normal goose excreted as uric acid, it is in the animal that has lost its liver eliminated in the urine unchanged.

(4) After removal of the liver in frogs, or in dogs which have survived the previous connection of the portal vein with the inferior vena cava by an Eck's fistula (p. 328), the quantity of urea excreted is markedly diminished, and the ammonium salts in the urine are increased. When the Eck's fistula is established and the portal vein tied, without any further interference with the hepatic circulation, the amount of urea in the urine is not lessened to nearly the same extent, evidently because the substances from which urea is formed still, for the most part, gain access to the liver through the hepatic artery and by means of the back-flow which is known to take place through the hepatic vein. If the animals are kept on a diet poor in proteids, no symptoms may develop for a considerable time. But if much proteid is given, characteristic symptoms, including convulsions, always appear. These seem to be produced by the saturation of the organism with ammonia compounds, which are formed from the proteids as in the normal animal, but which the liver, with its circulation crippled, is unable to cope with and to completely change into urea. Although the portal vein carries to the liver a much greater supply of blood than the hepatic artery, ligation of the latter causes a greater diminution in the ratio of the amount of urea to the total nitrogen in the urine than ligation of the former. This seems to indicate that oxidation plays an important part in the formation of urea in the liver (Doyon and Dufourt).

(5) In acute yellow atrophy, and in extensive fatty degeneration of the liver, urea may almost disappear from the urine, and leucin and tyrosin may appear in it along with a much larger amount of ammonia than normal. The leucin and tyrosin are formed in the intestine, and, passing unchanged through the degenerated liver, are excreted by the kidney.

If it be granted, as in the face of the evidence it must, that the liver plays an important part in the formation of urea, we have still to ask what the materials are upon which it works, and in what organs they are formed before being brought to the liver. To the latter question it may be at once replied that proteid metabolism, although its final stages may be worked out in the hepatic cells, must go on in all the organized elements of every tissue. The living substance everywhere contains proteid; proteid is everywhere and at all times breaking down. In the muscles especially nitrogenous substances on the road to urea must be constantly produced. Can we lay our finger on any such intermediate substances? Can we with certainty state that any of the separate links of the chain of proteid metabolism, except the first and the last, have actually been discovered, identified, and labelled? The answer is that a whole series of bodies containing nitrogen, simpler than proteids and with a greater proportion of oxygen, more complex and less oxidized than urea, has been found in muscle and other tissues; but we cannot say definitely that any or all of them, although they are undoubtedly stages in the downward course of worn-out proteids, have arisen the one from the other, or must necessarily pass into the form of urea before being finally excreted.

Such substances are:

Guanin, $C_5H_5N_5O$	In the pancreas, liver, blood, and muscles.
Sarkin, or hypoxanthin, $C_5H_4N_4O$ ...	In spleen, liver, muscles, thymus, bone-marrow, and urine.
Xanthin, $C_5H_4N_4O_2$	In spleen, liver, muscles, brain, pancreas, thymus, and in the urine.
Uric acid, $C_5H_4N_4O_3$	In liver, spleen, lungs, pancreas, brain, and in urine.
Kreatin, $C_4H_9N_3O_2$	In muscles, blood, brain.

The increase in the proportion of oxygen from guanin to uric acid is very striking, and particularly the regular series formed by hypoxanthin, xanthin and uric acid. But while there is good evidence that the first three bodies in the list can be converted into uric acid, there is no reason to believe that they are stages on the way to urea. Kreatin exists in the body in greater amount than any of these,

muscle containing from 0·2 to 0·4 per cent. of it; and the total quantity of nitrogen present at any given time as kreatin is not only greater than that of the nitrogen present in urea, but greater than the whole excretion of nitrogen in twenty-four hours. To kreatin, then, we should naturally look first, among all these nitrogenous metabolites, in our search for a forerunner of urea. But there is a difficulty in accepting it as such, for although in the laboratory kreatin can be changed into kreatinin, and kreatinin into urea, there is no proof that in the body anything more than the first step in this process is accomplished. When kreatin is introduced into the intestine or injected into the blood, it appears in the urine, not as urea, but as kreatinin. Uric acid is, indeed, very closely related to urea, and can be made to yield it by oxidation outside the body. Not only so, but it is excreted as urea when given to a mammal by the mouth, and it replaces urea as the great end-product of nitrogenous metabolism almost wholly in the urine of birds and reptiles, and partially in the human subject in leukæmia. But none of these things can be admitted as evidence that in the normal metabolism of mammals uric acid lies on the direct line from proteid to urea.

Then, again, the amido-acids, leucin, glycin and asparaginic acid, when given by the mouth, increase the output of urea, so that the leucin formed in the intestine during digestion is doubtless a precursor of a small portion of the urea. And since leucin and tyrosin are very widely spread in the solids and liquids of the body, it has been asserted that the amido-acids are the form in which nitrogen leaves the tissues to be converted into urea in the liver. But it is against this view that there is not enough carbon in proteids to convert all their nitrogen into amido-acids (Bunge). It may be, however, that a portion of the proteid is changed into amido-acids relatively rich in carbon, and the remainder into simple ammonia compounds relatively rich in nitrogen, the amido-acids being then further split up into simpler bodies, which combine with each other to form urea. Lea has suggested that the amido-acids have quite another significance than that of intermediate steps in the downward metabolism of proteids—that they are destined, in fact, to take part in synthetic processes within the liver—that they are on the up, and not on the down, grade. And he points out, in support of this view, that even when the urea in the urine is increased by the administration of these substances, the increase does not correspond to the whole of their nitrogen; a part of it is therefore devoted to other purposes in the body. Outside of the body proteids can be decomposed so as to yield a large number of products, ammonium salts, leucin, tyrosin, aspartic and glutaminic acids, lysine and arginine. These can also be all obtained by tryptic digestion, and from the arginine urea can be artificially derived. But we must not conclude without special proof that in the body the course of proteid decomposition is the same.

The conclusion of the whole matter is that, if anyone

chooses to assert that the proteids of the tissues fall by a single descent nearly to the stage of urea, there is as yet little real evidence to contradict him. What is certain is that *from most tissues the nitrogen does not pass out chiefly in the form of urea, that it appears in the urine mainly as urea, and that the change is effected to a large extent, but not exclusively, in the liver. Among its precursors are probably ammonia compounds.*

Uric acid, like urea, is separated from the blood by the kidneys, not to any appreciable extent formed in them. In birds, and often in man, it can be detected in normal blood. It is present in increased amount in the blood and transudations of gouty patients, in whose joints and ear-cartilages it often forms concretions. 'Chalk-stones' may contain more than half their weight of sodium urate. The spleen yields a small quantity of uric acid, which may be increased by blowing air through a mixture of splenic pulp and blood.

As to the source of the uric acid, it is well established that in the bird it is formed both from the end-products of proteid metabolism and from nuclein compounds and their derivatives. In the mammal, the taking of food rich in nucleated cells, and therefore in nucleoproteids and nucleins (thymus gland, pig's pancreas, and herring roe), or of food rich in nuclein bases* (Liebig's meat extract), increases the quantity of uric acid in the urine. The increase is in part due to the production of uric acid from the nuclein substances (Jerome). But this is not the only source of the uric acid, since extracts of the thymus gland containing only traces of nucleins or nucleic acid cause, when injected, a characteristic increase in the uric acid excretion, just as the entire gland does when taken by the mouth. And during the period of increased nitrogen excretion caused by a meal containing proteid the increase in the uric acid occurs particularly in the hours immediately following the ingestion of the food, and does not last so long as the increase in the urea. Now, the nucleins of the food are comparatively little affected during the earlier stages of digestion (Hopkins and Hope). We may conclude, therefore, that in the mammal, as well as in the bird, a portion of the uric acid, although certainly a far smaller portion in the mammal, is derived from bodies other than the nuclein substances of the food; that is to say, from the nuclein substances of the tissues and from the proteids of both food and tissues.

* Nucleins, the chief constituents of the nuclei of cells, are compounds of proteid with nucleic acids. The nucleic acids, of which at least four are known, are compounds of an acid and one of the nuclein bases or alloxan bodies, such as adenin, guanin, xanthin, hypoxanthin.

Hippuric acid can undoubtedly be produced in the kidney. If an excised kidney is perfused with blood containing benzoic acid, or, better, benzoic acid and glycin, hippuric acid is formed. The kidney cells must be intact, for if a mixture of blood, glycin, and benzoic acid be added to a minced kidney immediately after its removal from the body, hippuric acid is produced, but not if the kidney has been crushed in a mortar. In herbivora hippuric acid cannot normally be detected in the blood; it is present in large quantities in the urine; it must therefore be manufactured in the kidney, not merely separated by it. In certain animals, as the dog, the kidney is the sole seat of the production of hippuric acid. But in the rabbit and the frog some of it may also be formed in other tissues, for after extirpation of the kidneys the administration of benzoic acid causes hippuric acid to appear in the blood. The benzoic acid comes mainly from substances of the aromatic group contained in vegetable food, but a small amount is produced in the body, since hippuric acid does not entirely disappear from the urine in starvation. It is not known in what form the nitrogenous glycin appears on the spot where it is wanted to form hippuric acid, since glycin has not been found anywhere in the tissues. But there is no doubt that it is a product of the metabolism of proteids (and gelatine). It is also a constituent of glycocholic acid, and may be derived in part from the bile which is reabsorbed.

Kreatinin can be so readily obtained from kreatin outside the body, that it is very tempting to suppose that the kreatinin of the urine is manufactured by the kidney from the kreatin of muscle carried to it by the blood. It has been shown, however, that most, at any rate, of the kreatinin of the urine is derived from ready-formed kreatin in the food. The kreatin of the muscular tissue may be ultimately changed into urea, but if this is the case, the intermediate steps are unknown. A small amount of kreatinin is excreted in the urine even in starvation, and this may come from the muscular kreatin.

Formation of Carbon Dioxide from Proteids.—We cannot say whether any carbon dioxide is normally produced at the moment when the nitrogenous portion of the proteid molecule

splits off, or whether a carbonaceous residue may not always hang together for a time and pass through further stages before the carbon is fully oxidized. We shall see that under certain conditions some of the carbon of proteids may be retained in the body as glycogen or fat; and this suggests that in all cases it may run through intermediate products as yet unknown, before being finally excreted as carbon dioxide.

2. **Metabolism of Carbo-hydrates—Glycogen.**—*The carbo-hydrates of the food, passing into the blood of the portal vein in the form of dextrose, are in part arrested in the liver, and stored up as glycogen in the hepatic cells, to be gradually given out again as sugar in the intervals of digestion.* The proof of this statement is as follows:

Sugar is arrested in the liver, for during digestion, especially of a meal rich in carbo-hydrates, the blood of the portal contains more sugar than that of the hepatic vein. In the liver there exists a store of sugar-producing material from which sugar is gradually given off to the blood, for in the intervals of digestion the blood of the hepatic vein contains more sugar (2 parts per 1,000) than the mixed blood of the body or than that of the portal vein (1 to 1·5 part per 1,000). When the circulation through the liver is cut off in the goose, the blood rapidly becomes free, or nearly free, from sugar (Minkowski). And a similar result follows such interference with the hepatic circulation as is caused by the ligation of the three chief arteries of the intestine in the dog, even when the animal has been previously made diabetic by excision of the pancreas (p. 483). The nature of the sugar-forming substance is made clear by the following experiments: (1) A rabbit after a large carbo-hydrate meal, of carrots for instance, is killed, and its liver rapidly excised, cut into small pieces, and thrown into acidulated boiling water. After being boiled for a few minutes, the pieces of liver are rubbed up in a mortar and again boiled in the same water. The opalescent aqueous extract is filtered off from the coagulated proteids. No sugar, or only traces of it, are found in this extract; but another carbo-hydrate, glycogen, an isomer of starch giving a port-wine colour with iodine and capable of ready conversion into

sugar by amylolytic ferments, is present in large amount. (See Practical Exercises, p. 511.)

(2) The liver after the death of the animal is left for a time *in situ*, or, if excised, is kept at a temperature of 30° to 40° C., or for a longer period at a lower temperature; it is then treated exactly as before, but no glycogen, or comparatively little, can now be obtained from it, although sugar (dextrose) is abundant. The inference plainly is that after death the hepatic glycogen is converted into dextrose by some influence which is restrained or destroyed by boiling. This influence may be due to an unformed ferment or to the direct action of the liver-cells, for both unformed ferments and living tissue elements are destroyed at the temperature of boiling water. Although there is no doubt that an amylolytic ferment can be extracted from the liver in small amount, as from other organs and from the blood, it has been shown that the vital action of the hepatic cells is the most important factor. The amylolytic activity of a fresh liver, for instance, is increased by chloroform, but this is not the case with a liver which has first been treated by alcohol and dried, and in which accordingly the cells have been killed while the unorganized ferments are unaffected (Paton). And sulphate of quinine, which does not hinder the activity of enzymes, causes when injected into the veins a diminution in the amount of sugar formed in the liver (Cavazzani). The post-mortem change is to be regarded as an index of a similar action which goes on during life: sugar in the intact body is changed into glycogen; glycogen is constantly being changed into sugar.

(3) With the microscope, glycogen, or at least a substance which is very nearly akin to it, which very readily yields it, and which gives the characteristic port-wine colour with iodine, can be actually seen in the liver-cells. The liver of a rabbit or dog which has been fed on a diet containing much carbo-hydrate is large, soft, and very easily torn. Its large size is due to the loading of the cells with a hyaline material, which gives the iodine reaction of glycogen, and is dissolved out by water, leaving empty spaces in a network of cell-substance. If the animal, after a period of starvation, has been fed on proteid alone, only a little glycogen is found

in the shrunken liver-cells; if the diet has been wholly fatty, no glycogen at all may be found.

In the liver-cells of the frog in winter-time, a great deal of this hyaline material—this glycogen, or perhaps loose glycogen compound—is present; in summer, much less. The difference is very remarkable if we consider that in winter frogs have no food for months, while summer is their feeding-time; and at first seems inconsistent with the doctrine that the hepatic glycogen is a store laid up from surplus sugar, which might otherwise be swept into the general circulation and excreted by the kidneys. It has been found, however, that the quantity of glycogen is greatest in autumn at the beginning of the winter-sleep, and slowly diminishes as the winter passes on, to fall abruptly with the renewal of the activity of the animal in the spring. The glycogen present at any moment is, therefore, believed to be a residue, which represents the excess of glycogen formed over glycogen used up; and the amount is larger in winter, not because more is manufactured than in summer, but because less is consumed. It is possible, indeed, to produce the 'summer' condition of the hepatic cells merely by raising the temperature of the air in which a winter frog lives; at 20° or 25° C., glycogen disappears from its liver. Conversely, if a summer frog is artificially cooled, a certain amount of glycogen accumulates in the liver. The meaning of this seems to be that at a low temperature, when the wheels of life are clogged and metabolism is slow, some substance, possibly dextrose, is produced in the body in greater amount than can be used up, and that the surplus is stored as glycogen; just as in plants starch is put by as a reserve which can be drawn upon—which can be converted into sugar—when the need arises.

When a fasting dog is made to do severe muscular work, the greater part of the glycogen soon disappears from its liver. When a dog is starved, but allowed to remain at rest, the glycogen still markedly diminishes, although it takes a longer time; and at a period when there is still plenty of fat in the body, there may be only a trace of hepatic glycogen left. The glycogen which is usually contained in the muscles also diminishes very rapidly in the first days of hunger. These facts have been taken to indicate that glycogen and the sugar formed from it are the readiest resources of the starving and working organism. The fat of the body is a good security, which, however, can only be gradually realized; its organ-proteids are long-date bills, which will be discounted sparingly and almost with a grudge; its glycogen, its carbo-hydrate reserves, are consols, which can be turned into money at an hour's warning. Glycogen is drawn upon for a sudden demand, fat for a steady drain, proteid for a life-and-death struggle.

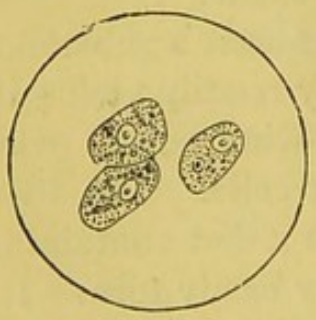


FIG. 134. — CELLS OF PLACENTA CONTAINING GLYCOGEN.

While the liver in the adult (containing as it does from 2 to 10 per cent of glycogen, or even more with a diet rich in sugar or starch) may be looked upon as the main storehouse of surplus carbo-hydrate, depots of glycogen seem to be formed, both in adult and fœtal life, in other situations where the strain of function or of growth is exceptionally heavy—in the muscles of the adult (0·3 to 0·5 per cent. of the moist muscle), in the placenta, in many developing organs in the embryo (lungs, epithelium of the trachea, œsophagus, intestine, ureter, pelvis of kidney, and renal tubules.) In the embryonic muscles the glycogen may constitute as much as 40 per cent. of the solids.

Although it cannot be doubted that much of the hepatic glycogen leaves the liver as sugar, there is no proof that it all does so. It is known that fat may be formed from carbo-hydrates (p. 458); and globules of oil are often conspicuous among the contents of liver-cells, side by side with glycogen. It is possible, therefore, that some of the glycogen may represent a half-way house between sugar and fat, or, since fat can also be formed from proteid, and a purely proteid diet produces some glycogen, a half-way house between proteid and fat. The so-called 'liver dextrin,' a nitrogenous substance containing a carbo-hydrate group, which reduces cupric oxide and yields a reducing sugar on being heated with dilute acid, may be an intermediate stage in the conversion of proteid into sugar. According to Seegen, its discoverer, the amount of this body in the liver sometimes exceeds that of the glycogen and sugar put together. That glycogen may be produced from proteids even during starvation is shown by the following experiment: A fasting animal was put under the influence of strychnia to remove all glycogen from the liver. Then the strychnia spasms were cut short by chloral, and the animal allowed to sleep for eighteen hours. At the end of that time a considerable amount of glycogen was found in the liver and muscles, and this must have come from the proteids of the body.

Pavy has put forward the heterodox view that the glycogen formed in the liver from the sugar of the portal blood is never reconverted into sugar under normal conditions, but is changed into some other substance or substances, and he denies that the post-mortem formation of sugar in the hepatic tissue is a true picture of what takes place during life. But in spite of the brilliant manner in which he has defended this thesis both by argument and by experiment, it must be said that the older doctrine of Bernard, which in the main we have followed above, is attested by such a cloud of modern witnesses that it seems to be firmly and finally established.

Fate of the Sugar.—What, now, is the fate of the sugar which either passes right through the portal circulation from the intestine without undergoing any change in the liver, or is gradually produced from the hepatic glycogen? When the proportion of sugar in the blood rises above a certain low limit (about 3 parts per 1,000), some of it is excreted by the kidneys (Practical Exercises, p. 526).

A large meal of carbo-hydrates is frequently followed by a temporary glycosuria, but something seems to depend upon the form in which the sugar-forming material is taken. Miura, for example, after an enormous meal of rice (equivalent to 6·4 grammes ash- and water-free starch per kilo of body-weight), which, as he mentions, tasked even his Japanese powers of digestion to dispose of, found not a trace of sugar in the urine. Glucose, cane-sugar and lactose, on the other hand, when taken in large amount, were in part excreted by the kidneys, as was also the case with levulose and maltose in a dog (Practical Exercises, p. 527).*

But, except as an occasional phenomenon, such an excretion is inconsistent with health; and therefore in the normal body the sugar of the blood must be either destroyed or transformed into some more or less permanent constituent of the tissues. The transformation of sugar into fat we have already mentioned, and shall have again to discuss; it only takes place under certain conditions of diet, and no more than a small proportion of the sugar which disappears from the body in twenty-four hours can ever, in the most favourable circumstances, be converted into fat. Accordingly, it is the *destruction* of sugar which concerns us here, and there is every reason to believe that this takes place, not in any particular organ, but in all active tissues, especially in the muscles, and to a less extent in glands.

It has been asserted that the blood which leaves even a resting muscle, or an inactive salivary gland, is poorer in sugar than that coming to it; and the conclusion has been drawn that in the metabolism of resting muscle and gland sugar is oxidized, the carbon passing off as carbon dioxide in the venous blood. This is indeed extremely likely, for we know that when the skeletal muscles of a rabbit or guinea-pig are cut off from the central nervous system by

* Twenty-four healthy students, whose urine had previously been shown to be free from sugar, ate quantities of cane-sugar varying from 250 grammes to 750 grammes. The urine was collected in separate portions for twelve to twenty-four hours after the meal. In only three cases was reducing sugar found in the urine (by Fehling's and the phenylhydrazine test), and then merely in traces. In eight cases cane-sugar was found, and estimated by the polarimeter, and, after boiling with hydrochloric acid, by Fehling's solution. The greatest quantity of cane-sugar recovered from the urine was 8 grammes (7·918 grammes by Fehling's method and 8·288 grammes by the polarimeter); the highest proportion of the quantity taken which appeared in the urine was 2·5 per cent. When glucose was found, cane-sugar was always present as well.

curara, the production of carbon dioxide falls much below that of an intact animal at rest; and the carbon given off by such an animal on its ordinary vegetable diet can be shown, by a comparison of the chemical composition of the food and the excreta, to come largely from carbo-hydrates. But, considering the relatively feeble metabolism of muscles and glands when not functionally excited, the large volume of blood which passes through them, the difficulty of determining small differences in the proportion of sugar in such a liquid, the possibility that even in the blood itself sugar may be destroyed, or that it may pass from the blood, without being oxidized, into the lymph, too much weight may easily be given to the results of direct analysis of the in-coming and out-going blood. And although the recent results of Chauveau and Kaufmann, obtained in this way, fit in fairly well with what we have already learnt by less direct, but more trustworthy, methods, they cannot be accepted as yielding exact quantitative information. They found that in one of the muscles of the upper lip of the horse the quantity of grape-sugar used up during activity (feeding movements) was 3·5 times as much as in the same muscle at rest, and this corresponded with the deficit of oxygen in the blood entering the muscle, and with the excess of carbon dioxide in the blood leaving it. More dextrose was also destroyed in the active than in the passive parotid gland of the horse, but the excess per unit of weight of the organ was far less than in muscle.

Diabetes.—In the disease known as *diabetes mellitus*, sugar accumulates in the blood, and is discharged by the kidneys, and it has been supposed that a derangement in the glycogenic function of the liver is the cause of this accumulation and of this discharge. An artificial and temporary diabetes, in which the sugar in the urine undoubtedly arises from the hepatic glycogen, can, indeed, be caused by puncturing the medulla oblongata in a rabbit at or near the region of the vaso-motor centre. If the animal has been previously fed with a diet rich in carbo-hydrates—that is, if it has been put under conditions in which the liver contains much glycogen—the quantity of sugar excreted by the

kidneys will be large. If, on the other hand, the animal has been starved before the operation, so that the liver is free or almost free from glycogen, the puncture will cause little or no sugar to appear in the urine. That nervous influences are in some way involved is shown by the absence of diabetes if the splanchnic nerves, or the spinal cord above the third or fourth dorsal vertebra, be cut before the puncture is made. But sometimes these operations are themselves followed by temporary diabetes. Section of the vagi has no effect either in causing glycosuria of itself or in preventing the 'puncture' diabetes, although stimulation of the central ends of these and of other afferent nerves may cause sugar to appear in the urine. Although several of the operations which lead to this temporary glycosuria undoubtedly bring about changes in the hepatic circulation, it is as yet impossible to say whether the whole phenomenon is at bottom a vaso-motor effect, or is due to direct nervous stimulation of the liver-cells, or to withdrawal of such stimulation or control.

The pancreas is intimately concerned in the metabolism of sugar. Excision of this organ in dogs causes permanent diabetes (v. Mering and Minkowski), which is prevented if a portion of the pancreas be left, or if it be transplanted under the skin of the abdomen (p. 483).

Curara, morphia, carbon monoxide, phloridzin (p. 527), and other substances, also cause diabetes. Phloridzin diabetes agrees with pancreatic, differs from 'puncture' diabetes in this, that it can be produced in an animal free from glycogen, and is accompanied by extensive destruction of proteids. It differs from other forms of diabetes in being associated, not with an increase, but with a diminution in the sugar of the blood. This is best explained by supposing that the phloridzin acts on the kidney in such a way as to increase the permeability of the glomerular epithelium for sugar, or (in terms of the vital theory of urinary secretion), to increase its sensitiveness to the stimulus of sugar circulating in the blood. The sugar is, therefore, rapidly swept out of the circulation, and this leads secondarily to an increased production of sugar to make good the loss.

In the natural diabetes of man it is possible that in some cases the sugar coming from the alimentary canal passes entirely or in too large amount through the liver, owing to a deficiency in its power of forming glycogen. But although in certain cases of diabetes specimens of the hepatic cells, obtained by plunging a trocar into the liver, have been found free from glycogen, in others glycogen has been present. And it is remarkable that levulose may be entirely used up in the tissues of a diabetic patient, or of a dog rendered diabetic by extirpation of the pancreas, while dextrose, which is so closely allied to it, and from which an identical form of glycogen is produced, is promptly cast out by the kidneys. In many cases even when carbo-hydrates are completely, or almost completely, omitted from the food, sugar, derived from the breaking-down of proteids, still continues to be excreted, although in smaller quantity. Other products of the deranged metabolism of proteids or of fats, such as acetone, aceto-acetic acid, and oxybutyric acid, may also appear in the urine, or, accumulating in the blood, may, by uniting with its alkalies, seriously diminish the quantity of carbon dioxide which that liquid is capable of carrying, and thus lead to the condition known as diabetic coma. This form of coma appears to be really an acid-poisoning comparable to the condition produced in animals by doses of mineral acids too large to be neutralized by the ammonia split off from the proteids. The administration of very large doses of alkalies (sodium bicarbonate, for instance, to the amount even of hundreds of grammes) has been recommended for the treatment of this serious complication. The most rational way of explaining many of the facts of diabetes is to suppose that, from some change in the tissue elements, sugar has ceased to be a food for them, or is used up in smaller amount than in the healthy body, while the actual production of sugar is no greater than in a normal person with the same diet and the same intensity of metabolism of substances other than carbo-hydrates.

Normal blood seems to contain a ferment which has the power of destroying sugar and forming lactic acid; and the statement of Lépine and Barral that extirpation of the pancreas, which is followed by diabetes, causes a diminution in the activity or in the amount of this ferment, appeared to afford the basis for a theory of diabetes. But Spitzer has asserted that the sugar-destroying power of blood taken from diabetic patients, or from animals in which glycosuria had been caused by phloridzin, is not at all inferior to that of healthy blood. And, indeed, results that depend upon the determination of minute differences in the quantity of sugar must be accepted with reserve.

3. **Metabolism of Fat.**—The fat, passing along the thoracic duct into the blood stream, is very soon removed from the circulation, for normal blood contains only traces, except during digestion. Where does it go? What is its fate?

The presence of adipose tissue in the body might suggest

a ready answer to these questions. The fat cells of adipose tissue are apparently ordinary fixed connective-tissue cells which have become filled with fat, the protoplasm being reduced to a narrow ring, in which the nucleus is set like a stone. It would, at first thought, seem natural to suppose that the fat of the food is rapidly separated by these cells from the blood, and slowly given up again as the needs of the organism require, just as carbo-hydrate is stored in the liver for gradual use. And it has been found that a lean dog, fed with a diet containing much fat and little proteid, puts on more fat, as estimated by direct analysis, or keeps back more carbon, as estimated by measurements of the respiratory interchange, than can be accounted for on the supposition that even the whole of the carbon of the broken-down proteid corresponding to the excreted nitrogen has been laid up in the form of fat. Even with a diet of pure fat—and with such a diet digestion and absorption are carried on under unfavourable conditions—more carbon is retained than can have come from the metabolism of the proteids of the body, as measured by the nitrogen given off in the urine and fæces: the fat passes rapidly from the blood into the organs, and especially into the liver (Hofmann, Pettenkofer and Voit). It is thus certain that some of the absorbed fat may be stored up as fat in the body.

This is borne out by the careful experiments of Munk and Lebedeff, who find that when dogs are fed with excess of foreign fat (linseed-oil, rape-oil, mutton-fat), a fat is laid down which is quite different from dog's fat, and has the greatest resemblance to the fat of the food. Thus, when rape-oil, which contains a fatty acid, erucic acid, not found in animal fat, was given, erucic acid could be detected in the fat laid on. When the dogs were fed with mutton-fat, whose melting-point is much higher than that of dog's fat, the fat laid on did not melt till it was heated to 40° C. or more. When they were fed with linseed oil, the body-fat was found liquid even at 0° C. We have already referred (p. 371) to the fact that neutral fat can be built up in the wall of the intestine from fatty acids given in the food. Munk has shown that fat formed in this way can also be laid down as body-fat.

But besides the fat and fatty acids of the food, the fat of the body has other sources, and some of it is produced by more complex processes.

The fat of a dog consists of a mixture of palmitin, olein, and stearin. When a starved dog was fed on lean meat and a fat containing palmitin and olein, but no stearin, the fat put on contained all three, and did not sensibly differ in its composition from the normal fat of the dog (Subbotin). Stearin must, therefore, have been formed in some way or other in the body. If it was formed from the olein and palmitin of the food, the portion of these deposited in the cells of the adipose tissue must have undergone changes before reaching this comparatively fixed position. But there is conclusive evidence that fat may be derived from proteids; and it is more likely that the stearin was formed from the proteids of the food or tissues than directly from fat. And if the stearin was produced from proteids, it is evident that the olein and palmitin *might* have been formed from proteids too, the portion of the latter devoted to this purpose being sheltered from oxidation by the combustion of the fats of the food. It is well known that not only neutral fats, but also fatty acids, exert such a 'proteid-sparing' action, and a portion, though not the whole, of the fat laid on when an animal is fed with fatty acids does arise from the carbonaceous residue of the proteids that are saved from complete combustion. It is possible also that the fat which is normally excreted into the intestine (p. 372), and which is perhaps derived from broken-down proteids, may be reabsorbed, and take its place among the fat 'put on.'

Formation of Fat from other Sources than the Fat of the Food.—(1) **From Proteids.**—Dry proteid contains on the average 15 per cent. of nitrogen and 50 per cent. of carbon; and urea contains 46 per cent. of nitrogen and 20 per cent. of carbon. Urea is therefore rather more than three times as rich in nitrogen as the proteid from which it is derived, but two and a half times poorer in carbon; and less than one-seventh of the carbon of proteid will be eliminated in the urea, which carries off all the nitrogen. A carbonaceous residue is left, which under certain circumstances may be

converted into fat. The proof of this statement is very complete, but only an outline of it can be given here.

In the experiments of Bauer, the amount of oxygen consumed and of carbon dioxide and nitrogen excreted was determined in starving dogs. Phosphorus, which, as is well known, causes extensive fatty degeneration, was then administered in small doses for several days. The excretion of nitrogen was doubled, the excretion of carbon dioxide and the consumption of oxygen diminished to one-half. When the animals died, in a few days, the organs were all found fattily degenerated. In one case 42·4 per cent. of the solids of the muscles and 30 per cent. of the solids of the liver consisted of fat. This is nearly three times the normal amount. The fat could not have been simply transferred from the adipose tissue, since the dog had been starved for twelve days before the phosphorus was given, and died on the twentieth day of starvation. Now, after such a period of hunger the amount of fat necessary to account for the excess found in the organs does not exist in the adipose tissue. The source of the fat could only have been the broken-down proteid. Since the nitrogen excretion was increased, while the carbon excretion was diminished, a residue rich in carbon must have been split off from the proteids and, remaining unburnt in the body, must have been converted into fat. The observations of Lusk and his pupils indicate that phosphorus does not directly increase the amount of proteid broken down, but does so indirectly, by favouring the conversion of the carbo-hydrate-like radicle of the proteid molecule into leucin, tyrosin, and fat, and therefore necessitating an increased consumption of proteid.

These experiments show that in abnormal circumstances fat may arise from proteids. An absolute proof of its formation in this manner, under strictly physiological conditions, although in a humble form of animal life, is afforded by the experiments of Hofmann on maggots allowed to develop from the egg on blood containing a known amount of fat. The quantity of fat in the eggs was also known. After the maggots had grown, ten times as much fat was found in them as had been contained in the blood and eggs together. The trifling quantity of sugar in the blood was utterly inadequate to account for the fat, which must have come from the proteids of the blood.

That in the higher animals also fat is formed from proteids under normal conditions is, although not perhaps strictly proved, yet extremely probable. A dog fed for a time on a liberal diet of lean meat may go on excreting a quantity of nitrogen equal to that in the food, while there is a deficiency in the carbon given off. Or if the dog is not in nitrogenous equilibrium (p. 460), but putting on nitrogen in the form of 'flesh,' the deficiency in the carbon given off may be too great in proportion to the nitrogen deficit to warrant the assumption that all the retained carbon has been put on in the form of proteid. In either case, carbon in large amount can only come from the proteids of the food, and can only be stored up in the body

in the form of fat; for lean meat contains but a trifling quantity of carbon in any other proximate principle than proteid, and the non-proteid carbon of the animal body is only to a very small extent contained in carbo-hydrates or other substances than fat.

For example, in an experiment of Pettenkofer and Voit on a 34-kilo dog in nitrogenous equilibrium, with a diet of 2,000 grammes of lean meat, the animal on the first day

		Grammes.		Grammes.	
Took in in the food			68·0 N		250·4 C
Gave out in	urine	66·5 N		39·9 C	
	fæces	1·4		9·2	
	respiration	0		158·3	
			67·9		207·4
Difference			+0·1 N		+43·0 C

Here the nitrogen of the body remained unaltered, but carbon was put on to the extent of 43 grammes, or 17 per cent. of the amount in the food, representing about 58 grammes of fat. It is very unlikely that the whole of this carbon, or even the greater part of it, could have been retained as glycogen. For 43 grammes of carbon correspond to nearly 100 grammes of glycogen, or nearly 3 grammes per kilo of body-weight; and there is nothing to indicate that such an increase in the glycogen store ever takes place in a single day.

Some exact quantitative proofs of the conversion of proteids into fat have been quoted. Qualitative indications of its possibility and of its actual occurrence are numerous. Such are the readiness with which fatty degeneration occurs in the tissues in pathological states—for example, after poisoning with phosphorus, arsenic, or antimony, the accumulation of fat between the hepatic cells caused by phloridzin, which, as we know, hastens the disintegration of proteids; the formation of adipocere (a cheesy substance, rich in fatty acids united with calcium or ammonium) sometimes seen in dead bodies which have remained a long time under water or in moist graveyards; the formation of fat in the cells of the sebaceous glands; and the transformation of the cell-substance of the mammary glands into the fat of milk. This last case is of great practical importance, for it explains the rule which experience has taught, that a woman during lactation requires an excess of proteids in her food corresponding not only to the proteids, but also to the fat given off in the milk.

(2) **From Carbo-hydrates.**—It has been found that the addition of proteid to a diet of fat, and especially to a diet

of carbo-hydrate, in larger amount than is just necessary for nitrogenous equilibrium, leads to a more rapid increase in the carbon deficit—that is, in the fat put on—than if the minimum quantity of proteid required for nitrogenous equilibrium had been given. From this it is inferred that the carbonaceous residue of the broken-down proteid is shielded from oxidation by the fat, and to a still greater extent by the carbo-hydrates, and so retained in the body as fat. And it is certain that the high repute of carbo-hydrates as fattening agents is in part due to their taking the place of proteids and fats in ordinary 'current' metabolism, and so allowing body-fat to be laid down from these. Voit, indeed, has gone so far as to assert that this is the only sense in which carbo-hydrates can be said to form fat, and that, in carnivorous animals at least, a direct conversion never occurs. But the experiments of Rubner have shown that in a dog fed with a diet rich in carbo-hydrates, and containing but little fat and no proteids at all, the carbon deficit was greater than could be accounted for by the proteids broken down in the body and the fat of the food. In the pig and goose, too, the direct formation of fat from carbo-hydrates has been demonstrated. It is probable that the carbo-hydrates are first split up to some extent, and that the fats are then constructed from their decomposition products, oxygen being lost in the process, since fat is poorer in oxygen than carbo-hydrate. The production of wax by bees, which used to be given as a proof of the formation of fat from sugar, is not decisive, for in raw honey proteids are present; and even when bees fed on pure honey or sugar manufacture wax, it may be derived from the broken-down proteids of their own bodies.

As to the ultimate fate of the fat, from whatever source it may be derived, our knowledge may be compressed into a single sentence: *Sooner or later it is oxidized to carbon dioxide and water, its energy being converted into heat or, directly or indirectly, into mechanical or chemical work; much of the fat absorbed from the intestine rapidly undergoes this combustion without entering the fat-cells of the adipose tissue.*

Summary.—At this point let us sum up what we have

learnt as to the relation between the proximate principles of the tissues and the proximate principles of the food. *Inside the body we recognise representatives of the three groups of organic food-substances in a typical diet—proteids, carbo-hydrates, and fats.* But we should greatly err if we were to imagine that the three streams of food-materials have flowed from the intestines into the tissues each in its separate channel, neither giving to nor taking from the others. *The fats of the body may, indeed, in part be composed of molecules which were present as fat in the food; but they may also be formed from proteids, and from carbo-hydrates. The carbo-hydrates of the body—the glycogen of the liver and muscles, the sugar of the blood—may undoubtedly be derived from carbo-hydrates in the food, but they may also be derived from proteids, although probably not from fats. The proteids of the body arise solely from the proteids of the food; neither fats nor carbo-hydrates can form proteids, although both can economize them and shield them from an over-hasty metabolism.*

4. **The Income and Expenditure of the Body.—(1) Income and Expenditure of Nitrogen.—**

Preliminary Data.—The purpose of food is to maintain the constituents of the body upon the whole in their normal proportions. A knowledge of the chemical composition of the body is, therefore, an important datum in the consideration of the statistics of its metabolism. The body of a man analyzed by Volkmann had the following composition:

Inorganic substances	Water		65·9 per cent.
	Mineral matter		4·4 ,,
Organic substances	Carbon	18·4 per cent.	29·7 ,,
	Hydrogen	2·7 ,,	
	Nitrogen	2·6 ,,	
	Oxygen	6·0 ,,	

The muscles, the adipose tissue, and the skeleton form nearly four-fifths of the total body-weight in the adult. The following table shows the percentage amount of each of these tissues in a man, a woman, and a child (Bischoff):

	Man.	Woman.	New-born Child.
Voluntary muscles	41·8	35·8	23·5
Adipose tissue	18·2	28·2	13·5
Skeleton	15·9	15·1	15·7
Rest of body	24·1	20·9	47·3

The nitrogen is contained chiefly in the muscles, glands and nervous system, and in the constituents of the connective tissues, which yield gelatin, chondrin, and elastin. The proteids make up about 9 per cent. of the weight of the body, or 22 per cent. of its solids; the albuminoids (gelatin-yielding material, etc.) about 6 per cent. of the body-weight. Nitrogen exists in proteids to the extent of 15 per cent., so that the 6·5 kilos of proteid of a 70-kilo body contain nearly 1 kilo of nitrogen.

The carbon is contained chiefly in the fat, which forms a very large proportion of the water-free substance of the body, and in the proteids. A small amount is present as calcium carbonate in the bones. In the body of a strong young man weighing 68·6 kilos, Voit found the following quantities of dry fat in the various tissues:

Adipose tissue	8809·4 grammes.
Skeleton	2617·2 ,,
Muscles	636·8 ,,
Brain and spinal cord	226·9 ,,
Other organs	73·2 ,,
Total	12363·5 ,,

equivalent to 18 per cent. of the whole body-weight, or 44 per cent. of the solids. In dry fat rather more than 75 per cent. of carbon is present, and in proteid about 50 to 55 per cent.; so that while the fat of the body analyzed by Voit contained more than 9 kilos of carbon, only about a third of this amount would be found in the proteids.

In the fat there is, roughly speaking, 12 per cent. of hydrogen, in proteids only 7 per cent.; so that from three to four times as much hydrogen is contained in the fat of the body as in its proteids.

Oxygen forms about 12 per cent. of fat, and 20 to 24 per cent. of proteids; the proteid constituents of the body, therefore, contain about as much of its oxygen as the fat.

Of the inorganic salts calcium phosphate, $Ca_3(PO_4)_2$ is much the most abundant owing to the large amount of it in bone, in the ash of which it is found to the extent of 83 per cent., along with 13 per cent. of calcium carbonate.

Nitrogenous Equilibrium.—It is a matter of common experience that the weight of the body of an adult may remain approximately constant for many months or years, even when the diet varies greatly in nature and amount. And not only may the weight remain constant, but the relative proportions of the various tissues of the body, so far as can be judged, may remain constant too. Here it is evident that the expenditure of the body must precisely balance its income: it must lose as much nitrogen as it takes in, otherwise it would put on flesh; it must lose as much carbon as it takes in, otherwise it would put on fat. Or, again, the body may be losing or gaining fat, giving off more or less carbon than it receives, while its 'flesh' (its proteid constituents) remains constant in amount, the expenditure of nitrogen being exactly equal to the income.

In both cases we say that the body is in nitrogenous equilibrium.

A starving animal or a fever patient, on the other hand, is living upon capital, the former entirely, the latter in part; the expenditure of nitrogen is greater than the income. A growing child is living below its income, is increasing its capital of flesh. In neither case is nitrogenous equilibrium present.

The **starving animal**, as long as life lasts, excretes urea and gives off carbon dioxide; but its expenditure, and especially

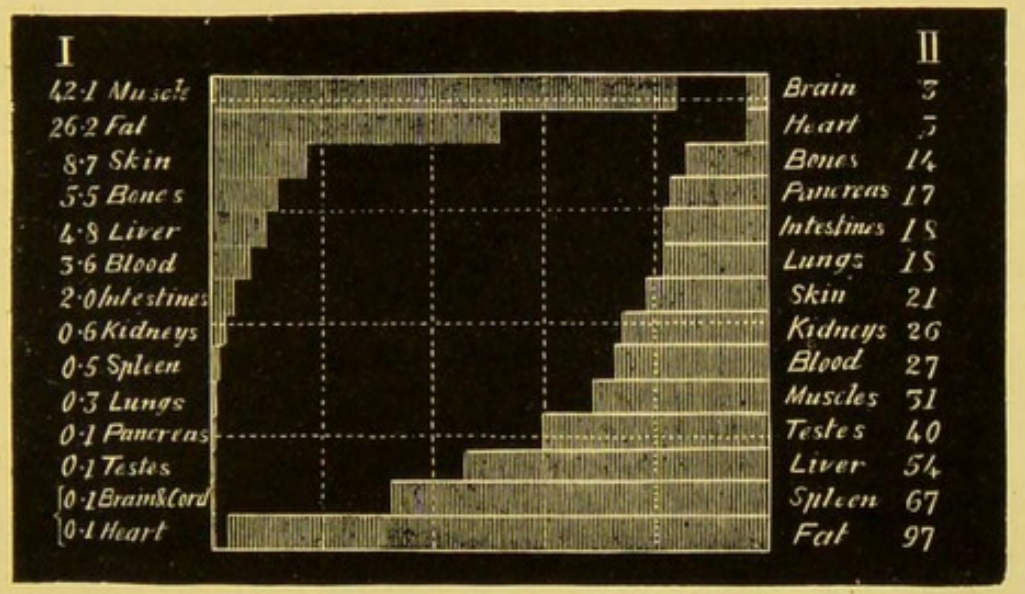


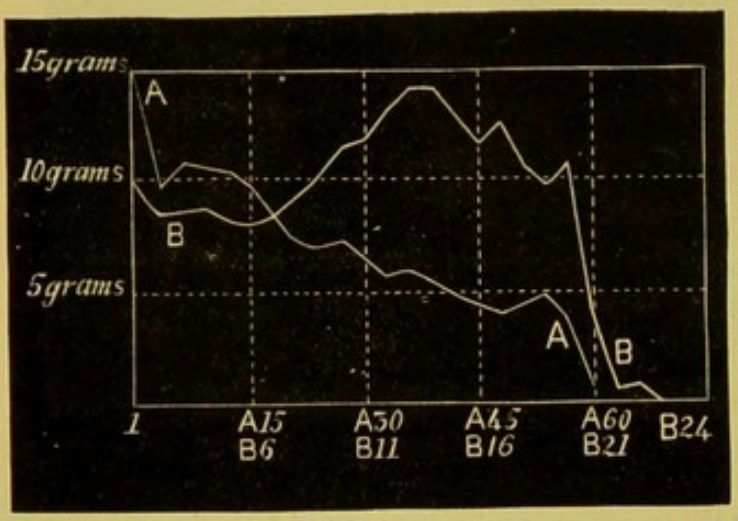
FIG. 135.—DIAGRAM SHOWING LOSS OF WEIGHT OF THE ORGANS IN STARVATION.

The numbers under I. are the percentages of the total loss of body-weight borne by the various organs and tissues. The numbers under II. give the percentage loss of weight of each organ calculated on its original weight as indicated by comparison with the organs of a similar animal killed in good condition.

its expenditure of nitrogen, is pitched upon the lowest scale. It lives penuriously, it spins out its resources; its glycogen goes, its fat goes, a certain part of its proteid goes, and when its weight has fallen from 25 to 50 per cent., it dies. At death the heart and central nervous system are found to have scarcely lost in weight; the other organs have been sacrificed to feed them. Fig. 135 shows the percentage loss of weight and the proportion of the total loss which falls upon each of the organs of a cat in starvation (Voit).

For the first day of starvation the excretion of urea in a dog or cat is not diminished; it takes about twenty-four hours

for all the nitrogen corresponding to the proteids of the last meal to be eliminated. On the second day the quantity of urea sinks abruptly; then begins the true starvation period, during which the daily output of urea remains constant or diminishes very slowly until a short time before death, when it rapidly falls and soon ceases altogether. An increase in the excretion may precede the final abrupt decline (pre-mortal increase). This seems to indicate the time at which all the available fat has been used up, and after which proteid is no longer 'spared' by the fat.* If the animal has little fat in its body to begin with, the rise in the urea excretion takes place even after the first few days. So long as the fat lasts, the rate at which it is destroyed—as estimated from the amount of carbon given off *minus* the carbon corresponding



A is a curve representing the quantity of urea excreted daily by a fat dog in a starvation period of sixty days. B is the curve of urea excretion in a lean young dog in a starvation period of twenty-four days. Both are constructed from Falck's numbers, but in A only every third day is put in, in order to save space. The numbers along the vertical axis represent grammes of urea; those along the horizontal axis days from the beginning of starvation.

FIG. 136.—EXCRETION OF UREA IN STARVATION.

to the broken-down proteids—remains very nearly constant after the first day. The fat to a certain extent economizes the proteids of the starving body, but however much fat may be present, a steady waste of the tissue-proteids goes on.

The results obtained on **fasting men** differ in some respects from those obtained on starving animals. In ten days of hunger, Cetti, a professional 'fasting man' of meagre habit, excreted 112 grammes nitrogen, or an average of 11 grammes a day. The excretion was least on the eighth, ninth, and tenth days, namely, about 9 grammes a day. On the third day it was higher than on the second, and almost as high on

* If the animal has been for some time on a diet containing an abundance of proteids, several days may elapse before the constant excretion of urea is reached; if the previous diet has been poor in proteid, the constant starvation output may be at once established.

the fourth as on the third. A similar rise in the nitrogen excretion on the second day has been observed in other fasting men, but is either rare or absent in fasting dogs. The explanation apparently is that in the ordinary food of man there is a greater abundance of carbo-hydrates and fats the proteid-sparing action of which is most pronounced at the very beginning of the starvation period. The quantity of chlorine and alkalies in the urine was also diminished, while the phenol was increased. The respiratory quotient sank to 0·66 to 0·69—even less than the quotient corresponding to oxidation of fats alone. The meaning of this, in all probability, is that some of the carbon of the broken-down proteids was laid up in the body as glycogen (*Zuntz*). In another professional fasting man (Succi) with a considerable amount of body-fat, the excretion of nitrogen was found to diminish continuously during a fast of thirty days, being less than 7 grammes on the tenth day, and, what seems almost incredible, not much over 3 grammes on the last day. The surprisingly small nitrogenous waste in this case is perhaps to be accounted for by the proteid-sparing action of the abundant body-fat. The nitrogenous metabolism has also been investigated during long-continued hypnotic sleep (Hoover and Sollmann). The results were very much the same as in an ordinary starvation experiment.

It might be supposed that if an animal was given as much nitrogen in the food in the form of proteids as corresponded to its daily loss of nitrogen during starvation, this loss would be entirely prevented and nitrogenous equilibrium restored. The supposition would be very far from the reality. If a dog of 30 kilos weight, which on the tenth day of starvation excreted 11·4 grammes urea, had then received a daily quantity of proteid equivalent to this amount—that is to say, about 34 grammes of dry proteid, or 175 grammes of lean meat—the excretion of nitrogen would at once have leaped up to nearly double its starvation value. If the quantity of proteid in the diet was progressively increased, the output of urea would increase along with it, but at an ever-slackening rate; and at length a condition would be reached in which the income of nitrogen exactly balanced the

expenditure, and the animal neither lost nor gained flesh. In an experiment of Voit's, for instance, the calculated loss of flesh in a dog with no food at all was 190 grammes a day. The animal was now fed on a gradually increasing diet of lean meat with the following result:

Flesh in the Food.	Flesh used up in the Body.	Net Loss of Body-flesh.
0	190	190
250	341	91
350	411	61
400	454	54
450	471	21
480	492	12

The loss of nitrogen in the urine and fæces is what was measured. Knowing the average composition of 'body-flesh' (muscles, glands, etc.), it is easy to translate results stated in terms of nitrogen into results stated in terms of 'flesh.' Muscle contains approximately 3·4 per cent. nitrogen. Here, with a diet of 480 grammes meat, the dog was still losing a little flesh; it would probably have required from 500 to 600 grammes for equilibrium. The results are graphi cally represented in Fig. 137.

The quantity of **proteid food necessary for nitrogenous equilibrium** varies with the condition of the organism: an emaciated body requires less than a muscular and well-nourished body. The least quantity which would suffice to maintain in nitrogenous equilibrium the famous 35 kilo dog of Voit, even in very meagre condition, was 480 grammes of lean meat, corresponding to 16 grammes of nitrogen, or 35 grammes of urea; that is, about three times the daily loss during starvation. From this lower limit up to 2,500 grammes of meat a day nitrogenous equilibrium could always be attained, the animal putting on some flesh at each increase of diet, until at length the whole 2,500 grammes were regularly used up in the twenty-four hours. A further increase was only checked by digestive troubles. A man, or at least a civilized man, can consume a much smaller amount both absolutely and in proportion to the body-weight. Rubner, with a body-weight of 72 kilos, was able to digest and absorb over 1,400 grammes of lean meat: Ranke, with about the same body-weight, could only use up

1,300 grammes on the first day of his experiment, and less than 1,000 grammes on the third.

So much for a purely proteid diet. When **fat is given in addition to proteid**, nitrogenous equilibrium is attained with a smaller quantity of the latter (7 to 15 per cent. less). A dog which, with proteid food alone, is putting on flesh, will put on more of it before nitrogenous equilibrium is reached if a considerable quantity of fat be added to its diet. Fat, therefore, economizes proteid to a certain extent, as we have already recognised in the case of the starving animal. On the other hand, when proteid is given in large quantities to a fat animal, the consumption of fat is increased; and if the food contains little or none, the body-fat will diminish, while at the same time 'flesh' may be put on. The Banting cure for corpulence consists in putting the patient upon a diet containing much proteid, but little fat or carbohydrate; and the fact just mentioned throws light upon its action.

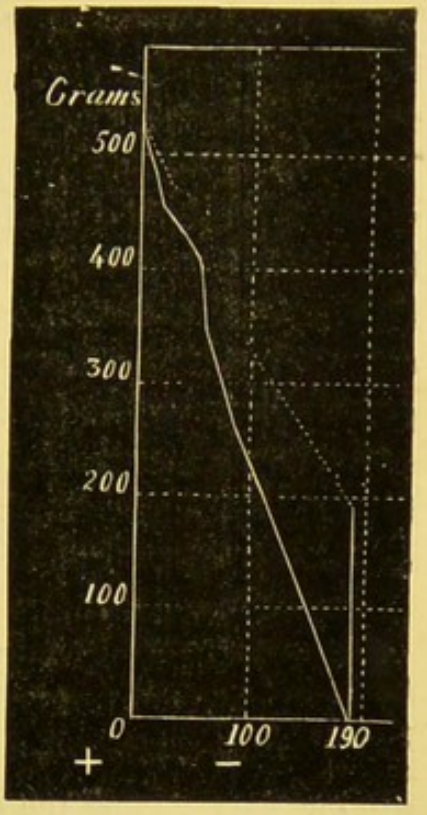


FIG. 137. — CURVES CONSTRUCTED TO ILLUSTRATE NITROGENOUS EQUILIBRIUM (FROM AN EXPERIMENT OF VOIT'S).

The loss of flesh in grammes is laid off along the horizontal axis. The income and expenditure corresponding to a given loss are laid off (in grammes of 'flesh') along the vertical axis. The continuous curve is the curve of income; the dotted curve, of expenditure. With no income at all the expenditure is 190 grammes; with an income of 480 grammes the expenditure is 492 and the loss 12 grammes. Nitrogenous equilibrium is represented as being reached with an income of about 530 grammes; here the two curves cut one another.

All that we have here said of fat is true of **carbo-hydrates**. To a great extent these two kinds of food substances are complementary. Carbo-hydrates economize proteids as fat does, but to a greater extent, and they also economize fat, so that when a sufficient quantity of starch or sugar is given to an otherwise starving animal, all loss of carbon from the body, except that which goes off in the urea still excreted, can be prevented. Of course the animal ultimately dies, because the continuous, though diminished, loss of proteid cannot be made good.

It is only necessary to add that peptone can, while gelatin cannot, completely replace the natural proteids in the food. Fully five-sixths, however, of the necessary nitrogen may be obtained from

gelatin, at least for a few days (Munk); so that gelatin economizes proteid in a much greater degree than fat and carbo-hydrates do.

The Laws of Nitrogenous Metabolism.—Within the limits of nitrogenous equilibrium, which is the normal state of the healthy adult, the body lives up to its income of nitrogen; it lays by nothing for the future. In the actual pinch of starvation the organism becomes suddenly economical. When a plentiful supply of proteid is presented to the starving tissues, they pass at once from extreme frugality to luxury; some flesh may be put on for a short time, some nitrogen may be stored up; but the tissues soon pitch their wants to the new scale of supply, and spend their proteid income as freely as they receive it. This is the first great law of nitrogenous metabolism, and we may formulate it thus: *Consumption of proteid is largely determined by supply* (p. 529).

Various hypotheses have been offered to explain this remarkable fact. It has been suggested that a large proportion of a heavy proteid meal may be broken up into leucin and tyrosin in the alimentary canal, and may pass by this short-cut to the stage of urea without ever joining the proteid of the blood, much less that of the organs. This would be a form of true *luxus-consumption*, of really, and not apparently, wasteful expenditure. The surplus proteids would be shunted out of the main metabolic current at its very source; and it is conceivable that in this short-cut from proteid to urea we have a kind of physiological safety-valve to protect the tissues from the burden of an excessive metabolism. But it is doubtful whether such a process occurs to any great extent in normal digestion. If it does occur, it may bear a different interpretation, and in any case it probably plays only a subordinate part, and cannot of itself explain all the facts of nitrogenous equilibrium.

Then, again, it has been said that the luxus-consumption takes the form of oxidation of the surplus proteids in the blood and lymph. Here the shunting would take place farther down the stream, but still high enough up to shield the tissue elements from excessive metabolic work. This theory of luxus-consumption breaks down, however, under the accumulating evidence that the oxidative changes go on chiefly in the living cells and not in the extra-cellular fluids.

We seem driven to locate the metabolism of actually absorbed proteids, as well as of other food substances, within the cells of the body; and there are three chief views as to the manner of this metabolism:

(*a*) That the actual protoplasmic substance, the living framework of the cell, is comparatively stable; that it does not break down

rapidly; and that only a relatively small and fairly constant amount of food- or circulating-proteid is required to supply the waste of the organ-proteid. It is assumed that the greater part of the former, without being incorporated with the protoplasm, is nevertheless acted upon, rendered unstable, shaken to pieces, as it were, by the whirl of life in the organized framework, the interstices of which it fills.

(*b*) That we have no right to draw a distinction between the consumption of organ- and circulating-proteid; that the whole of the latter ultimately rises to the height of organ-proteid, and passes on to the downward stage of metabolism only through the topmost step of organization. An increase in the supply of nitrogenous material in the blood must, on this view, be accompanied with an increased tendency to the break-up, the dissociation, as Pflüger puts it, of the living substance. The actual organised elements, however, the existing cells, are not supposed to be destroyed; the building remains, for although stones are constantly crumbling in its walls, others are being constantly built in.

(*c*) That the tissue elements themselves are short-lived; that the old cells disappear bodily and are replaced by new cells; and that the whole of the proteids of the food take part in this process of total ruin and reconstruction.

Histological evidence is on the whole strongly against (*c*). Although the cells of certain glands, such as the mammary, sebaceous, and perhaps the mucous glands, are known to break down bodily as an incident of functional activity, in most organs there is no proof of the production of new cells on the immense scale which this theory would require. There is but little evidence which would enable us to decide with confidence between (*a*) and (*b*), although the observation of Munk, that a dog fed with proteids and carbo-hydrates after a thirty days' fast used up less proteid than the minimum in starvation, certainly suggests that, under those conditions at least, the proteids of the food were all built up into the protoplasm of the tissues.

A second law of nitrogenous metabolism is that within normal limits *it is nearly independent of muscular work*, that is to say, the quantity of nitrogen excreted by a man on a given diet is practically the same whether he rests or works. Before this was known it was maintained by Liebig that proteids alone could supply the energy of muscular contraction—that, in fact, proteids were solely used up in the nutrition and functional activity of the nitrogenous tissues, while the non-proteid food yielded heat by its oxidation. As exact experiments multiplied, it was found that muscular work, the production of which is the function of by far the greatest mass of proteid-containing tissue, had little or no effect upon the excretion of urea in the urine. More than

this, it was shown that a certain amount of work accomplished (by Fick and Wislicenus in climbing a mountain) on a non-nitrogenous diet had double the heat equivalent of the whole of the proteid consumed in the body, as estimated by the urea excreted during, and for a given time after, the work. On the assumption that all the urea corresponding to the proteid broken down was eliminated during the time of this experiment, a part at least of the work must have been derived from the energy of non-nitrogenous material. And the increase in the carbon dioxide given off, which is as conspicuous an accompaniment of muscular work as the constancy of the urea excretion, showed that during muscular exertion carbonaceous substances other than proteids—that is to say, fats and carbo-hydrates—are oxidized in greater amount than during rest.

So the pendulum of physiological orthodoxy came full-swing to the other side. Liebig and his school had taught that proteids alone were consumed in functional activity; the majority of later physiologists have denied to the proteids any share whatever in the energy which appears as muscular contraction. The proteids, they say, 'repair the slow waste of the framework of the muscular machine, replace a loose rivet, a worn-out belt, as occasion may require; the carbo-hydrates and fats are the fuel which feeds the furnaces of life, the material which, dead itself, is oxidized in the interstices of the living substance, and yields the energy for its work.'

Now, it is a singular circumstance, and full of instruction for the ingenuous student of science, that the facts which have been supposed absolutely to disprove the older theory, and absolutely to establish its modern rival, do neither the one thing nor the other. The fact—and it is a fact—that the excretion of nitrogen is but little affected by muscular contraction, does not prove that none of the energy of muscular work comes from proteids; the fact that, under certain conditions, some of the muscular energy must apparently come from non-nitrogenous materials, does not prove that these are the normal source of it all. The distinction has again been made too absolute. The pendulum

must again swing back a little; and the recent experiments of Pflüger and others have actually set it moving.

In the first place, it is not perfectly correct to say that work causes no increase in the excretion of nitrogen; excessive work in man, and work, severe but not excessive, in a flesh-fed dog (Pflüger), do cause somewhat more nitrogen to be given off. On the first day of work the increase is always much less than on the second and third; and on the first and second rest days, following work, the elimination of nitrogen is still increased. After excessive exercise in man not only is the urea increased, but also the ammonia, kreatinin, and if the subject is in poor training, the uric acid and xanthin bases (Paton, Stockman, etc.). Moderate exercise causes no increase on the first day, but a slight increase on the second.

In the second place, even if the excretion of nitrogen were entirely unaffected by work, this would not prove that none of the energy of the work comes from proteids. For the animal body is a beautifully-balanced mechanism which constantly adapts itself to its conditions. If it saves proteids by the use of fat and carbo-hydrates when its nitrogenous food is restricted or its organ-proteid runs low, it may also, when called upon to labour, save proteids from lower uses to devote them to muscular contraction. In this case the excretion of nitrogen would not necessarily be altered; the proteids which, in the absence of work, would have been oxidized within the muscular substance or elsewhere, their energy appearing entirely as heat, may, when the call for proteid to take the place of that broken down in muscular contraction arises, be diverted to this purpose.

Thirdly, there is no doubt that a dog fed on lean meat may go on for a long time performing far more work than can be yielded by the energy of fat and carbo-hydrates occurring in traces in the food, or taken from the stock in the animal's body at the beginning of the period of work. A large portion, and perhaps the whole, of the work, must in this case be derived from the energy of the proteids (Pflüger). On the other hand, it is well established that when fats and carbo-hydrates are present in sufficient

quantity in the tissues or the food, they constitute the main source of the energy of muscular contraction (p. 584).

Experience has shown that the minimum quantity of nitrogen required in the food of a man whose daily work involves hard physical toil is higher than the minimum required by a person leading an easy sedentary life. This is evidently in accordance with the view that proteid is actually used up in muscular contraction; but it is not inconsistent with the opposite view. For the body of a man fit for continuous hard labour has a greater mass of muscle to feed than the body of a man who is only fit to handle a composing-stick, or drive a quill, or ply a needle; and the greater the muscular mass, the greater the muscular waste. But if an animal just in nitrogenous equilibrium on a diet of lean meat when doing no work, is made to labour day after day, it will lose flesh unless the diet be increased. This must mean that some of the proteid is being diverted to muscular work, and that the balance is not sufficient to keep up the original mass of 'flesh' (see p. 479).

(2) **Income and Expenditure of Carbon.**—This division of the subject has been necessarily referred to in treating of the nitrogen balance-sheet, and may now be formally completed.

Carbon Equilibrium.—A body in nitrogenous equilibrium may or may not be in carbon equilibrium. It has been repeatedly pointed out that the continued loss or gain of carbon by an organism in nitrogenous equilibrium means the loss or gain of fat; and, since the quantity of fat in the body may vary within wide limits without harm, carbon equilibrium is less important than nitrogen equilibrium. It is also less easily attained when the carbon of the food is increased, for, although the consumption of fat is to a certain extent increased with the supply of fat or fat-producing food, there is by no means the same prompt adjustment of expenditure to income in the case of carbon as in the case of nitrogen.

Carbon equilibrium can be obtained in a flesh-eating animal, like a dog, with an exclusively proteid diet; but a far higher minimum is required than for nitrogenous equilibrium alone. Voit's dog required at least 1,500

grammes of meat in the twenty-four hours to prevent his body from losing carbon. For a man weighing 70 kilos, the daily excretion of carbon on an ordinary diet is about 300 grammes. More than 2,000 grammes of lean meat would be required to yield this quantity of carbon; and, even if such a mass could be digested and absorbed, more than three times the necessary nitrogen would be thrown upon the tissues.

Not only may carbon equilibrium be maintained for a short time in a dog on a diet containing fat only, or fat and carbo-hydrates, but the expenditure of carbon may be less than the income, and fat may be stored up. But, of course, if this diet is continued, the animal ultimately dies of nitrogen starvation.

So far we have spoken only of the income and expenditure of carbon and nitrogen; and from these data alone it is possible to deduce many important facts in metabolism, since, knowing the elementary composition of proteids, fats and carbo-hydrates, we can, on certain assumptions, translate into terms of proteids or fat the gain or loss of an organism in nitrogen and carbon, or in carbon alone. But the hydrogen and oxygen contained in the solids and water of the food, and the oxygen taken in by the lungs, are just as important as the carbon and nitrogen; it is just as necessary to take account of them in drawing up a complete and accurate balance-sheet of nutrition. Fortunately, however, it is permissible to devote much less time to them here, for when we have determined the quantitative relations of the absorption and excretion of the carbon and nitrogen, we have also to a large extent determined those of the oxygen and hydrogen.

(3) **Income and Expenditure of Oxygen and Hydrogen.**—The oxygen absorbed as gas and in the solids of the food is given off chiefly as carbon dioxide by the lungs; to a small extent as water by the lungs, kidneys, and skin; and as urea and other substances in the urine and fæces. The hydrogen of the solids of the food is excreted in part as urea, but in far larger amount as water. The hydrogen and oxygen of the ingested water pass off as water, without, so

far as we know, undergoing any chemical change, or existing in any other form within the body. But it is important to recognise that although none of the water taken in as such is broken up, some water is manufactured in the tissues by the oxidation of hydrogen. We have already considered (p. 225) the gaseous interchange in the lungs, and we have seen that all the oxygen taken in does not reappear as carbon dioxide. It was stated there that the missing oxygen goes to oxidize other elements than carbon, and especially to oxidize hydrogen. We have now to explain more fully the cause of this oxygen deficit.

The Oxygen Deficit.—The carbo-hydrates contain in themselves enough oxygen to form water with all their hydrogen; they account for a part of the water-formation in the body, but for none of the oxygen deficit.

The fats are very different; their hydrogen can be nothing like completely oxidized by their oxygen. A gramme of hydrogen is contained in 8·5 grammes of dry fat, and needs 8 grammes of oxygen for its complete combustion. Only 1 gramme of oxygen is yielded by the fat itself; so that if a man uses 100 grammes of fat in twenty-four hours, rather more than 80 grammes of the oxygen taken in must go to oxidize the hydrogen of the fat.

The proteids also contribute to the deficit. In 100 grammes of dry proteids there are 15 grammes of nitrogen, 7 grammes of hydrogen, and 21 grammes of oxygen. The carbon does not concern us at present. The 33 grammes of urea, corresponding to 100 grammes of proteid, contain 15 grammes of nitrogen, a little more than 2 grammes of hydrogen, and a little less than 9 grammes of oxygen. There remain 5 grammes of hydrogen and 12 grammes of oxygen. But 5 grammes of hydrogen need for complete combustion 40 grammes of oxygen; therefore 28 grammes of the oxygen taken in must go to oxidize the hydrogen of 100 grammes of proteid. Taking 140 grammes of proteid as the amount in the diet of a man, we get 39 grammes as the required quantity of oxygen. This, added to the 80 grammes needed for the hydrogen of the fat, makes a total of, say, 120 grammes, equivalent to about 85 litres of oxygen. A small amount of oxygen also goes to oxidize the sulphur of proteids. With a diet containing less fat and proteid and more carbo-hydrate, the oxygen deficit would of course be less.

The Production of Water in the Body.—One gramme of hydrogen corresponds to 9 grammes of water. In 140 grammes of proteids and 100 grammes of fat there are, in round numbers, 22 grammes of hydrogen; in 350 grammes of starch, 21·5 grammes. With this diet, 43·5 grammes of hydrogen are oxidized to water within the body in twenty-four hours, corresponding to a water-production of 391 grammes, or 15 to 20 per cent. of the whole excretion of water. It has been observed that during starvation the tissues sometimes

become richer in water, even when none is drunk. The only explanation is, that the elimination of water does not keep pace with the rate at which it is produced from the hydrogen of the broken-down tissue-substances, or set free from the solids with which it is (physically?) united.

Inorganic Salts.—The inorganic salts of the excreta, like the water, are for the most part derived from the salts of the food, which do not in general undergo decomposition in the body. A portion of the chlorides, however, is broken up to yield the hydrochloric acid of the gastric juice. Within the body some of the salts are intimately united to the proteids of the tissues and juices, some simply dissolved in the latter. The chlorides, phosphates and carbonates are the most important; the potassium salts belong especially to the organized tissue elements, the sodium salts to the liquids of the body; calcium phosphate and carbonate predominate in the bones. The amount and composition of the ash of each organ only changes within narrow limits. In hunger the organism clings to its inorganic materials, as it clings to its proteids; the former are just as essential to life as the latter. In a starving animal chlorine almost disappears from the urine at a time when there is still much chlorine in the body; only the inorganic salts which have been united to the used-up proteids are excreted, so that a starving animal never dies for want of salts.

On the other hand, when an animal is fed with a diet as far as possible free from salts, but otherwise sufficient, it dies of *salt-hunger*. The blood first loses inorganic material, then the organs. The total loss is very small in proportion to the quantity still retained in the body; but it is sufficient to cause the death of a pigeon in three weeks, and of a dog in six, with marked symptoms of muscular and nervous weakness. A **deficiency of lime salts** causes changes particularly in the skeleton, although the nutrition of the rest of the body is also interfered with. These changes are of course most marked in young animals, in which the bones are growing rapidly. In pigeons on a diet containing very little calcium the bones of the skull and the sternum become extremely thin and riddled with holes, while the bones concerned in movement scarcely suffer at all (E. Voit).

It is not indifferent in what form the calcium is taken, nor can it be replaced to any great extent by other earthy bases, as magnesium or strontium. Weiske fed five young rabbits of the same litter on oats, a food relatively poor in calcium. One of the rabbits received in addition calcium carbonate, another calcium sulphate, a third magnesium carbonate, and a fourth strontium carbonate. At the end of a certain time it was found that the skeleton of the rabbit fed with calcium carbonate was the heaviest and strongest of all, and contained the greatest proportion of mineral matter. Then came the rabbit fed with calcium sulphate. The animal which received only oats had the worst-developed skeleton; the condition of the animals fed with magnesium and strontium carbonates was but little better.

Milk is a food rich in calcium and also in phosphorus, a circumstance evidently related to the rapid development of the skeleton in the young child. As in the other natural foods, the calcium and phosphorus are partly in the form of organic compounds, united with the proteids and with the nucleo-proteid, caseinogen, and partly in the form of inorganic salts. Both of these elements are more easily assimilated by the body in the organic than in the inorganic form. And the same is true of **iron**, which exists in organic combination in the bran of wheat, in the hæmoglobin of the blood and of muscular fibres, in the nuclei of most cells, vegetable and animal, and conspicuously in the nuclein of the yolk of the egg. It was supposed by Bunge that only such organic compounds of iron could be absorbed, and that the undoubted benefit derived from the administration of inorganic iron compounds, such as ferric chloride, in anæmia, was due not to their direct absorption, but to their shielding the organic compounds from the attack of the sulphuretted hydrogen in the intestine (p. 359). But this theory has been shown to be inconsistent with the facts. For instance, after the administration of salts of iron, the iron in the blood, liver, spleen, and other organs increases, but there is no accumulation of iron in the liver of an animal to which salts of manganese have been given, although these are equally decomposed by sulphuretted hydrogen. It is certainly the case, however, that under ordinary conditions all the iron that the body receives or needs is taken in the form of organic compounds, since there is no inorganic iron in the natural food-substances. Stockman, from careful estimations of the

quantity of iron in a number of actual dietaries, finds that it only amounts to about 8 to 10 milligrammes a day. He concludes that the greater part of it must be retained in the body and used over and over again.

Milk is poor in iron, but this does not hinder the development of the young child, except when it is weaned too late, when it is apt to become anæmic, unless the milk is supplemented with a food rich in iron, such as yolk of egg. The explanation is that the fœtus, especially in the last three months of intra-uterine life, accumulates a store of iron in the liver and other organs; so that, in proportion to its body-weight, it is at birth several times richer in iron than the adult. This iron, of course, all comes from the mother, and the loss is not exactly balanced by the excess of iron in her food; certain of her organs, the spleen, for instance, though not apparently the liver, are impoverished as regards their content of iron.

(4) **Dietetics.** — There are two ways in which we can arrive at a knowledge of the amount of the various food substances necessary for an average man: (*a*) By considering the diet of large numbers of people doing fairly definite work, and sufficiently, but not extravagantly, fed—*e.g.*, soldiers, gangs of navvies, or plantation labourers; (*b*) by making special experiments on one or more individuals.

Voit, bringing together a large number of observations, concluded that an 'average workman,' weighing 70 to 75 kilos, and working ten hours a day, required in the twenty-four hours 118 grammes proteid, 56 grammes fat, and 500 grammes carbo-hydrate, corresponding to about 18·3 grammes nitrogen and at least 328 grammes carbon.

Ranke found the following a sufficient diet for himself, with a body-weight of 74 kilos:

Proteids	100 grammes.
Fat	100 „
Carbo-hydrates	240 „

This corresponds to only 14 grammes nitrogen and, say, 230 grammes carbon.

A German soldier in the field receives on the average

Proteids	151 grammes.
Fat	46 „
Carbo-hydrates	522 „

representing about 21 grammes nitrogen and 340 grammes carbon. But the diet of certain miners (Steinheil) and lumberers (Liebig) contained respectively 133 and 112 grammes proteid, 113 and 309 (!) grammes fat, and 634 and 691 grammes carbo-hydrates. The diet of prize-fighters and of athletes in training is richer in proteid than any of these. So that a definite and typical diet for severe labour does not exist. And although perhaps the hardest work ever done in the world is to break athletic records, to cut and handle timber, to mine coal and to make war, the diet on which these things are accomplished is very variable.

Nevertheless, we may conclude that, for a man of 70 kilos, doing fairly hard, but not excessive work, 20 grammes nitrogen and 300 grammes carbon are a sufficient, and indeed a liberal, allowance, while many men are sufficiently fed with 15 grammes of nitrogen. The 20 grammes nitrogen will be contained in 140 grammes dry proteid, which will also yield 70 grammes of the required carbon. The balance of 230 grammes carbon could theoretically be supplied *either* in 517 grammes starch *or* in 300 grammes fat. But it has been found by experiment and by experience (which is indeed a very complex and proverbially expensive form of experiment) that for civilized man a mixture of these is necessary for health, although the nomads of the Asian steppes, and the herdsmen of the Pampas, are said to subsist for long periods on flesh alone, and a dog can live very well on proteids and fat. The proportion of fat and carbo-hydrates in a diet may, however, be varied within wide limits. Probably no 'work' diet should contain much less than 50 grammes of fat, but twice this amount would be better; 100 grammes fat give about 75 grammes carbon, so that from proteids and fat we have now got 145 grammes of the necessary 300, leaving 155 grammes carbon to be taken in 350 grammes starch, or an equivalent amount of cane-sugar or glucose. Adding 30 grammes inorganic salts, we can put down as the solid portion of a good normal diet for a man of 70 kilos:

140	grammes	proteids	$= \frac{1}{500}$ of body-weight.
100	„	fat	$= \frac{1}{700}$ „
350	„	carbo-hydrates	$= \frac{1}{200}$ „
30	„	salts.	
620			

Now, knowing the composition of the various food stuffs we can easily construct a diet containing the proper quantities of nitrogen and carbon, by using a table such as the following:

	Quantity required to yield 20 grms. N.	Quantity required to yield 300 grms. C.	N. in 100 grms.	C. in 100 grms.	Proteid in 100 grms.	Fat in 100 grms.	Carbohydrate in 100 grms.	Water in 100 grms.
Cheese* (Gruyère)	400	770	5	39	31	31	—	34
Peas (dried)	570	840	3·5	35·7	22	2	55	15
Lean meat	590	2230	3·4	13·5	21	3·5	—	74
Wheat-flour	870	750	2·3	39·8	12	2	70	15
Oatmeal	760	740	2·6	40·3	13	5·5	65	15
Eggs	1040	2040	1·9	14·7	11·5	12	—	75
Maize	1080	730	1·85	40·9	10·5	7	65	15
Wheat bread	1590	1340	1·25	22·4	8	1·5	49	40
Rice	2040	820	0·9	36·6	5	1	83	10
Milk	3170	4250	0·6	7	4	4	5	85
Potatoes	5000	2860	0·4	10·5	2	0·15	21	75
Good butter	13000	430	0·15	69	1	90	—	8

Economic and social influences—prices and habits—and not purely physiological rules, fix the diet of populations. The Chinese labourer, for example, lives on a diet which no physiologist would commend. In order to obtain 20 grammes nitrogen or 140 grammes proteid, he must consume nearly 2,000 grammes rice, which will yield 700 grammes carbon, or twice as much as is required; but if the Chinese labourer could not live on rice, he could not live at all. The Irish peasant is even in worse case; he must consume 5 kilos of potatoes to obtain his 20 grammes nitrogen, while little more than half this amount would furnish the necessary 300 grammes carbon.† A man attempting to live on flesh alone would be well fed as regards nitrogen with 600 grammes of meat, but nearly four times as much would be required to yield 300 grammes carbon. Oatmeal and wheat-flour contain nitrogen and carbon in nearly the right proportions (1 N : 15 C), oatmeal being rather the better of the two in this respect; and the best-fed labouring populations of Europe still live largely on wheaten bread, while, one hundred years ago, the Scotch peasant still cultivated the soil, as the Scotch Reviewer the Muses, 'on a little oatmeal.' But although bread may, and does, as a rule, form the great staple of diet, it is not of itself sufficient.

* A cheese manufactured from whole milk, curdled before the cream has had time to rise, and therefore rich in fat.

† Of course a diet consisting, week in week out, *entirely* of potatoes or rice, would represent an extreme case. A certain amount of the necessary nitrogen is often obtained even by the poorest populations, in the form of fish, milk, eggs or bacon.

We may take 500 grammes of bread and 250 grammes of lean meat as a fair quantity for a man fit for hard work. Adding 500 grammes milk, 75 grammes oatmeal (as porridge), 30 grammes butter, 30 grammes fat (with the meat, or in other ways), and 450 grammes potatoes, we get approximately 20 grammes nitrogen and 300 grammes carbon contained in 135 grammes proteid, rather less than 100 grammes fat, and somewhat over 400 grammes carbo-hydrates. Thus :

	N.	C.	Proteids.	Fat.	Carbo-hydrates.	Salts.
(9 oz.) 250 grms. lean meat	8	33	55	8·5	—	4
(18 oz.) 500 grms. bread -	6	112	40	7·5	245	6·5
(¾ pint) 500 grms. milk -	3	35	20	20	25	3·5
(1 oz.) 30 grms. butter -	—	20	—	27	—	0·5
(1 oz.) 30 grms. fat - -	—	22	—	30	—	—
(16 oz.) 450 grms. potatoes	1·5	47	10	—	95	4·5
(3 oz.) 75 grms. oatmeal -	1·7	30	10	4	48	2
	20·2	299	135	97	413	21

This would be a fair 'hard work' diet for a well-nourished labourer. But the great elasticity of dietetic formulæ is shown by comparing the ration of the English and German soldier as given in the following tables :

*Ration of the English Soldier.**

Bread - - - -	680 grammes.
Meat - - - -	340 ,,
Vegetables - - -	226 ,,
Potatoes - - - -	453 ,,
Milk - - - -	92 ,,
Sugar - - - -	37·7 ,,
Coffee - - - -	9·4 ,,
Tea - - - -	4·6 ,,
Salt - - - -	7 ,,

Ration of the German Soldier.

Peace.		War.	
Bread - - -	750 grammes.	Bread - - -	750 grammes.
Meat - - -	150 ,,	Biscuit - - -	500 ,,
Rice - - -	50 ,,	Meat - - -	375 ,,
or barley groats -	120 ,,	Smoked meat -	250 ,,
Legumes - -	230 ,,	or fat - - -	170 ,,
Potatoes - -	1500 ,,	Rice - - -	125 ,,
		or barley groats -	125 ,,
		Legumes - -	250 ,,

In prisons the object is to give the minimum amount of the

* This is given in Parkes's 'Practical Hygiene' as the usual dietary of the English soldier on home service. The free ration includes only one pound of bread, but the soldier buys, on the average, an extra half-pound.

plainest food which will suffice to maintain the prisoners in health A 'hard work' prison diet in Munich was found to contain 104 grammes proteids, 38 grammes fat, and 521 grammes carbo-hydrates; a 'no work' diet, only 87 grammes proteids, 22 grammes fat, and 305 grammes carbo-hydrates. Here we recognise the influence of price; carbon can be much more cheaply obtained in vegetable carbo-hydrates than in animal fats; the cheapest possible diet contains a minimum of fat and proteids.

Many poor persons live on a diet which would not maintain a strong man, for an emaciated body has a smaller mass of flesh to keep up, and therefore needs less proteid; it can do little work, and therefore needs less food of all kinds. A London needlewoman, according to Playfair, subsists, or did subsist, thirty years ago, on 54 grammes proteid, 29 grammes fat, and 292 grammes carbo-hydrates. But this is the irreducible minimum of the deepest poverty; and a woman, with a smaller mass of flesh and leading a less active life than a man, requires less food of all sorts. Even the Trappist monk, who has reduced asceticism to a science, and, instead of eating in order to live, lives in order not to eat, consumes, according to Voit, 68 grammes proteid, 11 grammes fat, and 469 grammes carbo-hydrates; but manual labour is a part of the discipline of the brotherhood, and this must be still above the lowest subsistence diet.

A growing child needs far more food than its weight alone would indicate; for, in the first place, its income must exceed its expenditure so that it may grow; and, in the second place, the expenditure of an organism is pretty nearly proportional, not to its mass, but to its surface. Now, speaking roughly, the cube of the surface of an animal varies as the square of the mass; when the weight is doubled, the surface only becomes $\sqrt[3]{4}$, or one and a half times as great. The surface of a boy of six to nine years, with a body-weight of 18 to 24 kilos, is two-fifths to one-half that of a man of 70 kilos; and he should have about half as much food as the man—say, 70 grammes proteids, 40 grammes fat, and 200 grammes carbo-hydrates. A child of four months, weighing 5·3 kilos, consumed *per diem* food containing ·6 gramme nitrogen per kilo of body-weight, or 3·18 grammes nitrogen altogether, as against a daily consumption of only ·275 gramme nitrogen per kilo in a man of 71 kilos (Voit) (p. 512).

An infant for the first seven months should have nothing except **milk**. Up to this age vegetable food is unsuited to it; it is a purely carnivorous animal. By careful observations on the amount of carbon dioxide and nitrogen excreted by a child nine weeks old, fed exclusively on its mother's milk, it has been shown that the absorption and assimilation of milk in the infant is very complete, over 91 per cent. of the total energy being utilized; while an adult, taking as much milk as is necessary for the maintenance of nitrogenous equilibrium, does not utilize at most more than 84 per cent. **Human milk** contains about 2 per cent. of proteid (mainly caseinogen), 3 per cent. of fat, 5 or 6 per cent. of carbo-hydrate (lactose or milk-sugar), and from ·2 to ·3 per cent. of salts. Cow's milk contains

about 4 per cent. of proteid, 4 to 6 per cent. of fat, 4 per cent. of lactose, and ·7 per cent. of salts. When given to infants it should be diluted with water, and some sugar should be added to it. Ass's milk has about the same amount of proteid, lactose and salts as human milk, but less than half as much fat. It is very well borne and very completely absorbed.

As to **the place of water and inorganic salts in diet**, it is neither necessary nor practicable to lay down precise rules. In most well-settled countries they cost little or nothing; very different quantities can be taken and excreted without harm; and both economics and physiology may well leave every man to his taste in the matter. Salt is indeed for the most part used, not as a special article of diet, but as a condiment to give a relish to the food, just as a great deal more water than is actually needed is often drunk in the form of beverages. It is certain that the quantity of salt required, in addition to the salts of the food, to keep the inorganic constituents of the body at their normal amount, is very small. A 30-kilo dog obtains in his diet of 500 grammes of lean meat only 0·6 gramme sodium chloride, and needs no more. An infant in a litre of its mother's milk, which is a sufficient diet for it, gets only 0·8 gramme sodium chloride. Bunge, however, has shown that the proportion of potassium and sodium salts in the food is a factor in determining the quantity of sodium chloride required. A double decomposition takes place in the body between potassium phosphate and sodium chloride, potassium chloride and sodium phosphate being formed and excreted; and the loss of sodium and chlorine in this way depends on the relative proportions of potassium and sodium in the food. In most vegetables the proportion of potassium to sodium is much greater than in animal food, so that vegetable-feeding animals and men as a rule desire and need relatively great quantities of sodium chloride. But it is stated that the inhabitants of a portion of the Soudan use potassium chloride instead of sodium chloride, obtaining the potassium salt by burning certain plants which leave an ash poor in carbonates, and then extracting the residue with water and evaporating (Dybowski). A beef-eating English soldier

consumes about 7 grammes (¼ oz.), a vegetarian Sepoy about 18 grammes (⅔ oz.), of common salt per day.

Wine, beer, tea, coffee, cocoa, etc., belong to the important class of **stimulants.** Some of them contain small quantities of food substances, but these are of secondary interest. In beer, for example, there are traces of proteids, dextrin, and sugar. But 18 litres of beer would be required to yield 20 grammes nitrogen, and 12 litres to give 300 grammes carbon; and nobody, except a German corps student, could consume such quantities.

In some cocoas there is as much as 50 per cent. of fat, 4 per cent. of starch, and 13 per cent. of proteids; and in the cheaper cocoas much starch is added. Still, a large quantity of the ordinary infusion would be needed for a satisfying meal. Frederick the Great, indeed, in some of his famous marches dined off a cup of chocolate, and beat combined Europe on it; but his ordinary menu was much more varied and substantial.

The great social and hygienic evils connected with the abuse of **alcohol**, as well as its applications in therapeutics, render it necessary, or at least permissible, to state a little more fully, though only in the form of summary, some of the chief conclusions that may be drawn as to its action and uses.

(1) In small quantities alcohol is oxidized in the body, a little of it, however, being excreted unchanged in the breath and urine. It is therefore to some extent a food substance, although it is never taken for the sake of the energy its oxidation can supply, but always as a stimulant.

(2) There is no reason to suppose that this energy cannot be utilized as a source of work in the body. Heat can certainly be produced from it, but this is far more than counterbalanced by the increase in the heat loss which the dilatation of the cutaneous vessels caused by alcohol brings about.

(3) It is a very valuable drug, when judiciously employed, as a cardiac and general stimulant in certain diseases, *e.g.*, pneumonia.

(4) Alcohol is occasionally of use in disorders not amounting to serious disease, *e.g.*, in some cases of slow and difficult digestion. In these cases it may act by increasing the flow of certain of the digestive secretions, as saliva and gastric juice. This effect seems to more than counterbalance the retarding influence which, except when well diluted, it exerts on the chemical processes of digestion.

(5) Alcohol is of no use for healthy men.

(6) Alcohol in strictly moderate doses, properly diluted and especially when taken with the food, is not harmful to healthy men, living and working under ordinary conditions.

(7) Recent experience goes to show that in severe and continuous exertion, coupled with exposure to all weathers, as in war and in exploring expeditions, alcohol is injurious, and it is well known that it must be avoided in mountain climbing.

Tea, coffee, and cocoa are more suitable stimulants for healthy persons, because they are less dangerous than alcohol, and they leave no unpleasant effects behind them. But it should be remembered that there is no stimulant which is not liable to be abused. It has been shown by ergographic experiments (p. 621) that, like alcohol, tea, coffee, maté, and cola nut, which all contain the alkaloid theine or caffeine, restore the power of performing muscular work after exhaustion, but only if food has been recently or is simultaneously taken.

Certain organic acids contained in fresh vegetables, although neither in the ordinary sense foods nor condiments, seem to be necessary for the maintenance of health, for in circumstances in which these cannot be obtained for long periods, scurvy is liable to break out. It is prevented by the use of lime or lemon-juice, in which citric and a trace of malic acid are contained.

INTERNAL SECRETION.

It is long since Caspar Friedrich Wolff expressed the idea that 'each single part of the body, in respect of its nutrition, stands to the whole body in the relation of an excreting organ,' and thus emphasized the importance of substances produced by the activity of one kind of cell for the normal metabolism of another. But it is only in recent years that it has become possible to illustrate this mutual relation by any large number of experimental facts.

Certain of the substances taken in from the blood by the liver find their way, after undergoing various changes, into the biliary capillaries, and are excreted as bile; certain other substances, such as sugar and the precursors of urea, are taken up by the hepatic cells, transformed and sometimes stored for a time within them, and then given out again to the blood. Bile we may call the *external secretion* of the liver, glycogen and urea constituents of its *internal secretion*. In one sense it is evident that all tissues, whether glands in the morphological sense or not, may be considered as manufacturing an internal secretion. For everything that an organ absorbs from the blood and lymph it gives out to them again in some form or other except in so far as it

forms or separates a secretion that passes away by special ducts. But it is usual to employ the term only in relation to organs of glandular build, whether provided with ducts or not.

It is known that in the case of the liver the internal secretion is more important than the external, for an animal cannot live without its liver, while it may be but little affected by the continuous escape of the bile through a fistulous opening. The internal secretions of the **pancreas** and the **kidney** are also indispensable. For when the pancreas is excised death follows in many species of animals, and especially in carnivorous animals; and in man severe and ultimately fatal diabetes is often associated with pancreatic disease, while the mere loss of the pancreatic juice through a fistula does not necessarily shorten life, although the absorption of fat is seriously interfered with. And when the half or two-thirds of one kidney and the whole of the other have been removed from a dog by successive operations (Bradford), death also ensues, although the quantity both of water and urea excreted by the fragment of renal substance that remains is far above the normal (polyuria). The cause of death in both these cases seems to be a profound disturbance of metabolism, of which the most significant token after extirpation of the pancreas is the increased production of sugar and its appearance in the urine, and after interference with the kidneys the increased production of urea. Both in pancreatic diabetes and in experimental polyuria the destruction of proteids is increased. When only one kidney is excised the other hypertrophies and no ill effects ensue; nor does diabetes appear after partial removal of the pancreas, so long as a comparatively small fraction (one quarter or one-fifth) of it is left, even when this remnant is transplanted from its original position and grafted in the peritoneal cavity or indeed under the skin. Although as yet we are entirely ignorant of the manner in which the kidney* and the pancreas influence the

* The announcement of Tigerstedt and Bergmann that extracts of the kidney when injected into the veins of an animal cause a rise of arterial blood-pressure, essentially through direct action on the peripheral vasomotor mechanism, although it may possibly, as they suggest, have some bearing on the rise of pressure and consequent hypertrophy of the heart associated with certain renal diseases, does not throw any light on the relation of the kidney to proteid metabolism.

metabolism of the body, it is impossible to doubt, in view of the facts we have mentioned, that both of these organs, like the liver, in addition to carrying on the exchanges necessary for the preparation of their ordinary or external secretions, have other important relations with the circulating fluids, giving to them or taking from them substances on the manufacture or destruction of which the normal metabolic processes depend. Schäfer has suggested that the seat of the internal secretion of the pancreas is the very vascular epithelioid tissue which is peculiar to this gland, and occurs in islands between the alveoli. For animals survive the complete atrophy of the ordinary secreting epithelium caused by the injection of paraffin into the ducts; no sugar appears in the urine, and the grafting of such an atrophied organ prevents pancreatic diabetes.

Ligation, or the establishment of a fistula, of the thoracic duct, causes glycosuria in dogs. It is possible that this is really a mild form of pancreatic diabetes, due to interference with the supply of the internal secretion of the pancreas, or of that part of it which reaches the blood by the lymph-stream (Tuckett).

Sexual Organs.—The influence of castration in preventing the physical and psychical changes that normally occur at puberty is no doubt also, in part at least, due to the loss of the internal secretion of the **testes.** In partially castrated cocks it was seen that so long as a portion of one testicle remained, the male characters were preserved, but after removal of this residue the comb and wattles withered in a few weeks (Hanau). The exact experiments of Loewy and Richter on the metabolism of bitches before and after castration throw light upon the changes which follow that operation, and afford decisive proof that they are connected with the absence of substances specific to the **ovary.** They conclude that in the castrated animal the oxidative energy of the cells is lessened. The oxygen consumption sinks, even although proteid is laid on and the total amount of active tissue thus increased. This lessening of the oxidative power is due to the loss of ovarian substance, for the administration of an extract of the ovary (oophorin) not only neutralizes it, but actually causes an increase in the gaseous metabolism to far

above the original amount, while it has no effect on the metabolism of the uncastrated animal. Oophorin also brings about a notable increase in metabolism in the castrated male dog, while, curiously enough, extract of testicle causes only a small increase. But the orchitic extract is not without influence in other ways. It certainly increases the capacity for muscular work, as tested by the ergograph (p. 621), and this distinct physiological action is sufficient to encourage the hope that it may possess some therapeutic value, although far from what has been claimed for it by its more enthusiastic advocates.

But the capacity of manufacturing internal secretions of high importance can neither be attributed to all glands with ducts nor denied to all other organs. For the salivary, mammary and gastric glands may be completely removed without causing any serious effects, while death follows excision of the, so far as mere bulk is concerned, apparently insignificant masses of tissue in the ductless thyroid, suprarenal and pituitary bodies.

Thyroid.—When the thyroid is completely removed, symptoms and pathological changes ensue which differ in different species of animals. In man, after excision of the whole thyroid for goitre, an operation not infrequently performed before the consequences of thyroidectomy were known, the condition called cachexia strumipriva supervenes. The symptoms resemble those of the disease known as myxœdema, in which the characteristic anatomical change is an increase (a hyperplasia) of the connective tissue in and under the true skin. Newly formed connective tissue always contains an excess of mucin, and for this reason in the early stages of myxœdema there is somewhat more than the usual amount of that substance in the subcutaneous tissue. The skin is dry, and the hair falls off. The features are swollen and heavy; the movements clumsy, trembling, and often spasmodic. As the disease progresses, the mental powers deteriorate too; the patient becomes stupid and slow, and perhaps, at last, imbecile. When the gland is extensively affected in early life a peculiar condition of idiocy (cretinism) results. Monkeys, after removal of the thyroids, develop symptoms resembling those of myxœdema. Carnivorous animals do

not, as a rule, survive the operation long enough for the changes in the skin to be developed (p. 530). In the dog and cat muscular weakness soon becomes marked; tremors of central origin appear, and increase in severity until at length they culminate in general spasmodic attacks. The tissues waste, the temperature becomes subnormal, and this is associated with changes in the heat regulation (p. 512). Dogs and cats often die in a few days after the operation; occasionally they survive some months, and in rare cases a year. In young animals the symptoms come on more rapidly, and are more severe than in old. If a portion of the thyroid be left, or a graft be made, these effects are entirely obviated. Not only so, but the administration of extracts of the thyroid glands by subcutaneous injection, or the glands themselves by the mouth, brings about a cure, permanent so long as the thyroid treatment is continued, in cases of myxœdema in man, and sometimes, but with far less certainty, prevents the development of the symptoms in animals or removes them when they have appeared. The same is true, although in a minor degree, of certain compounds rich in iodine, for instance the so-called iodothyrin or thyroiodin, which have been extracted from the organ. While the precise *rôle* played by the thyroid in the economy remains obscure, it is evident that its secretion is of the utmost importance, whether it be solely the quasi-external secretion of 'colloid,' containing the iodothyrin, that collects in its alveoli and slowly passes out of them by the lymphatics, or perhaps in addition some other substance, which, like the glycogen of the liver, never finds its way into the lumen of the gland tubes at all.

As in the case of other glands forming an internal secretion, it has been debated whether the function of the thyroid is to destroy toxic bodies or to form substances indispensable or advantageous to the organism. It is probable that it does both. The intra-vascular injection of iodothyrin (or extracts of the gland) increases the excitability of the inhibitory mechanism of the heart and of the depressor, and diminishes that of the augmentor and vaso-constrictor apparatus. A fall of blood-pressure takes place, partly due to the slowing

of the heart and partly to the dilatation of the vessels. Neutral inorganic salts of iodine, such as sodium iodide, have the opposite effect, paralyzing the vagus and depressor fibres, increasing the excitability of the augmentors and vaso-constrictors, and causing in both ways an increase of blood-pressure. Iodothyrin, in fact, acts much as muscarin does, and iodine salts act like atropia. Cyon bases upon these results the theory that it is the office of the thyroid, although not necessarily the only one, to transform into an organic combination the iodine salts taken into the body, which otherwise would act as poisons to the nerves of the heart and bloodvessels. Not only are the iodine salts thus rendered harmless, but the iodothyrin formed by their union with proteids or proteid-like bodies is beneficial to the action of the vascular mechanism. He attributes the circulatory symptoms that follow removal of the thyroid (constriction of the small arteries, marked acceleration and consequent weakening of the heart and diminution of the output) to the loss of this regulative influence. It is a remarkable and as yet unexplained fact that in birds thyroidectomy appears to be harmless. The apparent immunity of rodents to this operation is due, it has been suggested, to the presence of sporadic masses of thyroid tissue (accessory thyroid glands), or to the presence of small bodies in the neighbourhood of the thyroid but of a different structure (parathyroids). Some have even gone so far as to assert that, in animals which possess them, it is the parathyroids and not the thyroids which are important, and that the extirpation of the latter is harmless unless the former be also removed. But the matter is not yet beyond the pale of controversy.

Although no clear proof has yet been given that the secretion of the thyroid is influenced by nerves, it is probable that this is the case. Section of the superior and inferior thyroid nerves going to the gland is followed by degenerative changes in it; and, indeed, extirpation of the gland causes degeneration in the nerves from which the thyroid fibres come, viz., the vagus and its superior and inferior laryngeal branches (Katzenstein).

Suprarenal Capsules.—It had been observed by Addison that

the malady which now bears his name, and in which certain vascular changes, with muscular weakness and pigmentation or 'bronzing' of the skin, are prominent symptoms, was associated with disease of the suprarenals. This clinical result was soon supplemented by the discovery that extirpation of the capsules in animals is incompatible with life (Brown-Séquard). Our knowledge of the functions of these hitherto enigmatic organs has been greatly extended by the experiments of Oliver and Schäfer, who have investigated the action of extracts of the suprarenals (of calf, sheep, dog, guinea-pig and man) when injected into the veins of animals. The arteries are greatly contracted, and this mainly through direct action on the vaso-motor nerve-endings or the smooth muscle of the vessels, but partly through the vaso-motor centre. The blood-pressure rises rapidly, although the heart is strongly inhibited through the vagus centre. The heart is at the same time directly stimulated, so that although it beats slowly, the beats are stronger than before. When the vagi are cut the action of the heart is markedly augmented, and the arterial pressure rises enormously (to four or five times its original amount). Stimulation of the depressor is of no avail in combating this increase of blood-pressure. The vessels of the conjunctiva are constricted by local action when an extract of the capsules is dropped into the eye, a fact which has proved of value in ophthalmological practice. The smooth muscular fibres of the dilator pupillæ and the retractor of the nictitating membrane in the cat are stimulated by intravenous injection of it after all the nerves going to them have been severed. The curve of contraction of the skeletal muscles is lengthened as in veratria poisoning (p. 570), though to a less extent. The active principle that produces these effects is solely contained in the medulla of the gland, and such is its extraordinary power that a dose of one-millionth of a gramme per kilo of body-weight is sufficient to cause a distinct effect upon the heart and bloodvessels. It was entirely absent from the suprarenals of a person who had died of Addison's disease. Abel has isolated as a benzoyl compound the substance which causes the rise of blood-pressure. He

names it epinephrin. It is a base of alkaloidal nature, whose percentage composition corresponds to the formula $C_{17}H_{15}NO_4$. The function of the capsules is to secrete this substance, which is probably of great physiological importance for maintaining the tonicity of the muscular tissues in general, and especially of the heart and arteries. It is possible that in addition toxic bodies are neutralized or destroyed in the glands. The existence of secretory fibres for the suprarenal capsules in the splanchnic nerves has been rendered probable by the experiments of Dreyer, who finds that the amount of active substance in the blood of the suprarenal vein, as tested by its physiological effect when injected into an animal, is increased by stimulation of those nerves.

Pituitary Body.—When the pituitary body is removed (in cats or dogs), death generally occurs within a fortnight, with symptoms some of which—for instance, muscular tremors and spasms—resemble those that follow excision of the thyroid. It has been stated, too, that the pituitary undergoes (compensatory?) hypertrophy after thyroidectomy, and some observers have accordingly assumed a similarity of function for these organs. But, according to Schäfer, there is no basis for this assumption. For in man pathological changes in the pituitary body are associated, not with myxœdema, as disease of the thyroid is, but with another condition, called acromegaly, in which the bones of the limbs and face become hypertrophied. The effects on the vascular system of intravenous injection of extracts of the gland are also very different from those caused by thyroid extract. Extracts of the anterior lobe, or hypophysis, are inactive. The posterior lobe, or infundibular body, contains two active substances, one *pressor* and the other *depressor*. The former is soluble in salt solution, but insoluble in absolute alcohol and ether; while the latter is soluble in salt solution as well as in alcohol and ether. The pressor substance causes a great rise of blood-pressure, due partly to constriction of the arterioles and partly to an increase in the force of the heart-beat, both of which are brought about by direct action. This rise of pressure lasts for a considerable time, and is some-

times accompanied by a slowing of the heart. A second dose injected before the effect of the first has passed off is inactive; and this distinguishes the pituitary from the suprarenal extract. The depressor substance produces a marked fall of blood-pressure, even when it is injected during the rise of pressure caused by an injection of the pressor substance.

Extracts of **nervous tissue** (sciatic nerve, white matter of brain, spinal cord, but especially gray matter of brain) cause, on injection into the veins, a decided fall of arterial blood-pressure, which soon passes off, and can be renewed by a fresh injection. The fall of pressure is due to direct action upon the blood-vessels of a depressor substance in the extracts, and not to the action of vaso-motor nerves. It can be obtained after section of the vagi (Osborne and Vincent).

The removal of the **thymus** in the frog, in which animal the organ persists throughout life,* is said to be fatal. The chief symptoms are muscular weakness going on to paralysis, trophic disturbances, including discolouration of the skin and certain alterations in the blood (hydræmia, swelling of the red corpuscles and slight diminution in their number, with increase in the number of the white corpuscles). The chief effect of intravenous injection of extract of human or ox thymus is a lowering of blood-pressure. In this respect it resembles thyroid extract. The heart may be at the same time accelerated.

The **spleen** does not produce an internal secretion necessary to life, for it can be removed both in animals and in man, not only without causing death, but often without the development of any serious symptoms. Its blood-forming and blood-destroying functions (p. 32) are taken on by other structures (particularly the red bone-marrow), but the formation of the bile-pigment is interfered with, and its amount reduced by more than 50 per cent. (Pugliese). The production of trypsin by the pancreas is also said to be diminished, whereas if an extract of spleen be injected into the circulation of an animal deprived of its spleen, the amount of trypsin is increased. It has, therefore, been supposed that the spleen forms a substance (protrypsin) which, passing into the blood, is taken up by the pancreas and elaborated into trypsinogen.

The **salivary glands** may be extirpated without the slightest change being produced in the normal metabolism.

* In mammals (including man) the thymus does not completely disappear in the adult. Islands of thymus tissue are found at all ages among the fat by which the bulk of the organ is replaced.

CHAPTER VIII.

ANIMAL HEAT.

FROM the earliest ages it must have been noticed that the bodies of many animals, and particularly of men, are warmer than the air and than most objects around them. The 'vulgar opinion' of Bacon's time, 'that fishes are the least warm internally, and birds the most,' if it does not imply a very extensive knowledge of animal temperature, at least shows that the fundamental distinction of warm and cold-blooded animals, which is to-day more accurately expressed as the distinction between animals of constant temperature (homoiothermal) and animals of variable temperature (poikilothermal), had been grasped, and was even popularly known. Since that time the accumulation of accurate numerical results, and the advance of physical and physiological doctrine, have given us definite ideas as to the relation of animal heat to the metabolic processes of the body. It is impossible to understand the present position of the subject without an elementary knowledge of the science of heat. For this the student is referred to a text-book of physics. All that can be done here is to preface the physiological portion of the subject by a few remarks on the physical methods and instruments employed:

Temperature.—Two bodies are at the same temperature if, when placed in contact, no exchange of heat takes place between them. They are at different temperatures if, on the whole, heat passes from one to the other, and that body from which the heat passes is at the higher temperature. It is known by experiment that if two bodies of different temperature are placed in contact, heat will pass from one to the other till they come to have the same temperature. If, then,

we have the means of finding out the temperature of any one body, we can arrive at the temperature of any other by placing the two in contact for a sufficiently long time, under the proviso that the quantity of heat necessary to bring the temperature of the first body, which may be called the 'measuring' body, to equality with that of the second, is so small as not to make a sensible difference in the latter. This is the principle on which thermometric measurements depend. A mercurial thermometer consists of a quantity of mercury ordinarily contained in a thin glass bulb, the cavity of which is continued into a tube of very fine bore in the stem. Like most other substances, mercury expands when the temperature rises, and contracts when it sinks, and the amount of expansion or contraction is shown by the rise or fall of the mercurial column in the stem of the thermometer. The point at which the meniscus stands when the bulb is immersed in melting ice or ice-cold water is, on the centigrade scale, taken as zero; the point at which it stands when the thermometer is surrounded by the steam rising from a vessel of boiling water is taken as 100 degrees. The intermediate portion of the stem is divided into degrees and fractions of degrees. When, now, we measure the temperature of any part of an animal with such a thermometer, we place the bulb in contact with the part until the mercury has ceased to rise or fall. We know then that the mercury has ceased to expand or contract, and therefore that its temperature is stationary, and presumably the same as that of the part. It is to be noted that we have gained no information whatever as to the amount of heat in the body of the animal. We have only observed that the mercury of the thermometer when its temperature is the same as that of the given part expands to an extent marked by the division of the scale at which the column is stationary. And we know that if the mercury rises to the same point when the thermometer is applied to another part, the temperature of the latter is the same as that of the first part; if the mercury rises higher, the temperature is greater; if not so high, it is less. The thermometer, then, only informs us whether heat would flow from or into the part with which it is in contact if the part were placed in thermal connection with any other body of which the temperature is known. In other words, the temperature is a measure of the heat 'tension,' so to speak; and difference of temperature between two bodies is analogous to difference of potential between the poles of a voltaic cell (p. 533), or to difference of level between the surface of a mill-pond and the race below the wheel.

The temperature of an animal is measured in one of the natural cavities, as the rectum, vagina, mouth, or external ear, or in the axilla, or at any part of the skin. For the cavities a mercury thermometer is nearly always used; the ordinary little *maximum* thermometer is most convenient for clinical purposes. The temperature of the skin may be measured by an ordinary mercury thermometer, the outer portion of the bulb of which is covered by some badly conducting material. An uncovered thermometer, heated nearly to the temperature expected, will also give results sufficiently accurate for most

purposes, especially if the bulb is flat or in the form of a flat spiral, which can be easily applied to the surface. A theoretically better method, but more laborious in practice, is the use of a thermo-electric junction, or a resistance thermometer formed of a grating cut out of thin lead-paper or tinfoil (Fig. 138). This is especially useful for comparing the temperature of two portions of skin. The temperature of the solid tissues and liquids of the body may also be measured or compared by the insertion of mercurial or resistance thermometers or thermo-electric junctions (p. 579).

Calorimetry.—The quantity of heat given off by an animal is generally measured by the rise of temperature which it produces in a known mass of some standard substance. Sometimes, however, as in the ice-calorimeter of Lavoisier and Laplace and the ether calorimeter of Rosenthal, a physical change of state—in the one case liquefaction of ice, in the other evaporation of ether—is taken as token and measure of heat received by the measuring substance, the number of units of heat corresponding to liquefaction of unit mass of ice or evaporation of unit mass of ether being known. The unit generally adopted in the measurement of heat is the quantity required to raise the temperature of a kilogramme of water 1° C., which is called a calorie, or kilocalorie, or large calorie. The thousandth part of this, the quantity needed to raise the temperature of a gramme of water by 1°, is termed a small calorie or millicalorie.

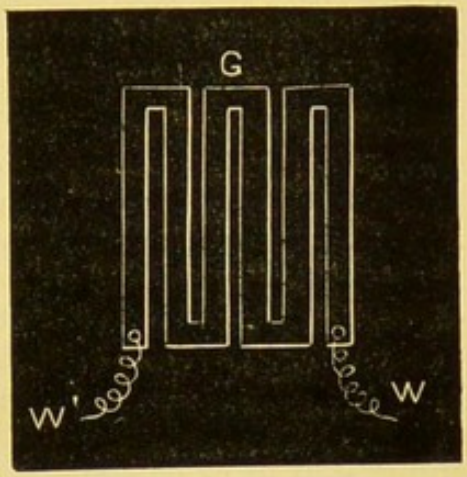


FIG. 138.—RESISTANCE THERMOMETER FOR MEASURING TEMPERATURE OF SKIN.

G, grating of lead-paper, attached to a cover-slip, and mounted on a holder; W, W', wires to the Wheatstone's bridge. An increase of temperature causes an increase in the resistance of the lead. The balance of the bridge is thus disturbed. By experimental graduation the temperature value of the deflection, or of the change of resistance that balances it, is known (p. 534).

In the calorimeters which have been chiefly used in physiology either water or air has been taken as the measuring substance. The most convenient form of water calorimeter is a box with double walls, the space between which is filled with a weighed quantity of water. The animal is placed inside the vessel, and the temperature of the water noted at the beginning and end of the experiment. Suppose that the quantity of water is 10 kilos, and that the temperature rises one degree in thirty minutes, then the amount of heat lost by the animal is 10,000 small calories in the half-hour, or 480,000 in the twenty-four hours; and *if* the rectal temperature is unchanged, this will also be the amount of heat produced. Here we assume (1) that all the heat lost by the animal has gone to heat the water, and none to heat the metal of the calorimeter; (2) that none has been radiated away from the outer surface of the latter. The first assumption will seldom introduce any sensible error in a prolonged physio-

logical experiment; but it is very easy to determine by a separate observation the water-equivalent of the calorimeter—that is, the quantity of water whose temperature will be raised 1° by a quantity of heat which just suffices to raise the temperature of the metal by 1° (p. 528). Then the water-equivalent is added to the quantity of water actually present, and the sum is multiplied by the rise of temperature. If the temperature of the room is constant, as will be approximately the case in a cellar, any error due to interchange of heat between the calorimeter and its surroundings may be eliminated by making the initial temperature of the water as much less than that of the air as the final temperature exceeds it. Then if the loss of heat by the animal is uniform, as much heat is gained during the first half of the experiment by the calorimeter from the air as is lost by it to the air during the last half. Or, without lowering the temperature of the water, the amount of heat lost by the calorimeter during an experiment may be previously determined by a special observation, and added to the quantity calculated from the observed rise of temperature. Or, finally, two similar calorimeters may be used, one containing the animal and the other a hydrogen flame, or a coil of wire traversed by a voltaic current, which is regulated so as to keep the temperature the same in the two calorimeters. From the quantity of hydrogen burnt, or electricity passed, the heat-production of the animal can be calculated.

Of late years air calorimeters have come into vogue for physiological purposes. A diagram of one is shown in Fig. 139. Such calorimeters are really thermometers with an immense radiating surface, for only a small proportion of the heat given off by the animal goes to heat the measuring substance. The heat required to raise the temperature of a litre of air by one degree is very small in comparison with that required to raise the temperature of a litre of water by the same amount. Hence a given quantity of heat raises the temperature of an air calorimeter much more than that of a water calorimeter of the same dimensions; and the loss of heat to the surroundings being proportional to the elevation of temperature, in the water calorimeter the chief part of the heat is actually retained in the water, while in an air calorimeter the greater portion passes through the air space, and is radiated away. When the amount of heat lost by the calorimeter becomes equal to that gained from the animal, the 'steady' reading of the instrument is taken, and from this the heat production can be deduced by an experimental graduation of the apparatus. One advantage of an air calorimeter is that it follows more closely rapid variations in the heat production of the animal, or, to speak more correctly, in the heat loss. It should be carefully noted that in calorimetry what is directly measured is the quantity of heat given out by the animal, not the quantity produced. The two quantities are identical only when the temperature of the animal has remained unchanged throughout the experiment. If the temperature has fallen, the quantity of heat produced is equal to the quantity measured by the calorimeter *minus* the difference between the quantity in the animal at the beginning

and at the end of the observation. This difference is equal to the average specific heat of the animal multiplied by its weight and by the fall of temperature. It can be approximately found by multiplying the weight (in kilogrammes or grammes) by the fall of rectal temperature (in degrees), since the average specific heat of the body (of a mammal at least) is not very different from that of water, and the specific heat of water is taken as unity.

All the higher animals (mammals and birds) have a practically constant internal temperature (fowl 41° to 44° C., mouse 37° to 38°, dog 38° to 39°, man 37° in the rectum), but

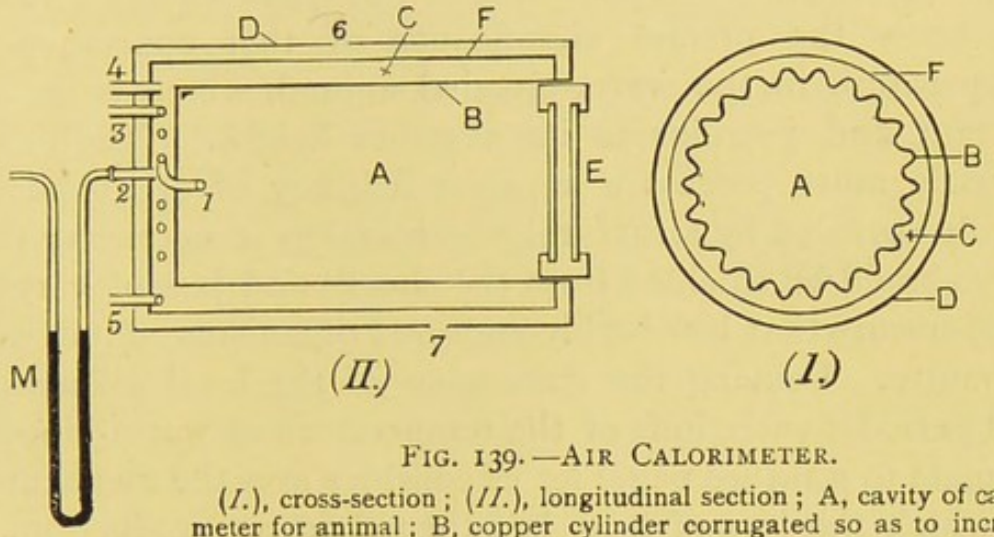


FIG. 139.—AIR CALORIMETER.

(*I.*), cross-section; (*II.*), longitudinal section; A, cavity of calorimeter for animal; B, copper cylinder corrugated so as to increase the radiating surface; C, air space enclosed between B and a concentric copper cylinder F; C is air-tight, and is connected by the tube 2 with the manometer M. The other end of the manometer is connected with an exactly similar calorimeter, in which a hydrogen flame is burnt in the space corresponding to A, or in which the air in A is heated by a coil of wire traversed by an electrical current. The flame or current is regulated so as to keep the coloured petroleum or mercury in the manometer M at the same level in both limbs; the amount of heat given off to the one calorimeter by the flame or current is then equal to that given off by the animal to the other. D is an external cylinder of copper or tin perforated by holes (6, 7) at intervals. The purpose of it is to prevent draughts from affecting the loss of heat from F; 4, 5, are tubes through which thermometers can be introduced into C; 1 is the terminal of a spiral tube, which is coiled in the end portion of the air space C. The sections of the coils are indicated by small circles. The other end of the spiral tube is 3; through this tube air is sucked out, and so the proper ventilation of the animal is kept up. The object of the spiral arrangement is that the air aspirated out of A may give up its heat to the air in C before passing out. E is a door with double glass walls.

a few hibernating mammals, such as the marmot, are homoiothermal in summer, poikilothermal during their winter sleep. In the lower forms the body temperature follows closely the temperature of the environment, and is never very much above it (frog 0·5° to 2° above external temperature). Both in a frog and in a pigeon heat is evolved as long as life lasts; but per unit of weight the amphibian produces far less than the bird, and loses far more readily what it does produce. The temperature of the frog may be 30° in June and 5° in January. The structure of its tissues is unaltered and their vitality un-

impaired by such violent fluctuations. But it is necessary, not only for health, but even for life, that the internal temperature (the temperature of the blood) of a man should vary only within relatively narrow limits around the mean of 37° to 38° C.

Why it is that a comparatively high temperature should be needed for the full physiological activity of the tissues of a mammal, while the in many respects similar tissues of a fish work perfectly, although perhaps more sluggishly, at a much lower temperature, is not quite clear; nor do we know the precise significance of that constancy of temperature in the warm-blooded animal, which is as important and peculiar as its absolute height. The higher animals must possess a superior delicacy of organization, hardly revealed by structure, which makes it necessary that they should be shielded from the shocks and jars of varying temperature that less highly-endowed organisms endure with impunity. Leaving the discussion of the local differences and periodic variations of the temperature of warm-blooded animals to a future page, let us consider now the mechanism by which the loss of heat is adjusted to its production, so that upon the whole the one balances the other.

Heat Loss.—Heat is lost (1) from the surfaces of the body by radiation, conduction, and convection; (2) as latent heat in the watery vapour given off by the skin and lungs; and (3) in the excreta. Even in the bulky excrement of herbivora a comparatively trifling part of the total heat is lost. The second channel of elimination is much more important; the first is in general the most important of all.

The loss of heat by direct **radiation** from a portion of the skin or clothes, or from hair, fur, or feathers covering the skin, may be measured by means of a thermopile or a resistance radiometer (bolometer). The latter instrument is similar in principle and allied in construction to the resistance thermometer used in measuring superficial temperatures, and already described (Fig. 138, p. 493). It may consist of a grating of lead-paper or tinfoil fixed vertically in a small box which protects it from draughts. The box has a sliding lid, which is kept closed till the moment of the observation, when it is withdrawn and the portion of skin applied to the opening at a fixed distance (5 to 10 cm.) from the grating. The intensity of radiation depends on the excess of temperature of the radiating surface over that of the surroundings, as well as on the nature of the

surface. The uncovered parts of the skin (face and hands in man) radiate more per unit of area than the clothes or hair; and the warm forehead more than the comparatively cool lobe of the ear or tip of the nose. When a man is sitting at rest in a still atmosphere, pure radiation plays a greater, and conduction and convection play a smaller, part in the total loss of heat from the skin than when he is walking about or sitting in a draught. The more rapidly the air in contact with the skin and clothes is renewed, the lower, other things being equal, is the temperature of the radiating surfaces kept, the greater is the loss of heat by conduction to the adjacent portions of air, and the smaller the loss by radiation to the walls of the room, the furniture, and other surrounding objects. It is probable that, under the most favourable conditions, the amount of heat lost from the surface by true radiation does not exceed the amount lost by conduction and convection.

The loss of heat by evaporation of water from the skin can be calculated if we know the quantity of water so given off. For a gramme of water at the ordinary temperature (say, 15° C.) needs 555 millicalories to convert it into aqueous vapour at the average temperature of the skin. If we take the average quantity of water excreted as sweat in twenty-four hours as 750 c.c., this will be equivalent to a heat loss of 416,250—say, in round numbers, 400,000 millicalories.

The quantity of heat given off by the lungs may be also deduced from calculation, the data being (1) the weight, temperature, and specific heat of the expired air, and (2) the excess of water it contains in the form of aqueous vapour over that contained in the inspired air. Helmholtz calculated the quantity of heat needed to warm the air expired by a man in twenty-four hours from an initial temperature of 20° to body temperature, at 70,000 small calories, and that required to evaporate the water given off by the lungs at 397,000, making the total heat-loss by the lungs from 400,000 to 500,000 small calories. By direct calorimetric observations it was found that a man of 70 kilos weight gave off in normal breathing, with an air temperature of 12° to 15° C., from 350,000 to 450,000 small calories. Forced respiration, as might be expected, increased the amount often to double or even treble. A diagram of a respiration calorimeter is shown in Fig. 140. (See Practical Exercises, p. 528.)

The following table gives an analysis of the heat-loss of an average man. It must be understood that the figures are only approximate. In round numbers we may say that two-thirds of the heat loss is due to radiation, conduction, and convection, and one-third to the evaporation of water.

		Per cent.		Millicalories.
Skin	Evaporation of water	15		400,000
	Radiation	30	80	750,000
	Conduction (and convection)	35		900,000
Lungs	Evaporation of water	15		400,000
	Heating the expired air	2·5	17·5	70,000
	Heating the excreta		2·5	70,000
			100	2,590,000

In the rabbit, according to Nebelthau, the heat lost by evaporation of water is about 16 per cent. of the whole, or about half the proportion in man, according to the above calculation. This is not surprising when we reflect that the rabbit does not sweat, and drinks comparatively little water.

Sources of the Heat of the Body.—Heat-production.—Some heat enters the body as such from without—in the food, and by radiation from the sun and from fires. The ultimate source of all the heat produced in the body is the chemical energy of the food substances. Whatever intermediate forms this energy may assume—whether the mechanical energy of muscular contraction; the energy of electrical separation by which the currents of the tissues are produced; the energy of the nerve impulse; or the energy, be it what it may, which enables the living cells to perform their chemical labours—it all ultimately, except so far as external mechanical work may be done, appears in the form of heat. We do not know at what precise stage of metabolism the chief outburst of heat takes place, but we may be sure that the food, whether it is burned in a calorimeter to simple end-products like carbon dioxide and water, or more slowly oxidized in the body, yields the same amount of heat, provided always that in both cases it is entirely consumed, and that no work is transferred to the outside. In the body the combustion of carbohydrates and fats is complete; but the nitrogenous residues of the proteids—urea, uric acid, etc.—can be further oxidized, and the remnant of energy which they yield must be taken into account in any calculation of the total heat-production founded on the heat of combustion of the food substances.

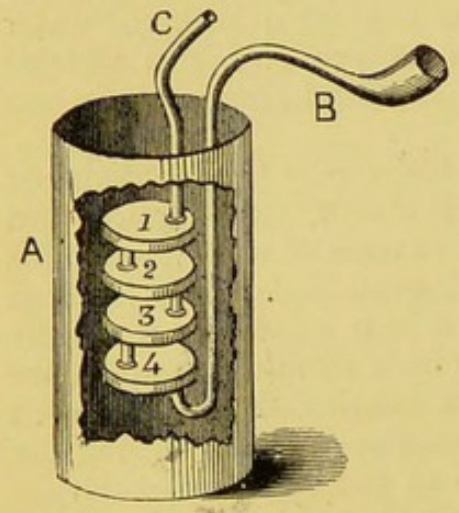


FIG. 140.—RESPIRATION CALORIMETER.

B, copper tube with mouthpiece, connected with the thin brass capsule 4; 4 is connected with a similar capsule 3 by a short tube, which passes out from it at the side opposite to that at which B enters; 2 and 1 are similar capsules. From 1 an outlet tube C passes off. The whole is set in a copper cylinder A filled with water. A piece is supposed to be cut out of A in order to show the capsules. A is placed in another wider copper cylinder.

From careful experiments, it has been found that a gramme of dry proteid (egg-albumin), when burned in a calorimeter, yields 5,735 millicalories of heat, a gramme of grape-sugar 3,742, and a gramme of animal fat 9,500 millicalories (Stohmann).

	Calories.
Heat equivalent of 1 gramme of albumin - -	5,735
Albumin (minus urea produced from it) -	4,949
Cane-sugar - - - - - - -	3,955
Kreatin (water-free) - - - - -	4,275
Starch - - - - - - -	4,182

In applying such results to the calculation of the heat-production of the body, it is not sufficient to deduct from the heat of combustion of the proteids the heat which the residual urea would yield if fully oxidized. For other incompletely oxidized products arise from proteids when consumed in the body, and Rubner has shown, by actually determining the heat of combustion of the urine and fæces, that the real equivalent of a gramme of albumin is at most only 4,420 millicalories. The heat-equivalent of our specimen diet (p. 476) will be approximately:

				Millicalories.
Proteid, 140 grammes	×	4,420	=	618,800
Fat, 100 grammes	×	9,500	=	950,000
Carbo-hydrate (reckoned as glucose), 350 grammes	×	3,742	=	1,309,700
				2,878,500

But this is the diet of a man doing a fair day's work; and to get the quantity of energy which actually appears as heat, the heat-equivalent of the mechanical work performed must be deducted. A fair day's work is about 150,000 kilogramme-metres—that is, an amount equal to the raising of 150,000 kilogrammes to the height of a metre. Now, a kilogramme-degree or calorie of heat is equivalent to (say) 427 kilogramme-metres of work, and a kilogramme-metre to $\frac{1000}{427}$ millicalories. The heat-equivalent of the day's work is, therefore, $150{,}000 \times \frac{1000}{427} = 351{,}000$ millicalories. Deducting this from the heat-equivalent of the food, we get in round numbers 2,530,000 millicalories as the quantity of heat given off. This corresponds fairly well with the calculated heat-loss (p. 497). Calorimetric observations have given results in some cases not widely different, in others considerably higher. Thus, Hirn found that a man of 73 kilos weight produced 140,000 millicalories per hour during rest, and 229,000 during an hour's work of 32,550 kilogramme-metres. At the same rate for the twenty-four hours these numbers would correspond respectively to 3,360,000 and 5,496,000 small calories. But it is not legitimate to apply the results of comparatively short observations in this way; for, on the one hand, the heat-

production during sleep is much less than in the 'rest' of ordinary waking life; and, on the other, continuous labour for twenty-four hours at the rate of more than 30,000 kilogramme-metres per hour would either be impossible, or would be associated with a greater consumption of food or of tissue than corresponds to the diet on which our calculation was based. During the normal eight hours of sleep the heat-production of a 73 kilo man is only about 45,000 millicalories per hour (Helmholtz), or 360,000. Adding to this 2,240,000 (16 × 140,000), for the sixteen resting but waking hours, we get 2,600,000 as the total heat-production of the 'resting' man. Dividing the day into eight hours of work at the rate of 32,550 kilogramme-metres per hour (a hard day's labour), eight hours' waking rest, and eight hours' sleep, we get a heat-production of 3,312,000 small calories in twenty-four hours, made up thus:

Eight hours' work	×	229,000	=	1,832,000
Eight hours' 'rest'	×	140,000	=	1,120,000
Eight hours' sleep	×	45,000	=	360,000
				3,312,000

Such direct observations as have been made on man by means of water or air calorimetes, or by simply immersing the subject in a bath, are still open to considerable errors, and the heat-production necessarily varies widely with the diet. But from the general agreement of calculated results with actual measurements we can safely conclude that *most healthy adults produce between* 2,000,000 *and* 3,000,000 *small calories on a 'rest' day, or a day of light labour, and between* 3,000,000 *and* 4,000,000 *on a day of hard manual work.*

Rubner has calculated from the diet the heat-production of various classes of men, reducing everything to the standard of a body-weight of 67 kilos. The fasting man, of 67 kilos body-weight, produces 2,303,000 calories in the twenty-four hours. The class of brain-workers, represented by physicians and officials, produce only a little more heat than the fasting man, viz., 2,445,000 calories. The second class, represented by soldiers (presumably in time of peace) and day-labourers (probably of a cautious and conservative type), work up to 2,868,000 calories. The third class, composed of men who work with machines and other skilled labourers, attain a heat-production of 3,362,000 calories. The fourth class, typified by miners (who are engaged, usually by the piece and not by the day, in severe and exhausting toil), produce as much as 4,790,000 calories. In the fifth and last class,

represented by lumberers and other out-of-door labourers (who, in addition to excessive exertion, have often to face intense cold), the heat-production rises to 5,360,000 calories.

The Seats of Heat-production.—We have already recognised the skeletal muscles as important seats of heat-production. A frog's muscle, contracting under the most favourable con-

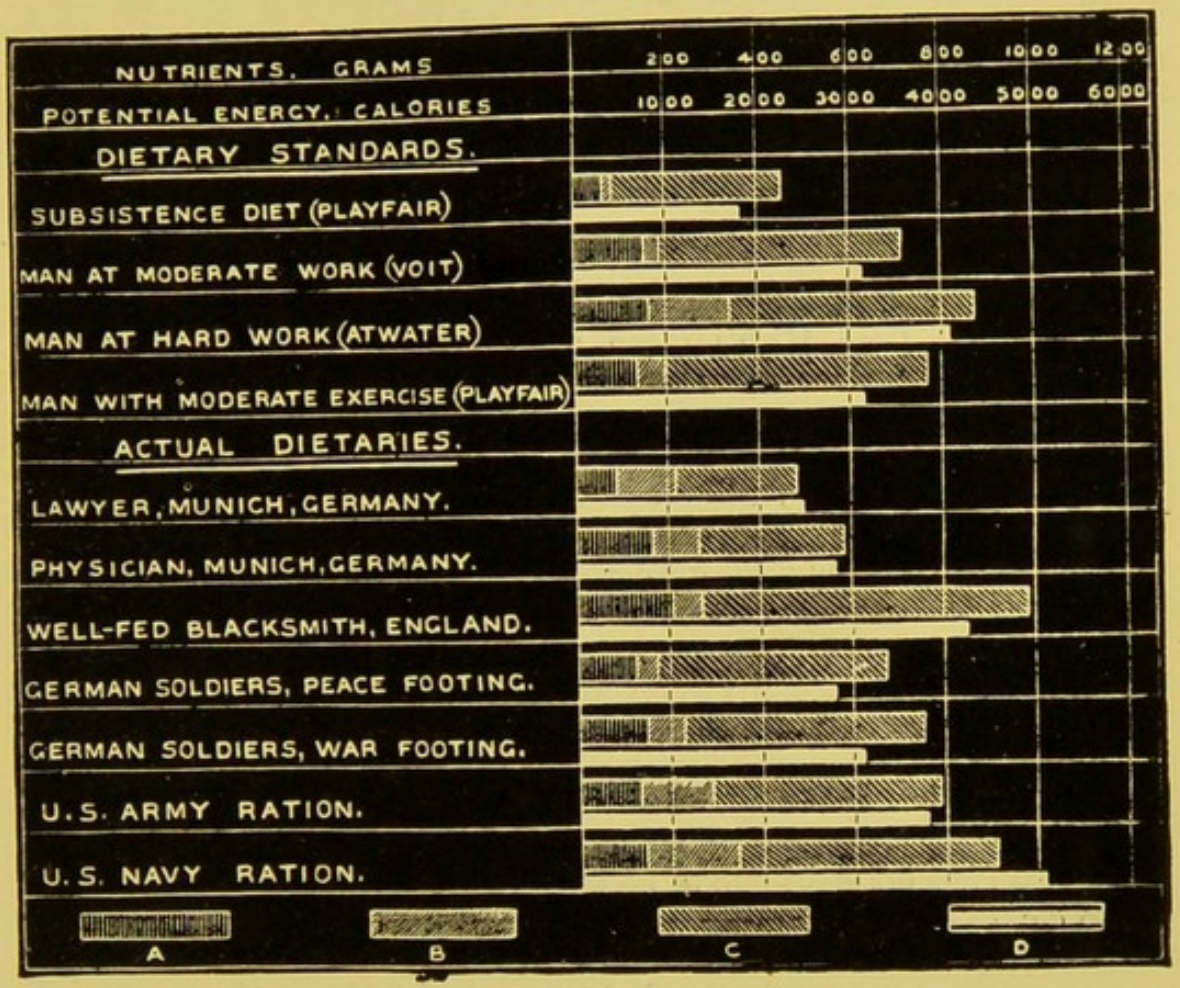


FIG. 141.—DIAGRAM SHOWING THE HEAT EQUIVALENT OF VARIOUS DIETARIES.

A, proteids; B, fats; C, carbo-hydrates; D, heat equivalent.

ditions, does not convert at most more than one-fourth or one-fifth of the energy it expends into mechanical work; at least three-fourths or four-fifths of the energy appears as heat. The muscles of mammals and of man in the intact body work, upon the whole, more economically than the excised frog's muscles at their maximum efficiency. Under the best conditions, that is when the work is moderate and not too rapidly done, about one-third of the chemical energy expended may be transformed into mechanical work; and

only two-thirds into heat (Zuntz). In hard work three-quarters of the energy may be changed into heat; but even then the efficiency of the muscles far outstrips that of the best steam-engines, which convert only an eighth of the total energy into work.

Notwithstanding the splendid efficiency of the muscular machine, the gaseous metabolism easily rises during muscular work to five times, and in severe labour to nine times its resting value, although persons inured to toil work more economically than amateurs. It is, indeed, not difficult to show that the greater part of the metabolism and heat-production of a man doing ordinary work is accounted for by the contraction of the voluntary and involuntary muscles.

It follows from Hirn's mean results that a 70 kilo man doing 27,700 kilogramme-metres of work in an hour gives off 283,000 small calories of heat. Now, 27,700 kilogramme-metres = say, 65,000 small calories; and on the assumption that the skeletal muscles produce four or even three times as much heat as work, the contraction of these alone, without reckoning the heat produced by the heart, would account for by far the greatest part of the heat-production during the hours of work. Taking the working day at eight hours, at least two-thirds of the total heat-production would be thus accounted for, particularly as a certain additional amount of muscular energy is expended in maintaining the position of the body necessary for the performance of the work. But even in muscles completely at rest metabolism goes on, and some heat is produced. The muscles of a dog's legs, through which an artificial circulation of defibrinated blood is kept up, consume at body temperature on the average about 150 c.c. of oxygen per kilo per hour. This is more than one-third of the rate of consumption per kilo of a resting dog, reckoned on the total weight of the animal. For Zuntz found that a fasting dog of 26 kilos, lying at rest, consumed oxygen at the rate of 10,260 c.c. per hour, or about 395 c.c. per kilo her hour. Taking the muscles as 40 per cent. of the body-weight, and assuming that oxygen consumption and heat-production are under the given conditions approximately proportional, we get $\frac{150}{395} \times \frac{40}{100}$ = say 1 : 6 or 1 : 7 as the ratio of the heat-production of the muscles when absolutely at rest, and removed from the influence of the nervous system, to the total heat-production of the resting animal.

It is probable that in the skeletal muscles of curarized animals the heat-production is not far different from that in isolated muscles at body temperature, and subjected to a good artificial circulation. Now, curara has been found to reduce the oxygen consumption of a rabbit from 770 c.c. to 500 c.c. per kilo per hour. On the assumption that the same proportion holds for a dog, we should get a reduction

from 395 c.c. to 256 c.c.; 139 c.c. (say 140 c.c.) per kilo of body-weight, or 350 c.c. per kilo of muscle, may therefore be taken as the portion of the oxygen consumption of the skeletal muscles of a dog at rest, which is under the control of the nervous system. Adding 150 c.c., the hourly oxygen consumption of a kilo of isolated muscles, we get 500 c.c. per kilo per hour as the total consumption of skeletal muscles connected with the nervous system, though not in active contraction.* In a dog of 26 kilos body-weight (with, say, 10·5 kilos of muscles) this would give 5,250 c.c. of oxygen as the consumption of the resting muscles in an hour. The 15·5 kilos of the animal's body left after deducting the muscles used up, therefore, in Zuntz's experiment about 5,000 c.c. of oxygen, or 320 c.c. per kilo per hour.

If the work of the heart is taken as 27,000 kilogramme-metres in twenty-four hours (p. 126), the total heat produced by this organ will be equivalent (on the assumption that it converts one-third of its energy into work) at least to 81,000 kilogramme-metres, or about 190,000 small calories, since, practically, the whole work is expended in overcoming the friction of the vessels, and finally appears as heat. Enough energy is transformed in twenty-four hours in the heart of the colonel of a regiment of 1,000 men to lift the whole regiment to a height of more than a metre, if it could be all changed into mechanical work. The work of the inspiratory muscles may be reckoned at 13,000 kilogramme-metres, equal to 30,500 small calories, and the heat produced by them at, say, 90,000 small calories. In sum, the muscular work of the circulation and respiration is responsible for the production of at least 280,000 small calories (without including the heat produced by the smooth muscle of the bronchi and bloodvessels), or nearly one-eighth of the total production of a man doing ordinary labour. During eight hours of sleep a man produces altogether about 320,000 small calories. Of this the share due to the heart and respiratory muscles may be taken as $\frac{280,000}{3} =$ 93,300; or, since the work of the circulation and respiratory system is less during the hours of rest, say, 90,000 small calories, *i.e.*, between one-third and one-fourth of the total heat-production during sleep.

The glands, and then the central nervous system, rank after the muscles, though at a great distance, as seats of heat-production. The liver and brain (?) are the hottest organs in the body; and that this is not altogether due to their being well protected against loss of heat is shown, in the case of the liver, by the excess of temperature of the blood of the hepatic over that of the portal vein. In view, however, of the exaggerated importance which some have given to these organs, as foci of heat-production, it may be well to point out that although many of the chemical

* Separation from the nervous system therefore cuts away more than two-thirds of the muscular metabolism, and leaves less than one-third intact.

changes in the animal body are undoubtedly associated with the setting free of heat, other, and not less weighty and characteristic, reactions may cause the absorption of heat; and it is possible that some of the syntheses which the hepatic and other glandular tissues seem to be capable of performing may be included in this latter category. For example, when urea is decomposed so as to yield ammonium carbonate (p. 388), heat is set free. We must assume, therefore, that if ammonium carbonate were transformed into urea in the liver, an equal amount of heat would be, on the whole, absorbed. So that the heat-production of an organ may depend, not only on the quantity, but also on the quality, of its chemical activity. When we consider the enormous tide of blood which during digestion sets through the portal system, we shall look with suspicion upon results that announce a difference of more than a small fraction of a degree in the temperature of the incoming and outgoing blood of the liver. Probably not less than 200 litres of blood pass in twenty-four hours through the liver of a 2 kilo rabbit. If the temperature of this blood is raised even one-tenth of a degree in its passage through the hepatic capillaries, this would correspond to a heat-production of 20,000 small calories, or one-tenth of the whole heat produced in the animal.

In the case of the brain it has been shown by comparison of the gases of blood taken from the carotid and from the venous sinuses (torcula Herophili) that the metabolism is feeble as compared even with that of resting muscles (Hill). Nor is it possible to demonstrate any marked or constant increase when the cerebral cortex is roused to such an active discharge of impulses as leads to general epileptiform convulsions. The rise of temperature of certain regions of the scalp observed by Lombard during mental activity cannot, therefore, be supposed to be due to conduction of heat from the brain through the skull. It is perhaps caused by vaso-motor changes in the scalp, associated, it may be, with corresponding changes in related areas of the cortex. And, indeed, if we remember how large a proportion of the central nervous system is made up of nerve-fibres, in which, or at any rate in the fibres of peripheral nerves, no sensible production of heat has ever been demonstrated, it will not appear surprising if even a considerable increase in the metabolism of the really active elements should fail to make itself felt.

With regard to the muscles, we are as yet in the dark as

to the precise relation of the energy which appears as heat and of that which is converted into work. The original source of both is, of course, the oxidation of the food substances; but it has been the subject of discussion whether in a muscle, as in a heat-engine, the chemical energy is first converted into heat, and part of the heat then transformed into work, or whether the chemical energy is immediately changed into work, or whether there is an intermediate form of energy other than heat. Some have supposed that the chemical energy is first converted into electrical energy. It is most probable, however, that the transformation is a direct one. It has been stated that under certain conditions a muscle, instead of becoming warmer, may become colder during contraction. If this were established, it would be in favour of the view that heat is directly transformed into muscular work. But it would not be an unequivocal proof; for the cooling might be due merely to chemical or physical reactions between the products formed in the active muscle and other muscular constituents.

It has been very generally admitted that the chief seat of excessive metabolism in fever is the muscles; but U. Mosso has stated that cocaine fever—the marked rise of temperature produced by injection of cocaine—can be obtained in animals paralyzed by curara. This, even if true, would not support the conclusion that a 'nervous fever'—that is to say, a fever due solely to increased metabolism in the nervous system—exists; for in a curarized animal a large amount of 'active' tissue (glands, heart, smooth muscle) still remains in physiological connection with the brain and cord. But, as a matter of fact, in an animal under a dose of curara sufficient to completely paralyze the skeletal muscles cocaine causes no rise of rectal temperature; and this is strongly in favour of the view that the fever produced in the non-curarized animal is connected with excessive muscular metabolism.

Thermotaxis.—What, now, is the mechanism by which the balance is maintained in the homoiothermal animal between heat-production and heat-loss? In answering this question we have to recognise that both of these quantities are

variable, that a fall in the production of heat may be compensated by a diminution of heat-loss, and an increase in the loss of heat balanced by a greater heat-production.

The loss of heat from the surfaces of the body may be regulated both by *involuntary* and by *voluntary* means. It is greatly affected by the state of the cutaneous vessels, and these vessels are under the influence of nerves. A cold skin is pale, and its vessels are contracted. In a warm atmosphere the skin is flushed with blood, its vessels are dilated, its temperature is increased; an effort, so to speak, is being made by the organism to maintain the difference of temperature between its surface and its surroundings on which the rate of heat-loss by radiation and conduction depends. A still more important factor in man, and in animals like the horse, which sweat over their whole surface, is the increase and decrease in the quantity of water evaporated and of heat rendered latent. It is owing to the wonderful elasticity of the sweat-secreting mechanism, and to the increase of respiratory activity, and the consequent increase in the amount of watery vapour given off by the lungs, that men are able to endure for days an atmosphere hotter than the blood, and even for a short time a temperature above that of boiling water. The temperature of a Turkish bath may be as high as 65° to 80° C. Blagden and Fordyce exposed themselves for a few minutes to a temperature of nearly 127° C. Although meat was being cooked in the same chamber by the heat of the air, they experienced no ill effects, nor was their body temperature even increased. But a far lower temperature than this, if long continued, is dangerous to life. In the summers of 1892 and 1896 hundreds of persons died in the United States within a few days from the excessive heat. During the unusually hot summer of 1819 the temperature at Bagdad ranged for a considerable time between 108° and 120° F. (42° to 49° C.), and there was great mortality. A much higher temperature may be borne in dry air than in air saturated with watery vapour. A shade temperature of 100° F. (37·7° C.) in the dry air of the South African plateaux is quite tolerable, while a temperature of 85° F. (29·4° C.) in the moisture-

laden atmosphere of Bombay may be oppressive. The reason is that in dry air the sweat evaporates freely and cools the skin, while in moist air, although according to Rubner the loss of heat by radiation and conduction is increased, the loss of heat by evaporation of sweat is diminished in a still greater degree. In saturated air at the body temperature no loss of heat by perspiration or by evaporation from the pulmonary surface is possible; the temperature of an animal in a saturated atmosphere at 35° to 40° C. soon rises, and the animal dies. In animals like the dog, which sweat little or not at all on the general surface, the regulation of the heat-loss by respiration is relatively more important than in man.

The winter fur of Arctic animals is a special device of Nature to meet the demands of a rigorous climate, and combat a tendency to excessive loss of heat. The experiments of Hösslin and the experience of squatters in Australia go to show that even domesticated animals have a certain power of responding to long-continued changes in external temperature by changes in the radiating surfaces which affect the loss of heat. It is said that in the hot plains of Queensland and New South Wales the fleeces of the sheep show a tendency to a progressive decrease in weight. And Hösslin found that a young dog exposed for eighty-eight days to a temperature of 5° C. developed a thick coat of fine woolly hairs. Another dog of the same litter, exposed for the same length of time to a temperature of 31·5° to 32° C., had a much scantier covering. The increased protection against heat-loss in the case of the 'cooled' dog was not sufficient fully to compensate for the lowered external temperature. The metabolism—that is to say, the heat-production—was also increased. And although the food was exactly the same for both animals in quantity and quality, the dog at 5° C. put on less than half as much fat in the period of the experiment as the 'heated' dog, but the same amount of 'flesh.'

The voluntary factor in the regulation of the heat-loss is of

great importance in man. Clothes, like hair and other natural coverings, retard the loss of heat from the skin chiefly by maintaining a zone of still air in contact with it, for air at rest is an exceedingly bad conductor of heat. A man clothed in the ordinary way has two or three concentric air-jackets around him. The air in the intervals between the inner and outer garments is of importance as well as that in the pores of the clothes themselves; and it is for this reason that two thin shirts put on one above the other are warmer than the same amount of material in the form of a single shirt of double thickness. When a man feels himself too hot, and throws off his coat, he really removes one of the badly conducting layers of air, and increases the rate of heat-loss by radiation and conduction. At the same time the water-vapour, which practically saturates the layer of air next the skin, is allowed a freer access to the surface, and the loss of heat by the evaporation of the sweat becomes greater. The power of voluntarily influencing the heat-loss must be looked upon in man as one of the most important means by which the equilibrium of temperature is maintained. In the lower animals this power also exists, but to a much smaller extent. A dog on a hot day puts out its tongue and stretches its limbs so as to increase the surface from which heat is radiated and conducted. The mere placing of a rabbit on its back, with its legs apart, may cause in an hour or two a fall of 1° to 2° C. in the rectal temperature. The power of covering themselves with straw or leaves, of burrowing and of forming nests, may be included among the voluntary means of regulation of the heat-loss possessed by animals. A man opens the window when he is too hot, and pokes the fire when he feels cold. Both actions are a tribute to his status as a homoiothermal animal, and illustrate the importance of the voluntary element in the mechanism by which his temperature is controlled.

The **production of heat,** like the loss, is to a certain extent **under voluntary control.** Rest, and especially sleep, lessen the production; work increases it. The inhabitants of the tropics, human and brute, often tide over the hottest part of the day by a siesta; and it is as natural, and as

much in accordance with physiological laws, that a man overpowered by the heat should lie down, as it is that he should walk about and stamp his feet or clap his hands on a cold winter morning. In the one case a diminution, in the other an increase, in the heat-production is aimed at by a corresponding change in the amount of muscular contraction. The quantity and quality of the food also influence the production of heat. The Eskimo, who revels in train-oil and tallow-candles, unconsciously illustrates the experimental fact that the heat of combustion of fat is high; the rice diet of the ryot of the Carnatic, with its low heat equivalent, seems peculiarly adapted to the dweller in tropical lands. But it would be easy to attach too much weight to considerations such as these. The Arctic hunter eats animal fat, and the Indian peasant vegetable carbo-hydrate, not only because fat has a high and carbo-hydrate a low heat-equivalent, but because in the climate of the far North animals with a thick coating of badly-conducting fat are plentiful, and vegetable food scarce; whereas in the river-valleys of India nature favours the growth of rice, and religion forbids the killing of the sacred cow.

The production of heat is also **controlled by an involuntary nervous mechanism**, upon which much light has been thrown by the researches of the last twenty years, and especially by those of Pflüger and his school (p. 228). It is a matter of everyday experience that cold causes involuntary shivering—involuntary muscular contractions—the object of which seems a direct increase in the heat-production. But besides this visible mechanical effect, the application of cold to a warm-blooded animal, when not carried so far as to greatly reduce the rectal temperature, is accompanied by a marked increase in the metabolism, as shown by an increased production of carbon dioxide and consumption of oxygen. In cold-blooded animals like the frog the metabolism, on the other hand, rises and falls with the external temperature; there is no automatic mechanism which answers an increased drain upon the stock of heat in the body by an increased supply. Or, in the light of recent experiments, we ought rather to say that, although the rudiments

of a heat-regulating mechanism may exist in such animals as the frog, the newt, and even the earthworm (Vernon), it is only able to modify to a certain extent the effects of changes of external temperature, not to balance or even override them, as in the homoiothermal animal. The warm-blooded animal loses its heat-regulating power when a dose of curara sufficient to paralyze the voluntary muscles is given. A curarized rabbit, kept alive by artificial respiration, reacts to changes of external temperature like the cold-blooded frog. Now, the only action of curara adequate to account for this effect is its power of paralyzing the motor nerve-endings, and so cutting off from the skeletal muscles impulses which in the intact animal would have reached them. The excitation by cold of the cutaneous nerves, or some of them, which in the unpoisoned animal is reflected along the motor nerves to the muscles, and causes the increase of metabolism, is now blocked at the end of the motor path; and the muscles, the great heat-producing tissues, are abandoned to the direct influence of the external temperature.

How is it, then, that nervous impulses from the skin produce in the intact animal their effect upon the chemical processes in the muscles? We know that the heat-production of a muscle is greatly increased when it is caused to contract; but it has not hitherto been possible by artificial stimulation to demonstrate that any chemical or physical effect is produced in a muscle by excitation of its motor nerve unless as the accompaniment of a mechanical change. When the gastrocnemius of a frog poisoned with not too large a dose of curara is laid on a resistance thermometer (p. 493), and its nerve stimulated from time to time as the curara paralysis deepens, heating of the muscle is observed as long as, and only as long as, there is any visible contraction. The gaseous metabolism of a rabbit immersed in a bath of constant temperature may sink by as much as 30 to 40 per cent. when curara is given. One obvious cause of this is the complete muscular relaxation. And the whole secret of the regulation of the heat-production might be plausibly supposed to lie in the bracing effect of cold upon the skeletal muscles and the relaxing effect of heat. And, indeed, in

man it has been observed that exposure to moderate cold causes no metabolic increase when shivering is prevented by a strong effort of the will (Loewy). Nevertheless, the explanation is inadequate in the case of small animals, such as guinea-pigs, rabbits, and cats; for very great changes in the metabolism may be brought about by external cold without any outward token of increased muscular activity. Lefèvre found that in man also a marked increase in the heat-loss, such as is caused by immersion for a considerable time (one to three hours) in cold water (at a temperature of 7° to 15° C.), was accompanied by a great increase in the production of heat, so that the axillary temperature fell comparatively little (*e.g.*, only 1° C. during a stay of three hours in a bath at 15° C.). With short periods of immersion, a characteristic reaction occurs after the person comes out of the bath. The rectal temperature falls to a minimum, which is reached in 20 to 30 minutes after exit from the bath, and then gradually returns to normal. This fall of internal temperature is due to the heating of the superficial portions of the body at the expense of the central portions. By training, the fall of temperature is greatly lessened, the heat-regulating mechanism acquiring, so to speak, with practice, greater promptitude and precision of adjustment.

It must be admitted, then, that—especially in the smaller homoiothermal animals—the metabolic changes normally going on in the resting muscles may be reflexly increased without the usual accompaniment of mechanical contraction, and that such an increase of 'chemical tone' is an important means by which the temperature is regulated. It is possible that other organs besides the muscles may be concerned, though not to a sufficient extent to secure the due regulation of temperature during curara paralysis. It is obvious that in man, whose environment is so much under his own control, a mere automatic regulation is less required than in the inferior animals, and that a regulative power, if present in rudiment, would tend to 'atrophy' by disuse, or, at all events, become less sensitive to slight changes of temperature. In the larger animals, again, mere bulk is an important safeguard against any sudden change of internal

temperature. To reduce the temperature of a horse or an elephant by 1°, a considerable quantity of heat must be lost, while a very slight loss would suffice to cool a mouse by that amount. Not only so, but the surface by which heat is lost is greater in proportion to the mass of the body in small than in large animals. The power of rapidly increasing the heat-production to meet a sudden demand is, therefore, far more important to the mouse than to the horse; and the fact (p. 479) that the metabolism of an animal varies approximately as its surface, and not as its mass,* is an illustration of the nice adjustment by which heat-equilibrium is maintained.

The following table, calculated by Rubner from the quantity of tissue-proteid and fat consumed, shows the relative intensity of heat-production in fasting dogs of different sizes:

Body-weight.	Small calories per kilo per hour.
31 K	1,580
24	1,700
20	1,870
18	1,920
10	2,550
6	2,840
3	3,780

Rubner has found that animals abundantly fed do not show so much change in the production of heat when the external temperature is varied as starving animals, perhaps because the thicker coat of subcutaneous fat so steadies the rate at which heat is lost that it becomes easy for the vaso-motor mechanism alone to hold the balance between loss and production. In well-fed animals it is the heat-loss which is chiefly affected, and it may be that this has something to do with the explanation of Loewy's results on man.

Lorrain Smith has discovered the curious and interesting fact that after removal of the thyroid glands (in cats), the heat-production, as

* The relation between mass (M) and surface (S) in man is approximately given by the equation $\frac{S\sqrt[3]{M}}{M}=K$, and the relation between surface, mass, length of body (L), and circumference of chest (C) just above the nipples in the 'mean' position of respiration, by the equation $\frac{S\sqrt[6]{M^4.\ L^4.\ C^2}}{M\ L\ C}=K'$. M is expressed in grammes, S in square centimetres, L and C in centimetres. K is a constant whose mean value is 12·3, and K′ a constant whose mean value is 4·5 (Meeh).

measured by the amount of carbon dioxide given off, is more sensitive to changes of external temperature than in the normal animal.

But it must not be imagined that the production of heat can be increased indefinitely to meet an increased heat-loss. The organism can make considerable efforts to protect itself, but the loss of heat may easily become so great that the increase of metabolism fails to keep pace with it. The internal temperature then falls, and if the fall be not checked, the animal dies. A mammal, when cooled artificially to the temperature of an ordinary room (15° to 20° C.), does not recover of itself, but may be revived by the employment of artificial respiration and hot baths, even when the rectal temperature has sunk to 5° to 10° C. If the skin of a rabbit be varnished, and the air which it is the function of the fur to maintain at rest around it be thus expelled, the animal dies of cold, unless the loss of heat is artificially prevented. If, without varnishing at all, the greater portion of the skin of a rabbit or guinea-pig be closely clipped or shaved, similar phenomena are observed. Prevented from covering itself with straw, the animal dies, sometimes in twenty-four hours. The radiation from the skin, as measured by the resistance-radiometer (p. 496), is greatly increased; the animal shivers constantly, and the rectal temperature falls. Placed in a warm chamber before the temperature in the rectum has fallen below 25°, the animal recovers perfectly. If the fall is allowed to go on, it dies. If it is kept from the first in the warm chamber, no fall of temperature occurs. When the increased loss of heat is less perfectly compensated—when, for example, the animal is left at the ordinary temperature, but supplied with sufficient straw to cover itself, or allowed to crouch among other animals—a curious phenomenon may sometimes be seen. The rectal temperature, which has fallen sharply during the operation, remains *subnormal* (as much as 2° to 3° below the ordinary temperature) for a time (a week or more), and then gradually rises as the coat again begins to grow. The meaning of this seems to be that the power of regulating the temperature by increasing the metabolism is overtasked by the removal of the natural protective covering, unless the escape of heat is artificially diminished. When the loss of the fur is entirely compensated, no fall of temperature occurs; when it is not compensated at all, the animal cools till it dies; when it is partially compensated, the increased metabolism may only suffice to maintain a temperature lower than the normal, although constant muscular contractions (shivering) are brought in to supplement the efforts of the regulative chemical processes.

Hitherto we have only spoken of a reflex regulation of the heat-production called into play by external cold. It might be supposed—and, indeed, has often been assumed—that heat would lessen the metabolism, as cold increases it; and there are indications that in the smaller animals this is the case, although the influence of heat seems to be much smaller than the influence of cold. But neither experi-

mental results nor general reasoning have as yet shown that in man, either in the tropics (Eykman) or in the north temperate zone (Loewy), the chemical tone is diminished by a rise of external temperature much above the mean of an ordinary English summer, apart from the effect of the muscular relaxation which heat induces. In a man, indeed, at rest in a hot atmosphere, the production of carbon dioxide and consumption of oxygen are, if anything, greater than at the ordinary temperature. The regulation of temperature in an environment warmer than the normal seems, in fact, to be brought about more by an increase in the loss than a decrease in the production of heat. Evaporation from the skin and lungs is an automatic check upon overheating as important as the involuntary increase of metabolism upon excessive cooling.

While it is known that the skeletal muscles, and perhaps the glands and other tissues, are at one end of the reflex arc by which the impulses pass that regulate the temperature through the metabolism, we are as yet ignorant of the precise paths by which the afferent impulses travel, of the nerve-centres to which they go, and even of the end-organs in which they arise. There are nerves in the skin which minister to the sensation of temperature (Chap. XIII.). A change of temperature is their 'adequate' and sufficient stimulus; and it is a tempting hypothesis, though nothing more, that these are the afferent nerves concerned in the reflex regulation of temperature—that impulses carried up by them to some centre or centres in the brain or cord are reflected down the motor nerves to control the metabolism of the skeletal muscles, and down the vaso-motor nerves to control the loss of heat from the skin.

Heat Centres.—It is known that certain injuries of the central nervous system are related to disturbance of the heat-regulating mechanism. Puncture of the median portion of the corpus striatum in the rabbit by a needle thrust through a trephine hole in the skull is followed by a rise of temperature in the rectum (1° to 2°), and still more in the duodenum, which is normally the hottest part of the body in this animal. The heat-production and respiratory exchange are also increased. These phenomena may last for several days (Ott, Richet, Aronsohn and Sachs), and are due to stimulation of the portions of the brain in the immediate neighbourhood of the injury. Electrical stimulation of this region has a similar effect. When the

temperature has returned to normal, a fresh puncture may again cause a rise. Injury to various portions of the cortex cerebri in the dog and other animals, and lesions of the pons, medulla oblongata and cord in man may also be followed by increase of temperature. When the spinal cord is cut below the level of the vaso-motor centre the increased loss of heat from the skin due to dilatation of the cutaneous vessels masks any increase of the heat-production which may possibly have taken place, and the internal temperature falls; but if the loss of heat is diminished by wrapping the animal in cotton-wool the temperature may rise. From such phenomena it has been surmised that certain 'centres' in the brain have to do with the regulation of temperature by controlling the metabolism of the tissues; that they cause increased metabolism when the internal temperature threatens to sink, diminished metabolism when it tends to rise. The cutting off, it is said, of the influence of the 'heat centres' by section of the paths leading from them allows the metabolism of the tissues to run riot, and the temperature to increase.

Fever is a pathological process generally caused by the poisonous products of bacteria, and characterized by a rise of temperature above the limit of the daily variation (p. 523). It is further associated with an increase in the rate of the heart and the respiratory movements, often with an increase in the excretion of urea and ammonia in the urine, and a diminution in the alkalies and carbon dioxide of the blood. It has been suggested that the proximate cause of fever is the action of bacterial poisons or of other substances on the 'heat centres,' and that antipyretics, or drugs which reduce the temperature in fever, do so by restoring the centres to their normal state, by preventing the development of the poisons, aiding their elimination, or antagonizing their action. In favour of this view, it has been stated that when the basal ganglia are cut off, by section of the pons, from their lower nervous connections, fever is no longer produced by injection of cultures of bacteria which readily cause it in an intact animal, while antipyrin has no influence upon the temperature (Sawadowski). But some observers have been unable to find any clear evidence of the existence of 'heat centres'—that is, of localized portions of the central nervous system specially concerned in the regulation of the body temperature. And while it is almost certain that some pyrogenic or fever-producing agents—cocaine, *e.g.*—act in-

directly, through the brain or cord, it is quite possible that others affect directly the activity of the tissues in general, just as some *antipyretics* or fever-reducing agents, such as quinine, act immediately upon the heat-forming tissues, so as to diminish their metabolism, while others, like antipyrin, affect them through the nervous system. A still more important action of antipyrin, and the group of antipyretics to which it belongs, is the increase in the heat-loss which they bring about by the dilatation of the blood-vessels of the skin. This effect is also produced through the nervous system.

Fever is a condition so interesting from a physiological point of view, and of such importance in practical medicine, that it will be well to consider a little more closely the possible ways in which a rise of temperature may occur. It must not be forgotten that the febrile increase of temperature is always accompanied by other departures from the normal, and that all the fundamental febrile changes may even, in certain cases, be present without elevation, and even with diminution of temperature. But here we have only to do with the disturbance of the normal equilibrium between the loss and the production of heat; and it is evident that any of the five conditions illustrated in the diagram may give rise to an increase of temperature. It is not necessary to discuss whether cases of fever can actually be found to illustrate every one of these possibilities. It is probable that not infre-

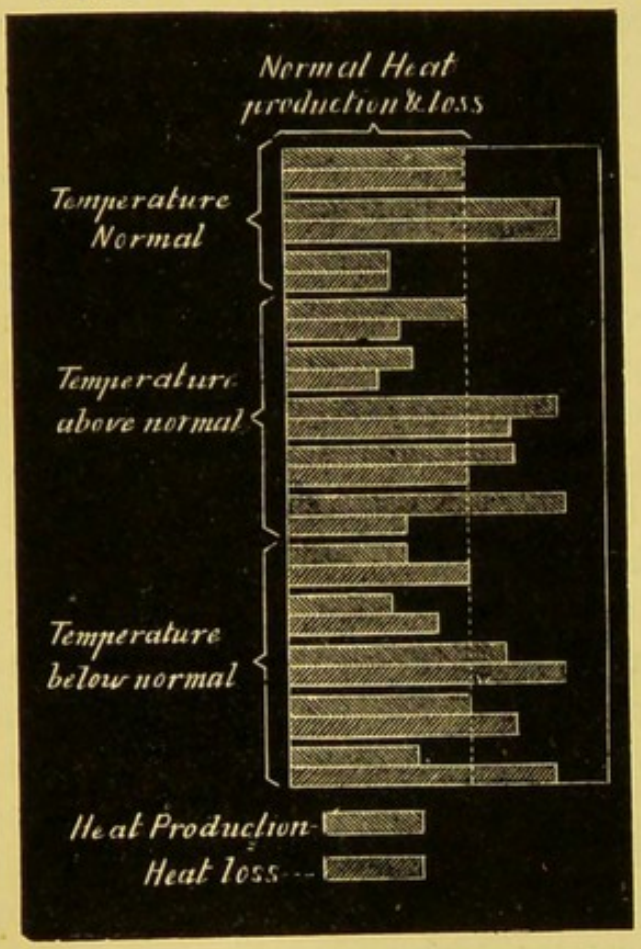


FIG. 142.—DIAGRAM TO SHOW THE POSSIBLE RELATIONS BETWEEN HEAT-PRODUCTION AND HEAT-LOSS IN FEVER.

quently diminished loss and increased production may be both involved; and it ought to be remembered that the healthy standard with which the heat-production of a fever patient should be compared is not that of a man doing hard work on a full diet, but that of a healthy person in bed, and on the meagre fare of the sick-room. When this is kept in view, the comparatively low heat-production and respiratory exchange which have sometimes been found in fever cease to excite surprise. But, in any case, no mere change in the relative proportions of heat formed and lost is sufficient to explain the febrile rise of temperature. That an increase in heat-production is not of itself enough to produce fever is proved by the fact that severe muscular work, which increases the metabolism more than high fever, only causes in a healthy man a rise of about 1° C. in the rectal temperature. When the work is over, the temperature comes rapidly back to normal. The essence of the change in fever is a *derangement* of the mechanism by which in the healthy body excess or defect of average metabolism, or of average heat-loss, is at once compensated and the equilibrium of temperature maintained.

This derangement only lasts as long as the temperature is rising. When it becomes stationary at its maximum we have again adjustment, again equality of production and escape of heat; but the adjustment is now pitched for a higher scale of temperature. A rough analogy, so far as one part of the process is concerned, may be found in the behaviour of the ordinary gas-regulator of a water-bath. It can be 'set' for any temperature. That temperature, once reached, remains constant within narrow limits of oscillation; but the regulator can be equally well adjusted for a higher or a lower temperature.

Rosenthal has concluded from calorimetric observations that, in the first stage of fever, while the temperature is rising, there is always increased retention of heat. Maragliano actually found evidence, by means of the plethysmograph, that the cutaneous vessels are at this stage constricted, and that the constriction may even precede the rise of temperature. Both observations lend support to the

famous 'retention' theory of Traube. At the height of the fever there is often, though apparently not always, an increase in the heat-production. After the crisis, while the fever is subsiding, the rate at which heat is being lost rises sharply. As to the explanation of the increase of metabolism in fever, various views have been held. Some have gone so far as to say that the increase is merely the consequence, not the cause, of the rise of temperature. But the rebutting evidence which has been brought against this view is strong and, indeed, overwhelming. The increase of urea, for example, is often much greater in fever than any increase which can be brought about by artificially raising the temperature of a healthy individual by means of hot baths. Further, this excessive excretion of urea does not run parallel with the rise of temperature in fever, but is generally most marked *after* the crisis. During the stage of defervescence an enormous amount of urea is sometimes given off. In a case of typhus, in the mixed urine of the third and fourth days after the crisis, no less than 160 grammes urea was found (Naunyn), or nearly three times the normal amount for a man on full diet. Again, when fever is caused by the injection of bacteria or their products, the increase in the carbon dioxide eliminated and oxygen consumed occurs even when the temperature is prevented from rising by cold baths. It seems perfectly clear, then, that the increase of metabolism is, in many cases at least, a primary phenomenon of fever, and it remains to ask whether the rise of temperature is anything more than a superficial, and, so to speak, an accidental, circumstance. The orthodox view for many ages has undoubtedly been that the increase of temperature is in itself a serious part of the pathological process, a symptom to be fought with, and, if possible, removed. And, indeed, it is not denied by anyone that the excessive rise of temperature seen in some cases of febrile disease (to 43° C., or even to 45°), is, apart from all other changes, a most imminent danger to life, unless, as is sometimes the case (in influenza, *e.g.*, where a temperature of 44° has been observed), the high temperature lasts only a short time. But some evidence has of late been brought forward, mostly from the field

of bacteriology, to support the idea that the rise of temperature is of the nature of a protective mechanism, that fever is, indeed, a consuming fire, but a fire that wastes the body, to destroy the bacteria. The streptococcus of erysipelas, for example, does not develop at 39° to 40° C., and is killed at 39·5° to 41° C. Anthrax bacilli, kept at 42° to 43° C. for some time, are attenuated,' and when injected into animals confer immunity to the disease. Heated for several days to 41° to 42° C., pneumococci render rabbits immune to pneumonia. These bacteriological results are supported to a certain extent by clinical experience. For it has been observed that a cholera patient with distinct fever has a better chance of recovery than a case which shows no fever. But too much weight ought not to be given to isolated facts of this sort, and adverse evidence can be produced both from the laboratory and the hospital. For although hens are immune to anthrax under ordinary conditions, but can be infected by inoculation when artificially cooled, frogs, equally immune at the temperature of the air, become susceptible when artificially heated. And it is impossible to deny that the use of cold baths in typhoid fever is sometimes of remarkable benefit.

Distribution of Heat.—The great foci of heat-formation—the muscles and glands—would, if heat were not constantly leaving them, in a short time become much warmer than the rest of the body; while structures like the bones, skin, and adipose tissue, in which chemical change and heat-production are slow, would soon cool down to a temperature not much exceeding that of the air. The circulation of the blood ensures that heat produced in any organ shall be carried away and speedily distributed over the whole body; while direct conduction also plays a considerable part in maintaining an approximately uniform temperature. The uniformity, however, is only approximate. The temperature of the liver is several degrees higher than that of the skin, and the temperature of the brain several degrees higher than that of the cornea. The blood of the superficial veins is colder than that of the corresponding arteries. The crural vein, for example, carries colder blood than the crural artery, and the external jugular than the carotid. The heat produced in the deeper parts of the regions which they drain is more than counterbalanced by the heat lost in the more superficial parts. When loss of heat from the surface is sufficiently diminished by an artificial covering, or prevented by the protected situation of

any organ with an active metabolism, the venous blood leaving it is warmer than the arterial blood coming to it. The temperature of the blood passing from the levator labii superioris muscle of the horse during mastication may be sensibly higher than that of the blood which feeds it; the blood in the vena profunda femoris, and in the crural vein of a dog with the leg wrapped in cotton-wool, is warmer by ·1° to ·3° than the blood of the crural artery. This difference of temperature is due to the heat produced in the muscles, and it is not difficult to show that the difference ought to be of this order of magnitude. The quantity of blood in a 7 kilo dog is about $\frac{1}{2}$ kilo; $\frac{1}{4}$ of this, or $\frac{1}{8}$ kilo, is in the skeletal muscles, and the average circulation-time through them may be taken as ten seconds. Six times in the minute, or 360 times in the hour, $\frac{1}{8}$ kilo of blood passes through the muscles, and is heated on the average by ·2°. If we take the specific heat of blood as about equal to that of water, this represents a heat-production of $\frac{360}{8} \times \frac{2}{10} \times 1{,}000$, or 9,000 small calories per hour. Now, the total heat-production of a 7 kilo dog is about 19,000 small calories per hour, of which somewhat less than one-half is probably formed in the skeletal muscles.

The blood of the inferior vena cava at the level of the kidneys may be ·1° colder than that of the abdominal aorta, but is warmer than the blood of the superior cava. The right heart, therefore, receives two streams of blood at different temperatures, which mingle in its cavities. A controversy was long carried on as to the relative temperature of the blood of the two sides of the heart; but the researches of Heidenhain and Körner have shown that a thermometer passed into the right ventricle through the jugular vein stands, as a rule, slightly higher than a thermometer introduced through the carotid into the left ventricle. They consider that the method gives not so much the temperature of the blood in the two cavities as that of their walls. The thin-walled right ventricle, according to them, is heated by conduction from the warm liver, from which it is only separated by the diaphragm, while the left ventricle loses heat to the cooler lungs. They deny that the difference of temperature is caused by cooling of the blood in its passage through the pulmonary capillaries, for even when respiration is suspended, they find a difference of temperature between the two sides of the heart. Under ordinary circumstances, they say, the inspired air is already heated almost to body temperature before it reaches the alveoli. But, while this is the case, it is possible that much of the water-vapour required to saturate it is evaporated from the alveolar walls, and a fall of less than $\frac{1}{10}$° in the temperature of the blood passing through the lungs would account for all the heat lost by the expired air. If half of the loss took place in the upper air-passages, less than $\frac{1}{20}$° would be sufficient. A slight difference of temperature in the blood of the two ventricles might be caused, even in the absence of respiration, by the heat developed in the cardiac muscle itself during contraction, a large proportion of which must be conveyed by the blood of the coronary veins into the right side of the heart.

The surface temperature varies between rather wide limits with the temperature of the environment. The temperature of cavities like the rectum, vagina, and mouth, and of secretions like the urine, approximates to that of the blood in the great vessels or the heart, and undergoes only slight changes. An increase in the velocity of the blood causes the internal and surface temperatures to come nearer to each other, the former falling and the latter rising. When the loss of heat from a portion of the surface is prevented, the temperature of this portion approaches the internal temperature. For this reason a thermometer placed in the axilla approximately measures the internal temperature, and not that of the skin; and a thermometer in the groin of a rabbit, and completely covered by the flexed thigh, may stand as high as, or, it is said, even higher than, a thermometer in the rectum (Hale White).

The surface temperature is a rough index of the rate of heat-loss; the internal temperature, of the rate of heat-production. A normal skin temperature and a rising rectal temperature would probably indicate increased production of heat; an increased rectal temperature, in conjunction with a diminished surface temperature, as in the cold stage of ague, might be due either to diminished heat-loss while the heat-production remained normal, or to diminished heat-loss *plus* increased heat-production.

The following tables illustrate the differences of temperature found in the body. It should be remembered that the numbers are not strictly comparable with each other; the temperature of the mammals in which direct observations have been made on the blood is not exactly the same as that of man, the temperature of the dog, for example, being a little (about 1° C.) higher. Then in the same animal there is no very constant ratio between the temperature of the blood in two vessels or of the skin at two points. Even in the same vessel the temperature may vary with many circumstances, such as the velocity of the stream, and the state of activity of the organ from which it comes. Apart from physiological variations, experimental fallacies sometimes cause a want of constancy, especially in measurements of blood temperature. The insertion of a mercurial thermometer into a vessel is very likely to obstruct the passage of the blood; and if the blood lingers in a warm organ, it will be heated beyond the normal.

Blood. (*Dog.*)

Right heart	38·8° C.
Left „	38·6
Aorta	38·7
Superior vena cava	36·8
Inferior „	38·1
Crural vein	37·2*
Crural artery	38·
Profunda femoris vein	38·2
Portal vein	38-39 } Varies with activity of
Hepatic vein	38·4-39·7 } digestive organs.

Tissues.

Brain	40
Liver	40·6-40·9
Subcutaneous tissue 2·1 lower than that of subjacent muscles (man).	
Anterior chamber of eye	31·9 } (rabbit).
Vitreous humour	36·1 }

Cavities. (*Man.*)

Axilla	36·3-37·5° C. (97·3-99·5° F.)
Rectum	36·-37·8
Mouth	37·25†
Vagina	37·5-38
Uterus	37·7-38·3
External auditory meatus	37·3-37·8
Bladder (temperature of the escaping urine)	36·-37·5

Natural Surfaces.

(Man) Room temperature, 17·5°	Cheek (boy, immediately after running)	36·25
	Anterior surface of forearm	33·5-34·4
	Posterior „ „	34·
	Skin over biceps	35·
	„ „ head of tibia	31·9
	„ immediately below xiphoid cartilage	34·7
	„ over sternum	33·2

* The following numbers were obtained (in an anæsthetized dog whose rectal temperature had fallen 2° C.) for the temperature of the *walls* of the crural artery and vein, as measured by an electrical resistance thermometer.

Leg of dog lightly wrapped in wool.		
Crural artery	34·95	Rectum, 36·2
„ vein	34·76	
Leg more carefully wrapped up.		Air, 16·3
Crural artery	34·70	
„ vein	34·82	

† The temperature in the mouth is not a very reliable index of the deep temperature of the body, especially in cold weather or after exercise, as it is apt to be influenced by the inspired air. The mouth must, of course, be kept closed during the measurement. On the average its temperature is about the same as that of the axilla, and 0·4° C. below that of the rectum. The rectal temperature is 0·2°, or 0·3° above that of the urine (Pembrey).

Natural Surfaces (continued).

On hair (boy)	30°
Under hair over sagittal suture (boy)	33·7-34°
Shaved skin of neck (rabbit)	36·5
On hair „ „ „	31·5
„ between eyes „	30·7

Artificial Surfaces.

(Man) Room temperature, 17·5°	Surface of trousers over thigh	23·7-28·7
	„ coat over arm	26·8
	„ waistcoat	26°

Normal Variations in the Temperature.—The internal temperature, as has been already said, is not strictly constant. It varies with the time of day; with the taking of food; with age; to some extent with violent changes in the external temperature, such as those produced by hot or cold baths; and possibly with sex.

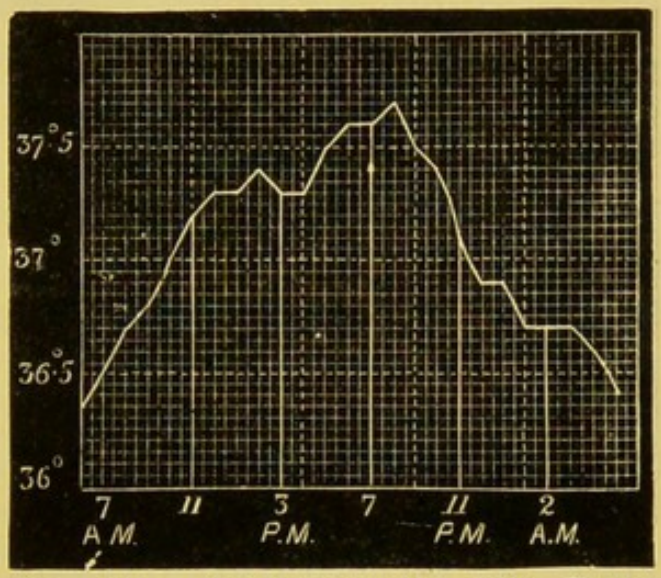


FIG. 143.—CURVE SHOWING THE DAILY VARIATION OF BODY TEMPERATURE.

The daily curve of temperature shows a minimum in the early morning, between two and six o'clock (36·3° C.), and a maximum in the evening, between five and eight o'clock (37·5° C.) (Fig. 143). The extreme daily range in health may be taken as a little over 1° C., or about 2° F. In fever it is generally greater, but the maximum and minimum fall at the same periods; and it is of scientific, and also of practical, interest that the early morning, when the temperature and pulse-rate are at their mininum, is often the time at which the flagging powers of the sick give way. From two to six o'clock in the morning the daily tide of life may be said to reach low-water mark. Even in a fasting man the diurnal temperature curve runs its course, but the variations are not so great. The taking of food of itself causes an increase of temperature, although in a healthy man this rarely amounts to more than half a degree. The rise of

temperature is certainly due in part to the increased work of the alimentary canal, but is also connected with the increase of metabolic activity which the entrance of the products of digestion into the blood brings about. The solution of the solids of the food by the digestive juices is associated with absorption of heat, as has been observed in artificial digestion, and even in a case of gastric fistula. The increased heat-production, however, is more than sufficient to prevent any fall of body temperature from this cause. The cause of the daily variation of temperature has been much discussed. There is no doubt that several factors are concerned, the most important being the variation in the amount of contraction of the skeletal muscles and the influence of food. This is shown by the fact that in persons who work at night and sleep during the day the curve of temperature is reversed.

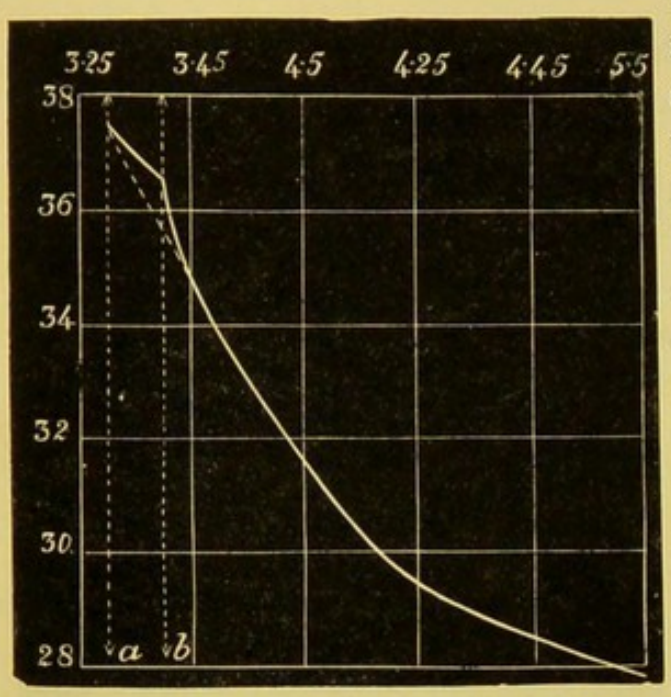


FIG. 144.—CURVE OF COOLING AFTER DEATH (GUINEA-PIG).

Time marked along horizontal, and temperature along vertical axis. At *a* ether and chloroform given to kill animal; death, as indicated by stoppage of the heart, took place at *b*. The dotted line shows the course the curve would have taken if death had occurred at the moment the anæsthetics were given. Air of room 17·6°.

As to the relation of age and sex to temperature, it is only necessary to remark that the mean temperature both of the young child and of the old man is somewhat higher than that of the vigorous adult; but a point of more importance is the relative imperfection of the heat-regulation in infancy and age, and the greater effect of accidental circumstances on the mean temperature. Thus, old people and young children are specially liable to chills, and a fit of crying may be sufficient to send up the temperature of a baby. The temperature of women is generally a little higher than that of men, and is also, perhaps, somewhat more variable.

After death the body cools at first rapidly, then more slowly (Fig. 144). But occasionally a **post-mortem rise of temperature** may take place. In certain acute diseases (like tetanus) associated with excessive muscular contraction this has been especially noticed; in bodies wasted by prolonged illness it does not occur. Nearly an hour after death, in a case of tetanus, the temperature was found to be 45·3°, while before death it was 44·7° (Wunderlich). In dogs a slight post-mortem rise may be demonstrated, especially when the body is wrapped up; but when an animal has been long under the influence of anæsthetics, no indication whatever of the phenomenon may be obtained. The explanation of post-mortem rise of temperature is to be found: (1) In the continued metabolism of the tissues for some time after the heart has ceased to beat, for the cell dies harder than the body. (2) In the diminished loss of heat, due to the stoppage of the circulation. (3) Possibly to a small extent in physical changes (rigor mortis, coagulation of blood) in which heat is set free.

PRACTICAL EXERCISES ON CHAPTERS VII. AND VIII.

1. **Glycogen**—(1) *Preparation.*—(*a*) Place in a mortar some fine sand and a mixture of equal volumes of saturated solution of mercuric chloride and Esbach's reagent.* Put one or two oysters in the mortar, rub up thoroughly, and let the mass stand till (*b*) and (*c*) have been done, stirring it occasionally. Then filter and precipitate the glycogen from the filtrate with alcohol. Filter again, wash the precipitate on the filter with a little alcohol, dissolve it in 1 or 2 c.c. of water, and test for glycogen as in (*b*). The mercuric chloride and Esbach's reagent are added to precipitate the proteids, which are more completely thrown down in this way than by the methods used in (*b*) and (*c*) (Huizinga).

(*b*) Cut an oyster into two or three pieces, throw it into boiling water, and boil for a minute or two. Rub up in a mortar with clean sand, and again boil. Filter. Precipitate any proteids which have not been coagulated, by adding alternately a drop or two of hydrochloric acid and a few drops of potassio-mercuric iodide so long as a precipitate is produced. Only a small quantity of these reagents will be required, as the greater part of the proteids has been already coagulated by boiling. Filter if any precipitate has formed. The filtrate is opalescent. Precipitate the glycogen from the filtrate (after concentration on the water-bath if it exceeds a few c.c. in bulk) by the addition of four or five times its volume of alcohol. Filter off the precipitate, wash it on the filter with alcohol, and dissolve it in a little water. To some of the solution add a drop or two of iodine; a reddish-brown (port wine) colour is produced, which disappears on heating, returns on cooling, is removed by an alkali, restored by an acid. Add saliva to some of the glycogen solution, and put in a bath at 40° C. In a few minutes reducing sugar (maltose) will be found in it by Trommer's test (p. 23).

* Esbach's reagent is a solution of 10 grm. picric acid and 20 grm citric acid in a litre of water.

Note that dextrin (erythrodextrin) gives the same colour with iodine as glycogen does. Dextrin is also precipitated by alcohol, but a greater proportion must be added to cause complete precipitation. Glycogen is completely precipitated by saturation with magnesium sulphate or ammonium sulphate, while a pure solution of erythrodextrin is not precipitated. Basic lead acetate also precipitates glycogen, but not dextrin. Maltose is formed when dextrin is digested with saliva.

(*c*) Cut another oyster into pieces, throw it into boiling water acidulated with dilute acetic acid, and boil for a few minutes. Rub up in a mortar with sand, boil again, and filter. Test a portion of the filtrate with iodine for glycogen. Precipitate the rest with alcohol, filter, dissolve the precipitate in water, and test again for glycogen.

(2) Deeply etherize a dog or rabbit five hours after a meal rich in carbo-hydrates (*e.g.*, rice and potatoes). Fasten it on a holder. Clip off the hair over the abdomen in the middle line. Make a mesial incision through the skin and abdominal wall from the ensiform cartilage to the pubis. The liver will now be rapidly cut out [by the demonstrator] and divided into two portions, one of which will be [distributed among the class and] treated as in (*a*) or (*b*); the other will be kept for an hour at a temperature of 40° C., and then subjected to process (*a*) or (*b*). Little, if any, sugar and much glycogen will be found in the portion which was boiled immediately after excision. Abundance of sugar will be found in the portion kept at 40° C.; it may or may not contain glycogen.

2. **Catheterism.**—In many physiological experiments it is necessary to obtain urine from the bladder by means of a catheter. The most suitable form for animals is the flexible vulcanized rubber tubes, which are also often employed in man. It is possible to pass a fine catheter into the bladder of a male dog. A larger one is easily passed in a male rabbit, and a still larger in a bitch, which is often used for experiments on metabolism. Even in the bitch the opening of the urethra lies entirely concealed within the vagina, much deeper than the cul-de-sac in the mucous membrane, into which the beginner usually tries to force the catheter. For a first attempt the animal should be etherized and fastened on a holder. The little or index finger of the left hand is passed into the vagina till the symphysis pubis can be felt. A little below this is the opening of the urethra. With the right hand the point of a flexible catheter of suitable calibre is directed along the finger, and after a little 'guess and trial' it slips into the bladder, its entrance being announced by the escape of urine.

When the bitch is to be used in a long series of experiments an operation is sometimes performed first of all to render the urethral orifice more accessible.

3. **Glycosuria.**—(1) Weigh a dog (female by preference) or rabbit. Give morphia to the dog or chloral to the rabbit, as described on pp. 176, 190. Fasten on a holder, and etherize. Insert a glass cannula into the femoral or saphena vein of the dog, or into the jugular of the rabbit (p. 177). Fill a large syringe with a 2 per cent. solution

of dextrose (glucose) in normal saline, connect it with the cannula by means of an indiarubber tube, taking care that there are no air-bubbles in the tube, and *slowly* inject as much of the solution as will amount to ½ to ¾ grm. sugar per kilo of body-weight. Tie the vein, remove the cannula, and in half an hour evacuate the bladder by passing a catheter, by pressure on the abdomen, or, if both of these methods fail, by tapping the bladder with a trocar pushed through the linea alba (supra-pubic puncture). In an hour again draw off the urine. Test both specimens for sugar.

In this experiment, the opportunity may also be taken to demonstrate that egg-albumin, when injected into the blood, is excreted by the kidneys, a filtered solution containing the albumin of one egg and sugar in the quantity mentioned being injected.

The catheter may be inserted before the injection is begun, and the bladder evacuated. After the injection the urine that drops from the catheter may be collected in test-tubes, first every two minutes, and then, as soon as sugar is found, every ten minutes. Determine the interval between injection and the appearance of the first trace of sugar and albumin. If a sufficient amount of urine is obtained, the quantity of sugar in successive specimens may be estimated and compared. The rate of flow of the urine as measured by the number of drops falling from the catheter may also be estimated from time to time, in order to determine whether diuresis is taking place.

If a rabbit is used for this experiment, the sugar solution may be injected into the ear vein. The vein is caused to swell up by pressing on it with the finger and thumb, and the hypodermic needle is then inserted towards the heart.

(2) *Phloridzin Diabetes.*—Dissolve ¼ grm. of phloridzin in warm water, and inject it subcutaneously into a rabbit. Obtain a sample of the urine at the end of two hours, by pressure on the abdomen with the thumb or by passing a catheter, and test for sugar. If none is present, wait for another interval, and again test the urine.

This experiment can also be performed without risk on man. One grm. of phloridzin has been injected twice a day without disturbing the individual. Much sugar is found in the urine, but it disappears the day after the administration of phloridzin is stopped. The phloridzin may also be given by the mouth, but more is required, and it is not very easily absorbed, and often causes diarrhœa (v. Mering).

(3) *Alimentary Glycosuria.*—The urine having been tested for sugar for two successive days, and none being found,

(*a*) a large quantity of cane-sugar is to be taken in the form which is most agreeable to the student. The urine of the next twenty-four hours is to be collected and measured. A sample of it is then to be tested for reducing sugar by Trommer's and the phenyl hydrazine test. If any sugar is found, the reducing power of a definite quantity of the urine is to be determined by titration with Fehling's solution (p. 432) (*α*) before and (*β*) after boiling with hydrochloric acid (p. 383).

Or (*b*) a large meal of rice or arrowroot, sweetened with as much dextrose as the observer can induce himself to swallow, is to be taken, and the urine treated as in (*a*).

Or (*c*) a large number of sweet oranges may be eaten.

If experiments (*a*), (*b*) and (*c*) are all unsuccessful, (*a*) and (*b*) may be repeated on a dog.

3. **Measurement of the Quantity of Heat given off in Respiration.**—This may be done approximately as follows: Put in the inner copper vessel, A, of the respiration calorimeter (Fig. 140, p. 498) a measured quantity of water sufficient to completely cover the series of brass discs. Place A in the wider outer cylinder, the bottom of which it is prevented from touching by pieces of cork. The outer cylinder hinders loss of heat to the air. Suspend a thermometer in the water through one of the holes in the lid. In the other hole place a glass rod to serve as a stirrer. Read off the temperature of the water. Put the glass tube connected with the apparatus in the mouth, and breathe out through it as regularly and normally as possible, closing the opening of the tube with the tongue after each expiration and breathing in through the nose. Continue this for five to ten minutes, taking care to stir the water frequently. Then read off the temperature again. If W be the quantity of water in c.c., and t the observed rise of temperature in degrees Centigrade, Wt equals the quantity of heat, expressed in small calories (p. 493), given off by the respiratory tract in the time of the experiment, on the assumptions (1) that all the heat has been absorbed by the water, (2) that none of it has been lost by radiation and conduction from the calorimeter to the surrounding air. Calculate the loss in twenty-four hours on this basis; then repeat the experiment, breathing as rapidly and deeply as possible, so as to increase the amount of ventilation. The quantity of heat given off will be found to be increased.*

In an experiment of short duration (2) is approximately fulfilled. As to (1), it must be noted that in the first place the metal of the calorimeter is heated as well as the water, and the water-equivalent of the apparatus must be added to the weight of the water (p. 494). The water-equivalent is determined by putting a definite weight of water at air temperature T into the calorimeter, and then allowing a quantity of hot water at known temperature T′ to run into it, stirring well, and noting the temperature of the water when it has ceased to rise. Call this temperature T″. Enough hot water should be added to raise the temperature of the calorimeter about 2° C. The quantity run in is obtained by weighing the calorimeter before and after the hot water has been added. Suppose it is m. Let the mass of the cold water in the calorimeter at first be M, and let M′ = the mass of water which would be raised 1° C. in temperature by a quantity of heat sufficient to increase the temperature of all the metal, etc., of the calorimeter by 1°—in other words, the water-equivalent of the calorimeter.

The mass m of hot water has lost heat to the amount of m (T′ − T″), and this has gone to raise the temperature of a mass of water M, and metal equivalent to a mass of water M′, by (T″ − T)

* The average heat-loss by the lungs for 51 men (calculated for the 24 hours) was 312,000 small calories for normal, 919,000 for the fastest, and 195,000 for the slowest breathing.

degrees. $\therefore m(T' - T'') = M(T'' - T) + M'(T'' - T)$. Everything in this equation except M′ is known, and $\therefore$ M′, the water-equivalent of the calorimeter, can be deduced, and must be added in all exact experiments to the mass of water contained in it.

Secondly, all the excess of heat in the expired over that in the inspired air is not given off to the calorimeter, for the air passes out of it at a slightly higher temperature than that of the atmosphere. At the beginning of the experiment this excess of temperature is zero. If at the end it is 1° C., the mean excess is 0·5° C. Now, when respiration is carried on in a room at a temperature of 10° C., the expired air has its temperature increased by nearly 30° C. About $\frac{1}{60}$ of the heat given off by the respiratory tract in raising the temperature of the air of respiration would accordingly be lost in such an experiment. But since the portion of the heat lost by the lungs which goes to heat the expired air is only $\frac{1}{7}$ of the whole heat lost in respiration (p. 497), the error would only amount to $\frac{1}{420}$ of the whole, and this is negligible.

Thirdly, the air leaves the calorimeter saturated with watery vapour at, say, 10·5°, while the inspired air is not saturated for 10° C. Now, the quantity of heat rendered latent in the evaporation of water sufficient to saturate a given quantity of air at 40° C. (the expired air is saturated for body temperature) is six times that required to saturate the same quantity of air at 10°. If, then, the inspired air is half saturated, the error under this head is $\frac{1}{12}$, or $8\frac{1}{2}$ per cent. If the inspired air is three-quarters saturated, the error is $\frac{1}{24}$, or about 4 per cent. If the air is fully saturated before inspiration, as is the case when it is drawn in through a water-valve (Fig. 145) by a tube fixed in one nostril, the only error is that due to the slight excess of temperature of the air leaving the calorimeter over that of the inspired air. The latent heat of the aqueous vapour in saturated air at 10·5° C. is about $\frac{1}{20}$ more than the latent heat of the aqueous vapour in the same mass of saturated air at 10° C., or about $\frac{1}{120}$ of the latent heat in saturated air at 40°. The error in this case would therefore be under 1 per cent. The tubes must be wide and the bottle large.

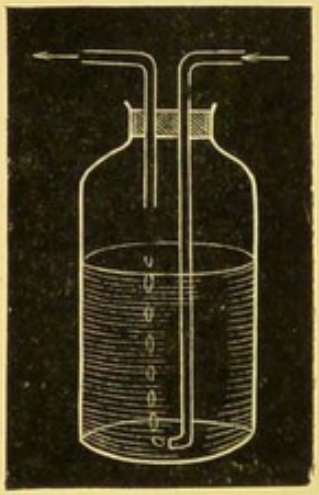


FIG. 145. — BOTTLE ARRANGED FOR WATER-VALVE.

4. **Variations in the Quantity of Urea excreted, with Variations in the Amount of Proteids in the Food.**—The student should put himself, or somebody else if he can, for two days on a diet poor in proteids, then (after an interval of forty-eight hours on his ordinary food) for two days on a diet rich in proteids. A suitable table of diets will be supplied. The urine should be collected on the six days of the period of experiment, on the day before it begins, and on the day after it ends. Small samples of the mixed urine of the twenty-four hours for each of these eight days should be brought to the laboratory, and the quantity of urea determined by the hypobromite method. The

volume of the urine passed in each interval of twenty-four hours being known, the total excretion of urea for the twenty-four hours can be calculated, and a curve plotted to show how it varies during the period of experiment.*

5. **Thyroidectomy.**—Study the anatomy of the neck and the relations and blood-supply of the thyroid glands in a dog used for some previous experiment.

(1) Then select a half-grown dog, weigh it, inject morphia subcutaneously (p. 176), and fasten on the holder back down. Clip the hair from the neck, and shave a wide space on each side of the middle line. Scrub with soap and water, then with corrosive sublimate solution (0·1 per cent.). Sponges, instruments, ligatures, etc., must have been boiled in water; the instruments are immersed in 5 per cent. carbolic acid solution, everything else in the corrosive solution. The hands and nails must be carefully cleansed and washed with the corrosive sublimate. A longitudinal incision is made through the skin and subcutaneous tissue in the middle line of the neck, beginning a little below the projecting thyroid cartilage. By separating the longitudinal muscles just external to the trachea on one side, the corresponding thyroid lobe will be seen as an oval red body. It is now to be carefully freed from its attachments; all vessels connected with it are to be tied with double ligatures, and divided between the ligatures. In tying the superior thyroid artery (a short large vessel coming off from the carotid), care must be taken not to put the ligatures too near its origin, as the rapid current in the carotid may prevent closure of the vessel by clot, and secondary hæmorrhage may occur some days after the operation. The thyroid lobe is thus shelled out of the tissues in which it lies. If, as rarely happens, an isthmus is present (connecting the two lobes across the front of the trachea), it must also be removed. All bleeding having been stopped, the wound is washed out with corrosive solution, and the muscles brought together over the trachea by a row of interrupted sutures, which should not be drawn too tight. The wound in the skin is then closed by a similar row, preferably of subcutaneous sutures (see p. 190). Collodion is painted over the wound, and the animal is returned to its cage. It should be kept for a week, or, better, a fortnight, and examined carefully during that time. Probably, unless the wound has become infected, its behaviour will be perfectly normal.

(2) The second part of the experiment, which consists in removing the remaining thyroid lobe, is now to be performed just as in (1). The animal must be examined next morning, and then twice a day for the following week, as the symptoms of cachexia strumipriva generally come on very rapidly in young dogs, and death may even ensue within two days. Trembling of the limbs, associated with instability of movement, spasms resembling those of tetany, sometimes passing into general epileptiform convulsions, and progressive emaciation,

* In 17 healthy students the average amount of urea excreted in twenty-four hours on the ordinary diet was 29·51 grm. (minimum 19·35 grm., maximum 46·007 grm.); on a diet poor in proteid, average 20·75 grm. (minimum 9·517 grm., maximum 32·857 grm.); on a diet rich in proteid, average 38·83 grm. (minimum 23·265 grm., maximum 67·82 grm.).

are the most marked symptoms. The animal must be weighed daily, the temperature taken in the rectum, the thermometer being always pushed in to the same distance ; and it will also be well to determine the number of the red corpuscles in samples of the blood. To obtain the samples punctures may be made in the gluteal region with the point of a narrow-bladed knife or lancet, the skin having been first shaved and thoroughly dried. The blood should flow freely without pressure (p. 61). A record of the experiment from the operation to the autopsy must be kept. At the autopsy search must be made to see whether the thyroid was completely removed, and whether any accessory thyroids exist. Such are occasionally found in the form of small reddish masses, either in the neck or within the chest in the neighbourhood of the aorta. If any are found, they must be hardened in alcohol and sections made. Portions of the muscles, spleen, and central nervous system are also to be preserved ; and it is to be observed whether the pituitary body has undergone any increase in size or other change (pp. 485, 489).

6. **Thyroidectomy with Thyroid Feeding.**—Some of the members of the class should modify experiment 5 by feeding the animal, as soon as symptoms have appeared, with fresh sheep's thyroid glands or commercial thyroid extracts, and noting any alleviation of the symptoms. If, as only rarely happens, they disappear, the animal is to be allowed to live for a considerable time, then killed by chloroform, an autopsy made, and portions of the tissues hardened and compared with those from experiments done as in 5.

CHAPTER IX.

MUSCLE.

It is impossible to understand the general physiology of muscle and nerve without some acquaintance with electricity. It would be out of place to give even a complete sketch of this preliminary but essential knowledge here; and the student is expressly warned that in this book the elementary facts and principles of physics are assumed to be part of his mental outfit. But in describing some of the electrical apparatus most commonly used in the study of this portion of our subject, it may be useful to recall the physical facts involved.

Batteries.—The Daniell cell is perhaps better suited for physiological work than any other voltaic element, although for special purposes Bunsen, Grove, Leclanché, and bichromate of potassium batteries may be employed.

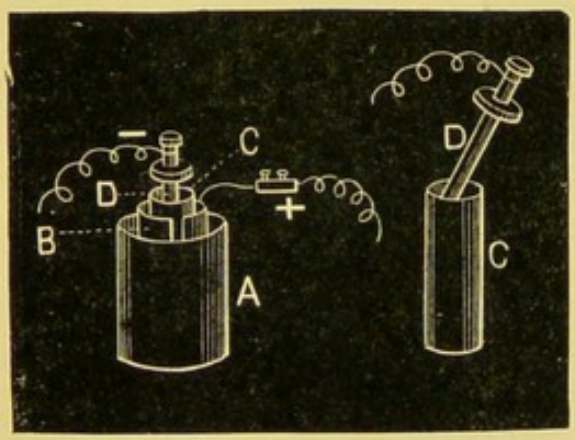


Fig. 146.—Daniell Cell.

A, outer vessel; B, copper; C, porous pot; D, zinc rod; D is supposed to be raised a little so as to be seen.

The Daniell is a two-fluid cell. Saturated solution of sulphate of copper is contained in an outer vessel, and a dilute solution of sulphuric acid in a porous pot standing in the copper sulphate solution. The latter is kept saturated by a few crystals of copper sulphate. A piece of sheet-copper, generally bent so as to form a hollow cylinder, dips into the sulphate of copper, and a piece of amalgamated zinc into the contents of the porous pot. Inside the cell the current (the positive electricity) passes from zinc to copper; outside, from copper to zinc. The copper is called the positive, the zinc the negative, pole. When the current is passed through a tissue, the electrode by which it enters is termed the anode, and that by which it leaves the tissue the kathode. The anode is, therefore, the electrode connected with the copper of the Daniell's cell; the kathode is connected with the zinc.

Potential—Current Strength—Resistance.—We do not know what in reality electricity is, but we do know that when a current flows along a wire energy is expended, just as energy is expended when water flows from a higher to a lower level. Many of the phenomena of current electricity can, in fact, be illustrated by the laws of flow of an incompressible liquid. The difference of level, in virtue of which the flow of liquid is maintained, corresponds to the difference of electrical level, or *potential*, in virtue of which an electrical current is kept up. The positive pole of a voltaic cell is at a higher potential than the negative. When they are connected by a conductor, a flow of electricity takes place, which, if the difference of level or potential were not constantly restored, would soon equalize it, and the current would cease; just as the flow of water from a reservoir would ultimately stop if it was not replenished. If the reservoir was small, and the discharging-pipe large, the flow would only last a short time; but if water was constantly being pumped up into it, the flow would go on indefinitely. This is practically the case in the Daniell cell. Zinc is constantly being dissolved, and the chemical energy which thus disappears goes to maintain a constant difference of potential between the poles. Electricity, so to speak, is continually running down from the place of higher to the place of lower potential, but the cistern is always kept full.

The difference of electrical potential between two points is called the *electromotive force;* and from its analogy with difference of pressure in a liquid, it is easy to understand that the *intensity or strength of the current*, that is, the rate of flow of the electricity between two points of a conductor, does not depend upon the electromotive force alone, any more than the rate of discharge of water from the end of a long pipe depends alone on the difference of level between it and the reservoir. In both cases the *resistance* to the flow must also be taken account of. With a given difference of level, more water will pass per second through a wide than through a narrow pipe, for the resistance due to friction is greater in the latter. In the case of an electrical current, a wire connecting the two poles of a Daniell's cell will represent the pipe. A thick short wire has less resistance than a thin long wire; and for a given difference of potential, of electric level, a stronger current will flow along the former. But for a wire of given dimensions, the intensity of the current will vary with the electromotive force. The relation between electromotive force, strength of current, and resistance were experimentally determined by Ohm, and the formula $C = \frac{E}{R}$, which expresses it, is called Ohm's Law. It states that the current varies directly as the electromotive force, and inversely as the resistance.

Although we do not know in what electrical resistance consists, it may be defined as that property of a conductor in virtue of which a flow of electricity cannot be kept up through it without the expenditure of energy. In treating of the circulation of the blood, we have already seen that the flow of a liquid along a tube involves the expenditure of energy to overcome the friction of the liquid molecules

on each other, and that this energy is transformed into heat (p. 72). In like manner electrical energy is transformed into heat whenever a current flows along a wire. The heat produced in a circuit in which no external work is done is exactly equal to the energy which has disappeared in the transference of the electricity from the place of higher to the place of lower potential; just as the heat produced in the flow of a liquid is equal to the difference in its total energy at the beginning and end of the path. If C is the current strength, and E the electromotive force, the energy represented by the transference of electricity in time t is $EC t$, or (since $E = CR$ by Ohm's Law), C^2Rt; and this represents the heat produced in the circuit when no work is done.

For the measurement of electrical quantities a system of units is necessary. The common unit of resistance is the *ohm*, of current the *ampère*, of electromotive force the *volt*. The electromotive force of a Daniell's cell is about a volt. An electromotive force of a volt, acting through a resistance of an ohm, yields a current of one ampère; but the current produced by a Daniell's cell, with its poles connected by a wire of 1 ohm resistance, would be less than an ampère, because the internal resistance of the cell itself, that is, the resistance of the liquids between the zinc and the copper, must be added to the external resistance in order to get the total resistance, which is the quantity represented by R in Ohm's Law.

Measurement of Resistance.—To find the resistance of a conductor, we compare it with known resistances, as a grocer finds the

FIG. 147.—WHEATSTONE'S BRIDGE.

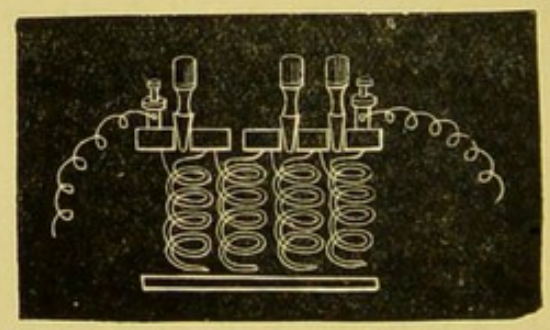


FIG. 148.—DIAGRAM OF RESISTANCE BOX.

weight of a packet of tea by comparing it with known weights. The Wheatstone's bridge method of measuring resistance depends on the fact that if four resistances, AB, AD, BC, CD, are connected, as in Fig. 147, with each other, and with a galvanometer G and a battery F, no current will flow through the galvanometer when $\frac{AB}{AD} = \frac{BC}{CD}$.

For when no current passes through the galvanometer, B and D are at the same potential. Let the fall of potential from C to B or from C to D be α; then, since the total fall of potential from C to A must be the same along either of the paths CBA or CDA, the fall from B to A must be equal to that from D to A. Call this β. Now, the

fall of potential which takes place in any given portion of a circuit is to the whole fall of potential in the circuit as the resistance of the given portion is to the whole resistance. That is,

$$\frac{\alpha}{\alpha+\beta}=\frac{BC}{BC+AB},$$

$$\frac{\beta}{\alpha+\beta}=\frac{AB}{BC+AB};\quad \therefore\quad \frac{\alpha}{\beta}=\frac{BC}{AB}.$$

Similarly: $\frac{\alpha}{\beta}=\frac{CD}{AD};\quad \therefore\quad \frac{BC}{AB}=\frac{CD}{AD}$, or $\frac{AB}{AD}=\frac{BC}{CD}$.

In making the measurement, a resistance-box, containing a large number of coils of wire of different resistances, is used (Fig. 148). The resistances corresponding to AB and AD, called the arms of the bridge, may be made equal, or may stand to each other in a ratio

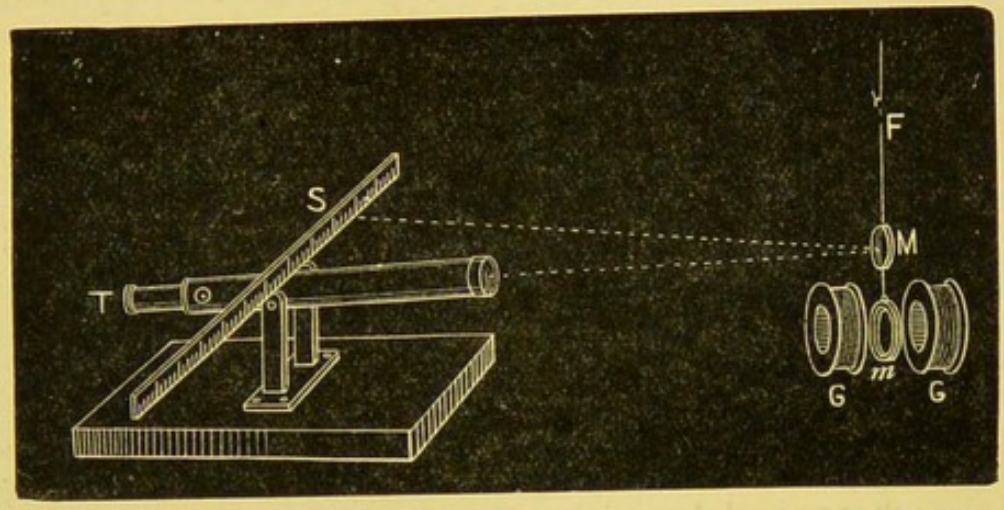


FIG. 149.—SCHEME OF WIEDEMANN'S GALVANOMETER (WITH TELESCOPE READING).

T, telescope; S, scale; M, mirror; *m*, ring magnet suspended between the two galvanometer coils G, the distance of which from *m* can be varied; F, fibre suspending mirror and magnet.

of 1 : 10, 1 : 100, etc. Then, the unknown resistance being CD, BC is adjusted by taking plugs out of the box till, on closing the current, there is either no deflection, or the deflection is as small as it is possible to make it with the given arrangement.

Galvanometer.—A galvanometer is an instrument used to detect a current, to determine its direction, and to measure its intensity. Since, by Ohm's law, electromotive force, resistance, and current strength are connected together, any one of them may be measured by the galvanometer. A galvanometer of the kind ordinarily used in physiology consists essentially of a small magnet suspended in the axis of a coil of wire, and free to rotate under the influence of a current passing through the coil. The most sensitive instruments possess a small mirror, to which the magnet is rigidly attached. A ray of light is allowed to fall on the mirror, from which it is reflected on to a scale; and the rotation of the mirror is magnified and measured by the excursion of the spot of light on the scale. In

the Thomson galvanometers the magnet is very light. A strip or two of magnetized watch-spring does very well. The magnet is 'damped,' that is, its tendency, when once displaced, to go on oscillating about its new position of equilibrium is overcome by enclosing it in a narrow air space. In the Wiedemann instrument the magnet is heavier (Fig. 149). It swings in a chamber with copper walls. Every movement of the magnet 'induces' currents in the copper; these tend to oppose the movement, and so 'damping' is obtained. It is usual to read the deflections of the Wiedemann galvanometer by means of a telescope. An inverted scale is placed over the telescope at a distance of, say, a metre from the mirror; an upright image of the scale is formed in the telescope after reflection from the mirror, and with every movement of the latter the scale divisions appear to move correspondingly. The method of reading by a telescope can be applied to any mirror galvanometer, and is often extremely convenient in physiological work. Sometimes a small scale is fastened on the mirror itself, and observed directly through a low-power microscope.

A suspended magnet, if no other magnets are near, takes up a definite position under the influence of the earth's magnetism; its long axis, in the position of rest, lies in a vertical plane, called the plane of the magnetic meridian at the given place. The 'marked' or north pole points north, the south pole south. If the magnet is disturbed from this position, it tends to return to it as soon as the disturbing force ceases to act. If, for instance, the north pole is displaced in an eastward direction, the earth's magnetism will produce a couple (a pair of parallel forces acting in opposite directions), one member of which may be considered to pull the north pole towards the west, and the other to pull the south pole towards the east. Displacement of the magnet, then, is opposed by this couple; and where the displacing force is small, that is, the current passing through the galvanometer weak, as is usually the case in physiological observations, it becomes important to reduce the effect of the magnetism of the earth, in other words, the strength of the magnetic field, as much as possible. This can be done by bringing a magnet into the neighbourhood of the galvanometer with its north pole pointing north. This pole, which is the one attracted by the earth's north pole, is magnetized in the opposite sense; and by properly adjusting its distance from the galvanometer magnet, the influence of the earth on the latter can be almost neutralized, and the system made nearly 'astatic.' In many galvanometers the magnets attached to the mirror form an 'astatic' pair (Fig. 150). Two small magnets of nearly equal strength are connected to a light slip of horn or an aluminium wire, with their poles in opposite directions. The earth's magnetism affects them oppositely, so that the resultant action is nearly zero. It is not possible to make the magnets exactly equal in strength, nor is it desirable, for then the system would not tend to come to rest in any definite position, and the zero point would be constantly shifting. Either one or both magnets may be surrounded by the galvanometer coils. If both are so surrounded, each must be within a separate

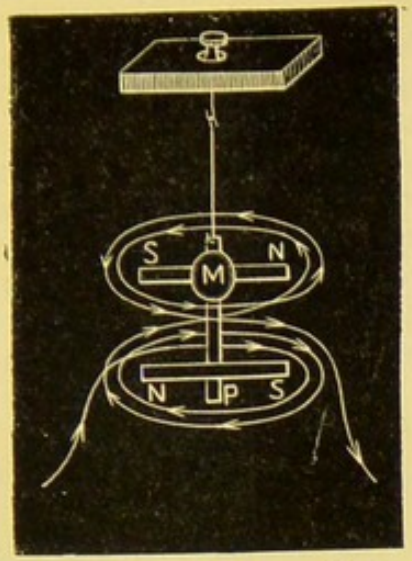


FIG. 150.—ASTATIC PAIR OF MAGNETS.

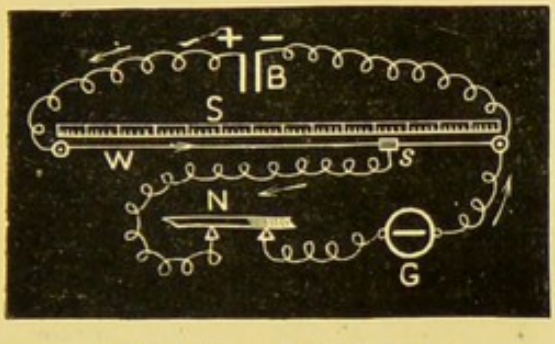


FIG. 152.—COMPENSATOR.

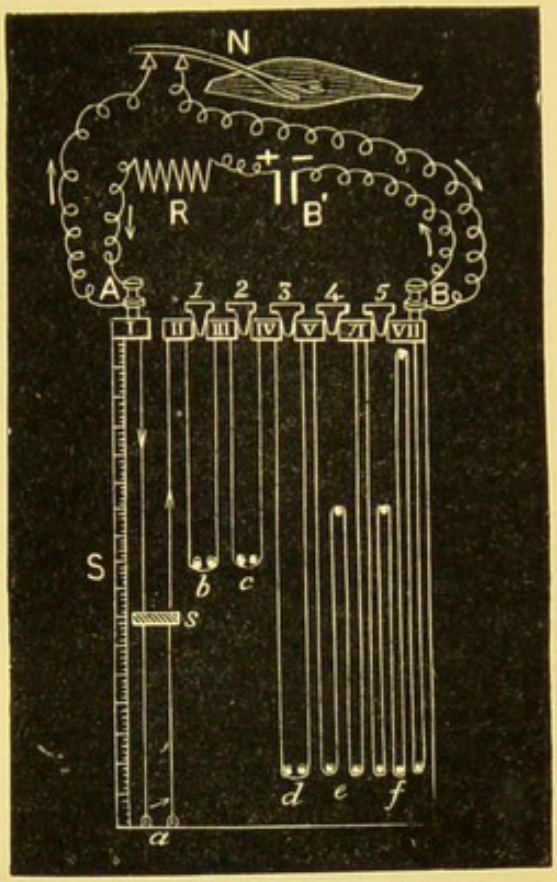


FIG. 151.—DIAGRAM OF RHEOCORD (AFTER DU BOIS-REYMOND'S MODEL).

Description of Fig. 150.—SN and NS are the magnets, fixed to the vertical piece P. M is a mirror. The arrow-heads show the direction of a current which deflects both magnets in the same direction.

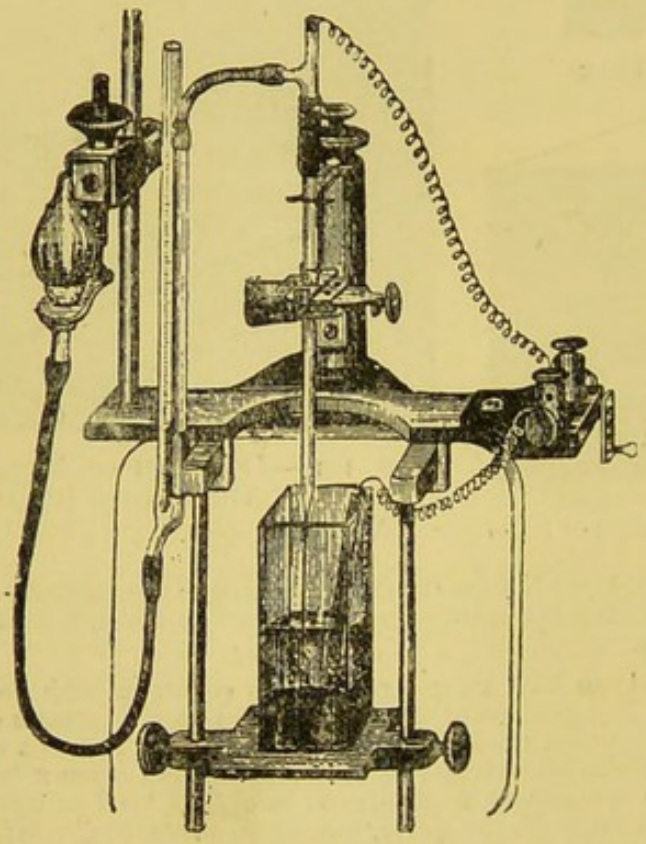
Description of Fig. 151.—I. to VII. are pieces of brass connected with the wires *a* to *f* in such a way that by taking out any of the brass plugs 1 to 5, a greater or less resistance may be interposed between the binding screws A and B. The two wires *a* are connected by a slider *s*, filled with mercury or otherwise making contact between the wires. The current from the battery B′ divides at A and B, part of it passing through the rheocord, part through N, the nerve, muscle, or other conductor which forms the alternative circuit. When a sufficient resistance R is interposed in the chief circuit to make the total strength of the current independent of changes in the resistance of the rheocord, the strength of the current passing through N will vary inversely as the resistance of the rheocord. When all the plugs are in, and the slider close up to A, there is practically no resistance in the rheocord, and all the current passes across the brass pieces and plugs to B, and thence back to the battery. As *s* is moved further away from A, the resistance of the rheocord is increased more and more, and the intensity of the current passing through N becomes greater and greater. The scale S shows the length of wire interposed for any position of *s*, and this gives a rough measure of the fraction of the current passing through N. When plug 1 or 2 is taken out, a resistance equal to that of the two wires *a* is interposed; plug 3, twice that of *a*; plug 4, five times; plug 5, ten times.

Description of Fig. 152.—W is a wire stretched alongside a scale S. A battery B is connected to the binding screws at the ends of the wire. A pair of unpolarizable electrodes are connected, one with a slider moving on a wire, the other through a galvanometer with one of the terminal binding screws. In the figure a nerve is shown on the electrodes, one of which is in contact with an uninjured portion, the other with an injured part. The slider is moved until the twig of the compensating current just balances the demarcation current of the nerve and the galvanometer shows no deflection.

coil, and the current must pass in opposite directions in the two coils, otherwise they would neutralize each other.

The deflection of a magnet by a current of given strength is proportional to the number of turns of wire around it. Where an increase in the number of turns does not sensibly cut down the current, as in experiments on tissues like nerves, whose resistance is large in comparison with that of the galvanometer, an instrument with a great number of turns of wire, that is, a high-resistance galvanometer, is suitable. The resistance of the galvanometers generally used in electro-physiology varies from 3,000 or 4,000 ohms up to five times as much.

A **rheocord** is an instrument by means of which a current may be divided, and a definite portion of it sent through a tissue (Fig. 151).



The electrometer consists (1) of a small table carrying a parallel-sided glass vessel containing mercury and sulphuric acid. (2) The capillary tube, which can be moved in two directions at right angles to each other, and so adjusted in the field of the microscope. (3) A pressure-vessel, and a manometer connected with it for measuring the pressure. (4) Two binding-screws connected by wires to the mercury in the capillary tube and in the parallel-sided vessel. The binding-screws can be short-circuited by closing the friction-key shown at the right side of the figure, thus preventing any difference of electromotive force between two points connected with the screws from affecting the electrometer.

FIG. 153.—CAPILLARY ELECTROMETER (AFTER FREY), AS ARRANGED FOR MOUNTING ON THE MICROSCOPE STAGE.

A **compensator** is simply a rheocord from which a branch of a current is led off, to balance or 'compensate' any electrical difference in a tissue, like that which gives rise to the current of rest of a muscle, for example (Fig. 152).

An **electrometer** is an instrument for measuring electromotive force, that is, differences of electric potential. Lippmann's capillary electrometer is being more and more employed in physiology. A convenient form of it is shown in Fig. 153. A simpler form, suitable for students working in a class where a considerable number of copies of the instrument is needed, can be conveniently made as follows. A glass tube is drawn out to a capillary at one end and

filled with mercury. The tube is inserted into a small glass bottle,* and fastened in its neck by a cork or a plug of sealing-wax which does not quite fill the opening, so that the interior of the bottle is still in communication with the external air. The upper end of the tube is connected by a short piece of rubber-tubing with a glass T-tube as in Fig. 154. The bottle is partially filled with 5 to 10 per cent. sulphuric acid, under which the capillary dips. By means of a small reservoir made from a piece of glass tubing filled with mercury,

B, bottle containing sulphuric acid; Hg, mercury; E, E′, platinum wires. E dips into the mercury in the vertical tube, and E′ is fused through the bottom of B, so as to make contact with the mercury in B, the other end of it passing out through a small hole in the wooden platform F, on which B rests. F is fastened to the stage of the microscope, S, by a pin, G, passing through one of the clip-holes, and to the wooden upright, D, by the pin, H. D fits tightly over the microscope stage, but can be moved laterally a little so as to bring the capillary into the middle of the field. I, stem of glass T-tube passing through a hole in D. L, rubber-tube connecting the capillary point with the vertical portion of the T-tube. A is a reservoir containing mercury connected by the rubber-tube M to I. A can be raised or lowered by sliding it in the clips K. In the figure the capillary tube appears as if the mercury extended to the very point of it. This should not be the case; the sulphuric acid should rise for some distance in the capillary, so that the mercury shows a sharply-bounded meniscus in the tube as is represented in C, the magnified image of the capillary as seen with the microscope.

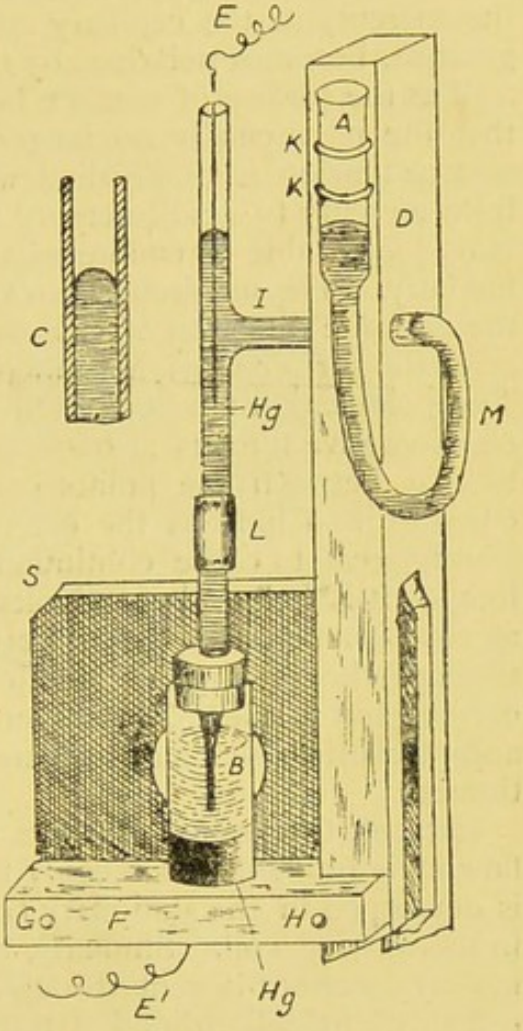


FIG. 154.—A SIMPLE CAPILLARY ELECTROMETER.

and connected with the stem of the T-tube, a little mercury is forced through the capillary so as to expel the air in it. When the pressure is lowered again, sulphuric acid is drawn up, and now lies in the

* A parallel-sided bottle is best, as it gives the clearest image of the meniscus. But it is easiest to make a cylindrical bottle from a piece of wide glass-tubing, and to insert a platinum wire into it before closing it at the bottom in the blow-pipe flame. The tube can then be firmly fastened with sealing-wax in a depression in a piece of wood, the wire being brought out through a hole in the wood. Once the instrument is arranged, there is little chance of the capillary getting broken, and there is very little evaporation of the acid.

capillary in contact with the meniscus of the mercury. A platinum wire fused through the tube, or simply inserted through its upper end, dips into the mercury. Another, passing through the cork, or, better, fused through the bottom of the bottle, makes contact with the sulphuric acid through some mercury. The bottle is fastened on the stage of a microscope, the capillary brought into focus, and the meniscus adjusted by raising or lowering the reservoir. When the platinum wires are connected with points at different potential, a current begins to pass through the instrument, and the meniscus of the mercury in the capillary tube, where the current density is the greatest, becomes polarized by the ions separated from the sulphuric acid at the surface of contact between the acid and the mercury, so that the meniscus is no longer in equilibrium in the tube. The surface tension is diminished when the direction of the current is from mercury to acid (mercury at a higher potential than acid), and is no longer able to counterbalance the hydrostatic pressure of the mercury. The meniscus therefore moves down in the tube. With the opposite direction of current (mercury at a lower potential than acid) the surface tension is increased, and the meniscus moves up. The polarization develops itself almost instantaneously, and thus an electromotive force is at once established in the opposite direction to that between the points connected with the electrometer, and equal to it so long as the external electromotive force is not sufficiently great to cause continuous electrolysis of the acid, that is, so long as it is below about 2 volts. The external current is therefore at once compensated, and after the first moment no current passes through the instrument, which is accordingly not a measurer of current, but of electromotive force. It is very suitable for detecting and measuring such small differences of potential as occur in animal tissues.

Induced Currents.—When a coil of wire in which a current is flowing is brought up suddenly to another coil, a momentary current is developed in the stationary coil in the opposite direction to that in the moving coil. Similarly, if instead of one of the coils being moved a current is sent through it, while the other coil remains at rest in its neighbourhood, a transient oppositely-directed current is set up in the latter. When the current in the first coil is broken, a current in the same direction is induced in the other coil.

Du Bois-Reymond's Sledge Inductorium (Fig. 155).—This consists of two coils, the primary and the secondary, the former having a comparatively small number of turns of fairly thick copper wire, the latter a large number of turns of thin wire. The object of this is that the resistance of the primary, which is connected with one or more voltaic cells, may not cut down the current too much; while the currents induced in the secondary, having a high electromotive force, can readily pass through a high resistance, and are directly proportional in intensity to the number of turns of the wire.

By means of various binding-screws and the electro-magnetic interrupter, or Neef's hammer, shown in the figure and explained

below it, the current can be made once in the primary or broken once, or a constant alternation of make and break can be kept up. We can thus get a single make or break shock in the secondary, or a series of shocks, sometimes called an interrupted current. Such a series of stimuli can also be got by making and breaking a voltaic current at any given rate.

A 'self-induced' current can also be obtained from a single coil; for instance, from the primary coil alone of the induction apparatus. The reason of this is, that when a current begins to flow through any turn of a coil of wire, it induces in all the other turns a current in the opposite direction, and, when it ceases to flow, a current in the same direction as itself. The former current, 'the make extra shock,' being in the opposite direction to the inducing current, is retarded in its development, and reaches its maximum more slowly than the break extra shock. But, as we shall see, the suddenness with which an

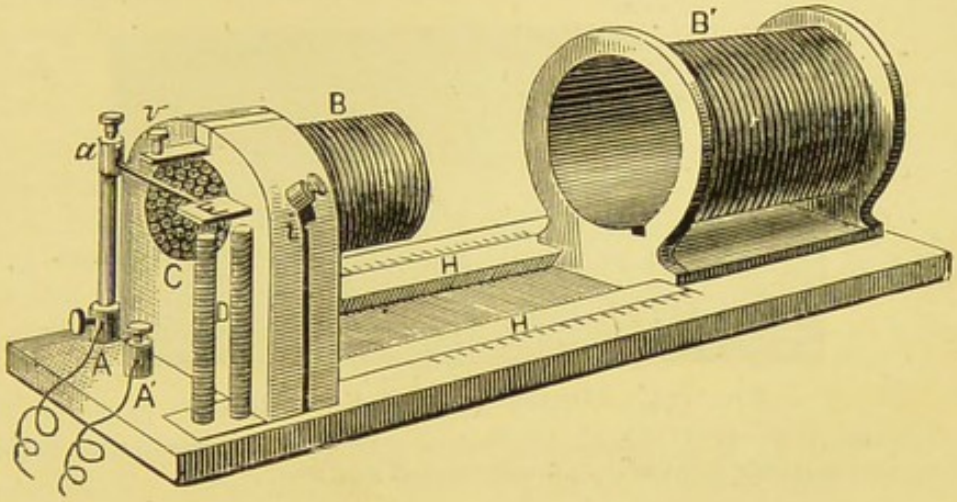


FIG. 155.—DU BOIS-REYMOND'S INDUCTORIUM.

B, primary, B', secondary, coil; H, guides in which B' slides, with scale; D, electro-magnet; E, vibrating spring; *i*, wire connecting wire of D to end of primary; *v*, screw with platinum point, connected with other end of primary; A, A', binding screws to which are attached the wires from battery. A' is connected with the wire of the electro-magnet D, and through it and *i* with the primary.

electrical change is brought about is one of the most important factors in electrical stimulation, and therefore the break extra shock is a much more powerful stimulus than the make. Owing to these self-induced currents, the stimulating power of a voltaic stream may be much increased by putting into the circuit a coil of wire of not too great resistance.

The self-induction of the primary also affects the stimulating power of the currents induced in the secondary; the shock induced in the secondary by break of the primary current is a stronger stimulus than that caused at make of the primary. The reason is, that with a given distance of primary and secondary, and a given intensity of the voltaic current in the primary, the abruptness with which the induced current in the secondary is developed depends upon the rapidity

with which the primary current reaches its maximum at closing, or its minimum (zero) at opening. Now, the make extra current retards the development of the primary current, while in the opened circuit of the primary coil the current intensity falls at once to zero.

The inequality between the make and break shocks of the secondary coil can be greatly reduced by means of Helmholtz's wire. Connect one pole of the battery with *v* (Fig. 155), and the other with A′. Join A and A′ by a short, thick wire. With this arrangement the primary circuit is never opened, but the current is alternately allowed to flow through the primary, and short-circuited when the spring touches *v*. The 'make' now corresponds to the sudden increase of intensity of the current in the primary when the short-circuit is removed, and the 'break' to its sudden decrease when the short-circuit is established. In both cases self-induced currents are developed, and therefore both shocks are weakened. But the opening stimulus is now slightly the weaker of the two,

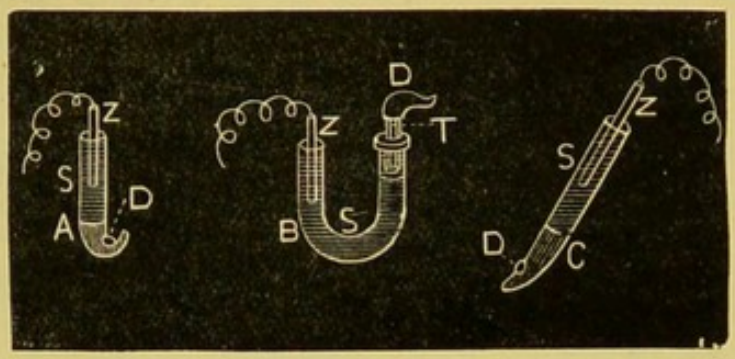


FIG. 156.—UNPOLARIZABLE ELECTRODES.

A, hook-shaped; B, U-tubes; C, straight. D, clay in contact with tissue; S, saturated zinc sulphate solution; Z, amalgamated zinc wire.

because the opening extra shock has to pass through a smaller resistance (the short-circuit) than the closing extra shock (which passes by the battery), and therefore opposes the decline of current intensity on short-circuiting, more than the closing shock opposes the increase of current intensity on long-circuiting through the primary.

By means of wires connected with the terminals of the secondary coil, and leading to electrodes, a nerve or muscle may be stimulated; and it is usual to connect the wires to a short-circuiting key (Fig. 158), by opening which the induced current is thrown into the tissue to be stimulated. For some purposes the electrodes may be of platinum; but all metals in contact with moist tissues become polarized when currents pass through them, that is, have decomposition products of the electrolysis of the tissues deposited on them. And as any slight chemical difference, or even perhaps a difference of physical state, between the two electrodes will cause them and the tissues to form a battery evolving a continuous current, it is often desirable to use *unpolarizable electrodes*.

Unpolarizable Electrodes.—Some convenient forms of these are represented in Fig. 156. A piece of amalgamated zinc wire dips into

saturated zinc sulphate solution contained in the upper part of a glass tube. The lower end of the tube may be straight, but drawn out so as to terminate in a not very large opening, or it may be bent into a hook, in the bend of which a hole is made. Before the tube is filled with the zinc sulphate solution, the lower part of it is plugged with china clay made up with normal saline. The clay just projects through the opening, and thus comes in contact with the tissue. When these electrodes are properly set up, there is very little polarization for several hours, but for long experiments, U-shaped tubes, filled with saturated zinc sulphate solution, are better. The amalgamated zinc dips into one limb, and a small glass tube filled with clay, on which the tissue is laid, into the other.

Pohl's Commutator (Fig. 157) consists of a block of paraffin or wood with six mercury cups, each in connection with a binding-screw (not shown in the figure). Cups 1 and 6 and 2 and 5 are connected by copper wires, which cross each other without touching. The bridge consists of a glass or vulcanite cross-piece *a*, to which are attached two wires bent into semicircles, each connected with a straight wire dipping into the cups 3 and 4 respectively. With the bridge in the position shown in the figure, a current coming in at 4 would pass out by the wire connected with 1, and back again by that connected with 2, in the direction shown by the arrows. When the bridge is rocked to the other side so that the bent wires dip into 5 and 6, the direction of the current is reversed. The cross-wires may be taken out altogether, and the commutator used to send a current at will through either of two circuits, one connected with 1 and 2, and the other with 5 and 6.

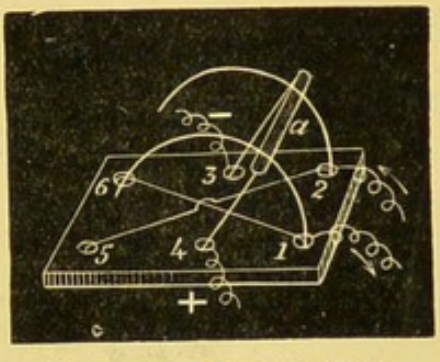


FIG. 157.—POHL'S COMMUTATOR.

Du Bois-Reymond's Short-circuiting Key.—A cheap and convenient form is shown in Fig. 158.

Time-Markers—Electric Signal.—It is of importance to know the time relations of many physiological phenomena which are graphically recorded; for example, the contraction of a skeletal muscle or the beat of a heart. For this purpose a tracing showing the speed of the travelling-surface in a given time is often taken simultaneously with the record of the movement under investigation. For a slowly-moving surface it is sufficient to mark intervals of one or two seconds, and this is very readily done by connecting an electro-magnetic marker (such as the electric signal of Deprez) with a circuit which is closed and broken by the seconds pendulum of an ordinary clock (Fig. 159) or a metronome (Fig. 60, p. 170). For shorter intervals a tuning-fork is used, which makes and breaks a circuit including an electro-magnetic marker, or writes on the drum directly by means of a writing-point attached to one of the prongs.

In all the great functions of the body we find that muscular movements play an essential part. The circulation and the respiration, the two functions most immediately essential to life, are kept up by the contraction and relaxation of muscles. The movements of the digestive canal, the regulation of the blood-supply to its glands and to all parts of the body, and that immense class of movements which we call voluntary, are all dependent upon muscular action, which, again, is indebted for its initiation, continuance, or control, to impulses passing along the nerves from the nerve-centres.

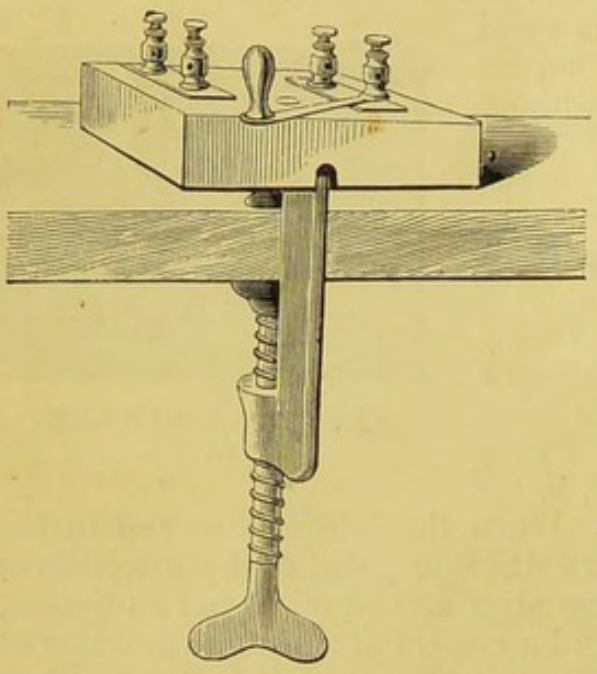


FIG. 158.—DU BOIS-REYMOND'S KEY.

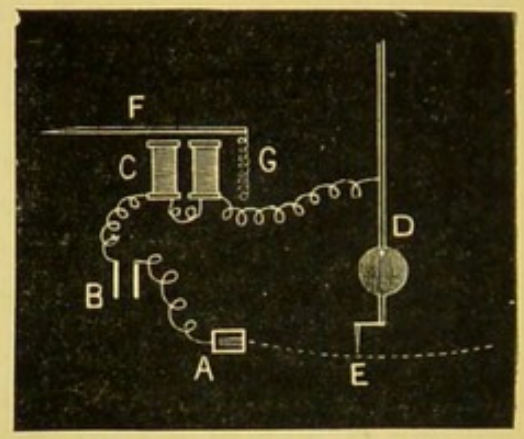


FIG. 159.—TIME-MARKER.

Arrangement for marking 2 intervals. D, seconds pendulum, with platinum point E soldered on; A, mercury trough, into which E dips at end of its swing; B, Daniell cell; C, electro-magnets, which draw down writing-lever F when the current is closed by E dipping into A; G, spring (or piece of indiarubber), which raises F as soon as current is broken.

Hitherto we have not gone below the surface fact, that muscular fibres have the power of contracting, either automatically, or in response to suitable stimuli. In this chapter and the two next we shall consider in detail the general properties of muscle, nerve, and the other excitable tissues.

Lying deeper than the peculiarities of individual muscles, muscular tissue has certain common properties, physical, chemical, and physiological. The biceps muscle flexes the arm upon the elbow, and the triceps extends it. The external rectus rotates the eyeball outwards. The intercostal muscles elevate the ribs. The sphincter ani seals up by a ring-like contraction the lower end of the alimentary

canal. These actions are very different, but the muscles that carry them out are at bottom very similar. And it cannot be doubted that the functional differences are due entirely, or almost entirely, to differences of anatomical connection, on the one hand with bones and tendons, on the other with the nerve-cells of the spinal cord and brain. The common properties in which all the skeletal muscles agree are the subject-matter of the general physiology of striated muscle.

The cardiac muscle differs more, both in structure and in function, from the skeletal muscles than these do among themselves; the smooth muscle of the intestines and blood-vessels still more. But every muscular fibre, striped or unstriped, resembles every other muscular fibre more than it does a nerve-fibre or a gland-cell or an epithelial scale. The properties common to all muscle make up the general physiology of muscular tissue.

A nerve-fibre is at first sight very different from a muscular fibre. It has diverged more widely from the primitive type of undifferentiated protoplasm. It has lost the power of contraction, or *contractility*, but it retains, in common with the muscle-fibre, susceptibility to stimulation, or *excitability*, the capacity for *growth*, and to a limited extent the capacity for *reproduction*. This inheritance of primitive properties, retained alike by both tissues, is the basis of the general physiology of muscle and nerve.

The electrical organ of the Torpedo or the Malapterurus is intermediate in some respects between muscle and nerve, and has properties common to both. In the gland-cell the chemical powers of native protoplasm have been specialized aud developed. Contractility has been, in general, entirely lost; but excitability remains. The idea that certain common endowments find expression in the action of muscle, nerve, electrical organ, gland, etc., in the midst of all their apparent differences is the basis of the general physiology of the excitable tissues.

Amœboid movement is the most primitive, the least elaborated form of contraction. An amœba may be seen under the microscope to send out pseudopodia, or processes, of its

substance, and to retract them, and it is even able by such movements to change place. Stimulation with induction shocks causes the whole of the processes to be drawn in, and the amœba to gather itself into a ball. This illustrates a universal property of protoplasm, **excitability**, or the power of responding to certain external influences, or stimuli, by manifestations of the peculiar kind which we distinguish as vital or physiological. Certain of the white blood-corpuscles behave like the amœba; and we have already dwelt upon some of the important functions fulfilled by such amœboid movement in the higher animals and in man. But a great distinction between this kind of contraction and that of a muscular fibre is that it takes place in any direction.

Cilia.—Cilia possess a higher and more specialized grade of contractility. They are very widely distributed in the animal kingdom; and analogous structures are also found in many low plants, such as the motile bacteria.

In the human subject ciliated epithelium usually consists of several layers of cells, the most superficial of which are pear-shaped, the broad end being next the surface and covered with extremely fine processes, or cilia, about 8 μ in length, which are planted on a clear band. It lines the respiratory passages, the middle ear and Eustachian tube, the Fallopian tubes, the uterus above the middle of the cervix, the epididymis, where the cilia are extremely long, and the central cavity of the brain and spinal cord.

Ciliary motion can be very readily studied by placing a scraping from the palate of a frog, or a small portion of the gill of a fresh-water mussel under the microscope in a drop of normal saline solution. The motion of the cilia is at first so rapid that it is impossible to make out much, except that a stream of liquid, recognised by the solid particles in it, is seen to be driven by them in a constant direction along the ciliated edge. When the motion has become less quick, which it soon does if the tissue is deprived of oxygen, it is seen to consist in a swift bending of the cilia in the direction of the stream, followed by a slower recoil to the original position, which is not at right angles to the surface, but sloping streamwards. All the cilia on a tract

of cells do not move at the same time; the motion spreads from cell to cell in a regular wave. The energy of ciliary motion may be considerable, although far inferior to that of muscular contraction. The work which cilia are capable of performing can be calculated by removing the membrane, fixing it on a plate of glass, cilia outwards, putting weights on the glass plate, and allowing the cilia, like an immense number of feet, to carry it up an inclined plane. Bowditch found in this way that the cilia on a square centimetre of mucous membrane did nearly 7 gramme-millimetres of work per minute (equal to the raising of 7 grammes to a height of a millimetre).

Since the cilia in the respiratory tract all lash upwards, they must play an important part in carrying up foreign particles taken in with the air, and the mucus in which they are entangled, as well as pathological products. Engelmann found that the energy of ciliary motion increases as the temperature is raised up to about 40° C., after which it diminishes quickly. Overheating causes cilia to come to rest, but if the temperature has not been too high, and has not acted too long, they recover on cooling.

Muscle.—Nearly all our knowledge of the physiology of muscle has been gained either from striped skeletal muscle or from the muscle of the heart, and chiefly from the former. Of non-striped muscle we know comparatively little except by inference, owing to the difficulty of obtaining it in sufficient quantity and in suitable preparations for experiments. In what follows we always refer to ordinary skeletal muscle, unless it is otherwise stated.

Physical Properties of Muscle—Elasticity.—All bodies may have their shape or volume altered by the application of force. Some require a large force, others a small force, to produce a sensible amount of distortion. The elasticity of a body is the property in virtue of which it tends to recover its original form or bulk when these have been altered. Liquids and gases have only elasticity of volume; solids have also elasticity of form. Most solids recover perfectly, or almost perfectly, from a slight deformation. The limits of distortion within which this occurs are called the limits of elasticity, and they vary greatly for different substances. Living muscle has very wide limits of elasticity; it may be deformed—stretched, for

example—to a very considerable extent, and yet recover its original length when the stretching force ceases to act.

The **extensibility** of a body is measured by the ratio of the increase of length, produced by unit stretching force per unit of area of the cross-section, to the original length of a uniform rod of the substance.

If e is the extensibility, $e = \frac{ls}{LF}$, where l is the increase of length, L the original length, s the cross-section, and F the stretching force. Suppose we wish to compare the extensibility of two substances. Let A and B be strips or rods of the substances, the length of A being 500 mm., that of B 1,000 mm.; the cross-section of A, 100 sq. mm., of B, 200 sq. mm. Let the elongation produced by a weight of 1 kilo be 10 mm. in each, then the extensibility of A is $\frac{10 \times 100}{500 \times 1} = 2$; and that of B is $\frac{10 \times 200}{1{,}000 \times 1} = 2$; that is, the substances are equally extensible. Young's modulus of elasticity, or the coefficient of elasticity is the quotient of the deforming force acting on unit area of the given body by the deformation produced (within the limits of elasticity). In the above example it is $\frac{F}{s} \div \frac{l}{L}$, that is $\frac{LF}{ls}$, the reciprocal of the extensibility e. For steel the coefficient of elasticity is very large, for muscle small. Or, as we may otherwise express it, living muscle within its limits of elasticity is very extensible; a small force per unit area of cross-section of a prism of it will produce a comparatively great elongation. The extensibility, however, diminishes continually with the elongation, so that equal increments of stretching force produce always less and less extension. If, for instance, the sartorius or semi-membranosus of a frog be connected with a lever writing on a blackened surface, and weights increasing by equal amounts be successively attached to it, the recording surface being allowed to move the same distance after the addition of each weight, a series of vertical lines, representing the amount of each elongation, will be traced. When the lower ends of all the vertical lines are joined, a smooth curve with the concavity upwards is obtained (Fig. 160). This is a property common to living and dead muscle and to other animal structures, such as arteries. Marey's method, in which the weight is continuously increased from zero and then continuously decreased to zero again by the flow of mercury into and out of a vessel attached to the muscle, gives directly the curve of extensibility.

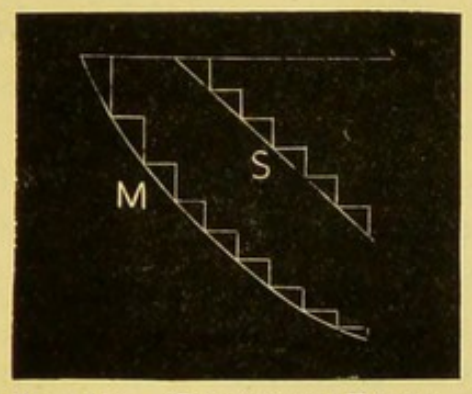


FIG. 160.—CURVES OF EXTENSIBILITY.

M, of muscle; S, of an ordinary inorganic solid.

The elongation of a steel rod or other inorganic solid is proportional within limits to the extending force per unit of cross-section;

and a curve plotted with the weights for abscissæ and the amounts of elongation for ordinates would be a straight line. But this is not a fundamental distinction between animal tissues, and the materials of unorganized nature, as some writers seem to suppose. For when the slow after-elongation which follows the first rapid increase in length in the loaded, excised muscle is waited for, the curve of extensibility comes out a straight line (Wundt), and within limits this is also the case for human muscles in the intact body. And although a steel rod much more quickly reaches its maximum elongation for a given weight when loaded, and its original length when the weight is removed, than does a muscle, time is required in both cases, and the difference is one of degree rather than of kind.

Dead muscle is less extensible and much less elastic than living. In the state of contraction the extensibility is increased in excised frog's muscle. When fatigue comes on after many excitations, the after-elongation becomes more pronounced, but the return after unloading is very incomplete. Donders and Van Mansveldt have found that contraction causes little difference in the muscles of a living man, although fatigue increases the extensibility. The great extensibility and elasticity of muscle must play a considerable part in determining the calibre of the vessels, and in lessening the shocks and strains which the heart and the vascular system in general are called upon to bear, and must contribute much to the smoothness with which the movements of the skeleton are carried out, and immensely reduce the risk of injury to the bones as well as to the muscles themselves, the tendons and the other soft tissues. And not only is smoothness gained, but economy also; for a portion of the energy of a sudden contraction, which, if the muscles were less extensible and elastic, might be wasted as heat in the jarring of bone against bone at the joints, is stored up in the stretched muscle and again given out in its elastic recoil. The skeletal muscles, too, are even at rest kept slightly on the stretch, braced up, as it were, and ready to act at a moment's notice without taking in slack. This is shown by the fact that a transverse wound in a muscle 'gapes,' the fibres being retracted, in virtue of their elasticity, towards the fixed points of origin and insertion.

If a muscle is so overweighted that it cannot contract, it elongates slightly on stimulation (Weber's paradox). This has by some been held to indicate that the increase of extensibility associated with contraction still occurs in the excited state when actual contraction is mechanically prevented.

In the further study of muscle it is necessary first of all to consider the means we have of calling forth a contraction—in other words, the various kinds of stimuli.

Stimulation of Muscle.—A muscle may be excited or stimulated either directly or through its motor nerve; and the stimulus may be electrical, mechanical, chemical, or thermal. Electrical stimuli are by far the most commonly

used, and will be discussed in detail. A prick, a cut, or a blow are examples of mechanical stimuli. A fairly strong solution of common salt or a dilute solution of a mineral acid will act as a chemical stimulus, which always tends to cause, not a single contraction, but a tetanus. Sudden cooling or heating acts as a stimulus for muscle, but thermal stimulation is somewhat uncertain. In all artificial stimulation there is an element of sudden or abrupt change, of shock, in other words; but we cannot tell in what the 'natural' or 'physiological' stimulus to muscular contraction in the intact body really consists, nor how it differs from artificial stimuli. All we know is that there must be a wide difference, and that our methods of excitation must be very crude and inexact imitations of the natural process.

Direct Excitability of Muscle.—The famous controversy on the existence of independent 'muscular irritability' has long been forgotten, and has no further interest except for the antiquaries of science, if such exist. The direct excitability of muscle in the modern sense is not quite the same as the 'muscular irritability,' the discussion of which occupied Haller and his contemporaries. What the modern physiologists have been called upon to decide is whether muscular fibres can be caused to contract except by an excitation that reaches them through their nerves. In this sense there can exist no doubt that muscle is directly excitable, and the proofs are as follows:

(1) The ends of the frog's sartorius contain no nerves, the apex of the frog's heart contains neither nerves nor nerve-cells, yet both respond to direct stimulation. (2) Certain chemical stimuli—ammonia, for instance—do not act on nerve, but excite muscle. (3) When the motor nerves of a limb are cut they degenerate, and after a certain time stimulation of the nerve-trunk causes no muscular contraction, while the muscles, although atrophied, can be made to contract by direct stimulation. (4) Finally, there is the celebrated curara experiment of Claude Bernard, which is described in a somewhat modified form in the Practical Exercises, p. 617. A ligature is tied firmly round one thigh of a frog, omitting the sciatic nerve; then curara is injected,

and in a short time the skeletal muscles are paralyzed. That the seat of the paralysis is not the muscles themselves is shown by their vigorous response to direct stimulation. The 'block' is not in the nerve-trunk, nor above it in the central nervous system, for the ligatured leg is often drawn up—that is, its muscles are contracted, although the poison has circulated freely in the sacral plexus and the spinal cord. Further, if the nerve of the ligatured leg be prepared as high up above the ligature as possible, where the curara must undoubtedly have reached it (just above the ligature the nerve has been isolated and the circulation in it more or less interrupted), stimulation of it will cause contraction of the muscles of the limb; while excitation of the other sciatic is ineffective.

It can be also shown, by means of the negative variation

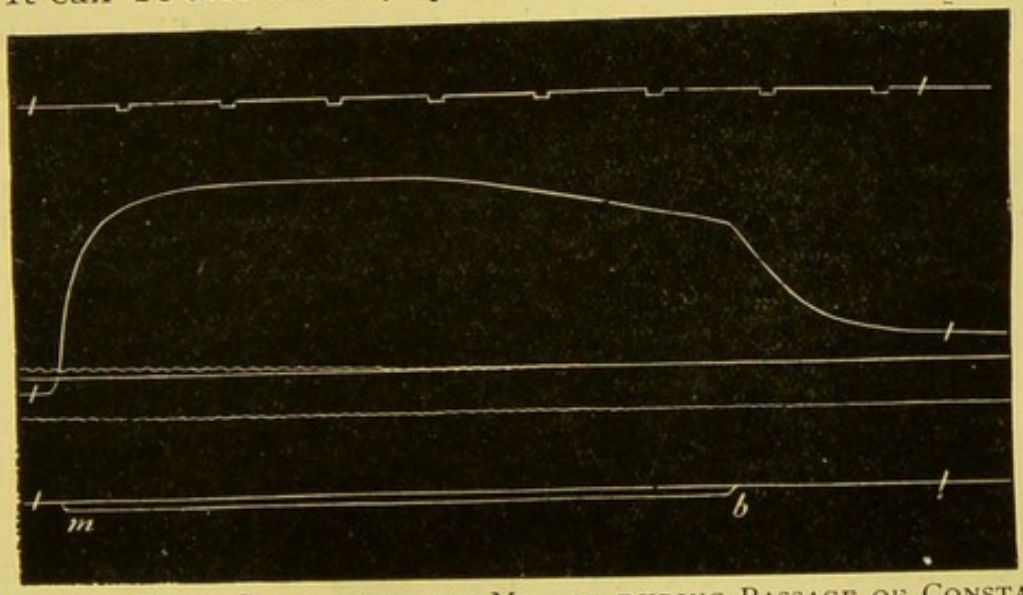


FIG. 161.—TONIC CONTRACTION OF MUSCLE DURING PASSAGE OF CONSTANT CURRENT.

Two sartorius muscles of frog connected by pelvic attachments. Current from 12 small Daniell cells in series passed through their whole length. Current closed at *m*, opened at *b*. Time trace, two-second intervals.

or current of action (p. 630), that a nerve-trunk on which curara has acted remains excitable, and capable of conducting the nerve-impulse. The conclusion, therefore, is that the curara paralyzes neither nerve-fibre nor muscular fibre, but the link between the two which we call the nerve-ending. In coming to this conclusion, the assumption is made that the nerve-fibres within the muscle, since they are anatomically similar to those in the nerve-trunk till near

their terminations, are similarly affected by curara. We must carefully remember that the 'nerve-endings' which are paralyzed by curara do not necessarily, nor even probably, coincide exactly with the 'nerve-endings' of histology. Still, it is significant that the histological differences between the nerve-terminations in striped and smooth muscle should correspond to a physiological difference in the action of curara on them. This drug paralyzes the nerve-endings in smooth muscle—the muscles of the bronchi, for instance—with much greater difficulty than those in ordinary skeletal muscle, and the same is true of the vagus-endings in the heart.

The action of curara gives us the means of stimulating muscle directly: when electrical currents are sent through a non-curarized muscle, there is in general a mixture of direct and indirect stimulation, for the nerve-fibres within the muscle are also excited. Induced currents stimulate nerve more readily than muscle. Voltaic currents may excite a muscle whose nerves have degenerated, while induced currents are entirely without effect.

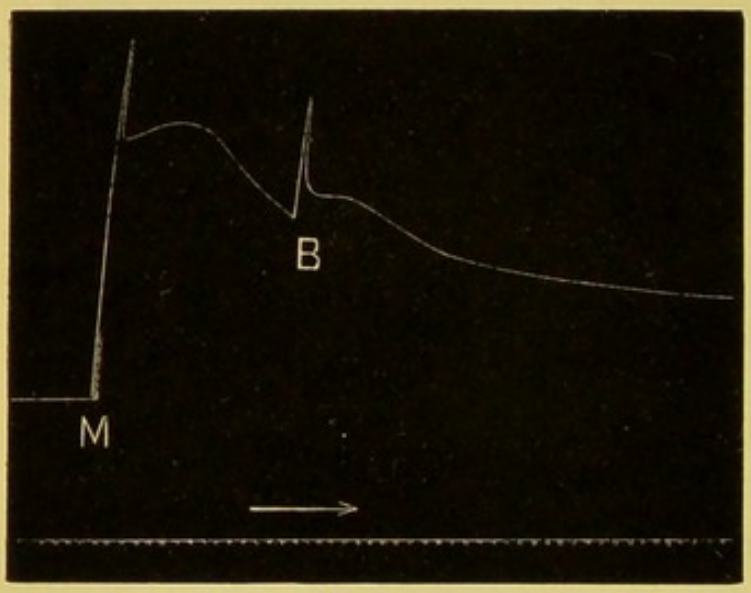


FIG. 162. — TONIC CONTRACTION DURING AND AFTER FLOW.

Curve from frog's gastrocnemius. At M constant current closed, at B broken. Contracture continues after opening of current. Time trace, two-second intervals.

For direct stimulation, a curarized frog's sartorius or semimembranosus is generally used on account of their long parallel fibres; for indirect excitation, a muscle-nerve preparation, composed of a frog's gastrocnemius with the sciatic nerve attached to it, is commonly employed, as it is easy to isolate the muscle without hurting its nerve.

Stimulation by the Voltaic Current.—While the current con-

tinues to pass through a nerve without any sudden or great change in its intensity, there is no stimulation, and the muscle connected with the nerve remains at rest. The same is true of muscle when a weak current is passed directly through it. But in muscle the constancy of the rule is more and more frequently broken by exceptional results as the current is strengthened, a state of permanent contraction being very apt to show itself during the whole time of flow (Wundt) (Fig. 161). Above a certain intensity of current a greater or less degree of permanent contraction is invariably produced. This is sometimes called the 'closing tetanus.' It is, however, not a true tetanus, but a tonic contraction, which is strongest in the neighbourhood of the cathode, and does not spread far from it. A similar condition, the so-called *galvanotonus*, is normally seen in human muscles when they or their motor nerves are traversed by a stream of considerable intensity. Under certain conditions, too, *e.g.*, when a strong current is allowed to flow for a comparatively long time through a muscle, the muscle remains contracted after the opening of the current (so-called 'opening tetanus').

For nerve, and with these qualifications for muscle, too, we may lay down the law that *the voltaic current stimulates at make and at break, but not during its passage.* Or, generalizing this a little, since it has been shown that a sudden increase or decrease in the strength of a current already flowing also acts as a stimulus, we may say that the *voltaic current stimulates only when its intensity is suddenly and sufficiently increased or diminished, but not while it remains constant.**

When a strong current is closed through a muscle there is an immediate sharp contraction (initial contraction). The muscle then promptly relaxes, but incompletely. When the current is opened, there is another contraction (Fig. 162). The force of the initial contraction, as measured by the resistance necessary to prevent it, is greater than that of the tonic contraction which follows it.

A second law of great theoretical importance is that *at make the stimulation occurs only at the cathode; at break only*

* This law of du Bois-Reymond has been questioned by Hoorweg and others. It seems to need modification, but the subject cannot be discussed here.

at the anode; and that the make is stronger than the break contraction. This is true both for muscle and nerve, but it is most directly and simply demonstrated on muscle. A long parallel-fibred curarized muscle is supported about its middle; the two ends, which hang down, are connected with levers writing on a revolving drum, and a current is sent longitudinally through the muscle. It is not difficult to see from the tracings that at make the lever attached to the cathodic end moves first, and that the other lever only moves when the contraction started at the cathode has had time to reach it in its progress along the muscle. Similarly, at break the lever connected with the anodic end moves first.

The Muscular Contraction.—When a muscle contracts, its two points of attachment, or, if it be isolated, its two ends, come nearer to each other; and in exact proportion to this shortening is the increase in the average cross-section. The contraction is essentially a change of form, not a change of volume. The most delicate observations fail to detect the smallest alteration in bulk (Ewald). Living fibres kept contracted by successive stimuli can be examined under the microscope; or fibres may be 'fixed' by reagents like osmic acid, and sometimes a very good opportunity of studying the microscopic changes in contraction is given by a group of fibres in which the 'fixing' reagent has caught a wave of contraction, and, so to speak, pinned it down. It is then seen that the process of contraction in the fibre is a miniature of that in the anatomical muscle. The individual fibres shorten and thicken, and the sum-total of this shortening and thickening is the muscular contraction which we see with the naked eye. The phenomena of the muscular contraction may be classified thus: (1) Optical, (2) Mechanical, (3) Thermal, (4) Chemical, (5) Sonorous, (6) Electrical. (5) will be treated under 'Voluntary Contraction'; (6) in Chapter XI.

(1) **Optical Phenomena — Microscopic Structure of Striped Muscle.**—The structure of striped muscle has long been the enigma of histology; and the labours of many distinguished men have not sufficed to make it clear. On the contrary, as investigations have multiplied, new theories, new interpretations of what is to be seen, have multiplied in proportion, and a resolute brevity has become the

chief duty of a writer on elementary physiology in regard to the whole question.

The muscle-fibre, the unit out of which the anatomical muscle is built up, is surrounded by a structureless membrane, the sarcolemma. The length and breadth of a fibre vary greatly in different situations. The maximum length is about 4 cm.; the breadth may be as much as 70 μ and as little as 10 μ. When we come to analyze the muscle-fibre and to determine out of what units it is built up, the difficulty begins. The fibre shows alternate dim and clear transverse stripes, and can actually be split up into discs by certain reagents. It also

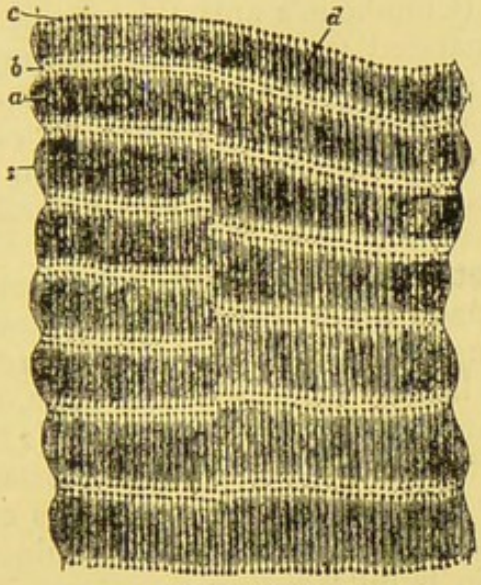


FIG. 163. — LIVING MUSCLE OF WATER-BEETLE (highly magnified). (SCHÄFER.)

s, sarcolemma; *a*, dim stripe; *b*, bright stripe; *c*, row of dots in bright stripe, which represent expansions of the interstitial substance (sarcoplasm).

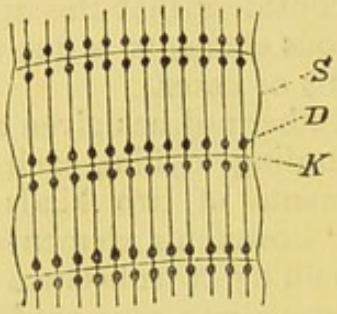


FIG. 164.—PORTION OF LEG MUSCLE OF INSECT, treated with dilute acetic acid. (SCHÄFER.)

S, sarcolemma; D, dot-like enlargement of sarcoplasm; K, Krause's membrane. The sarcous elements have been swollen and dissolved by the acid.

shows a longitudinal striation, and can be separated into fibrils. Some have supposed that the discs are the real structural units which, piled end to end, make up the fibre. The fibrils they consider artificial. This view is erroneous. It seems certain that the fibres are built up from fibrils ranged side by side, and that the discs are artificial. The contents of the muscle-fibre appear to consist of two functionally different substances, a contractile substance, and an interstitial, perhaps nutritive, non-contractile material of more fluid nature. The contractile substance is arranged as longitudinal fibrils embedded in interfibrillar matter (sarcoplasm). In a muscle impregnated with chloride of gold, the interfibrillar matter appears as a network.

Schäfer has described the contractile elements of the muscle-fibre (Figs. 163, 164) as fine columns (sarcostyles), divided into segments (sarcomeres) by thin transverse discs (Krause's membranes), occupying the position of the middle of each light stripe. Krause's membrane is probably only an optical appearance. If an actual partition

exists, it must either be incomplete, or much more easily ruptured than the sarcolemma; for Kühne, who was fortunate enough to find one day a small nematode worm moving in the interior of a fibre, saw it pass along the fibre with perfect freedom, ignoring Krause's membrane. Each sarcomere, according to Schäfer, contains a sarcous element (a portion of the dark stripe) with a clear substance at its ends, filling up the space between the sarcous element and Krause's membrane, and constituting a portion of the light stripe. The sarcous element is itself double, and if the fibre be stretched, the two portions separate at a line which runs transversely across the middle of the dim stripe (Hensen's line). The small polygonal areas seen in a cross-section of a fibre (Cohnheim's areas) represent the cross-sections of the sarcostyles separated from each other by sarcoplasm. Schäfer's muscle-columns or sarcostyles are units of greater transverse diameter than the fibrils of Kölliker, Rutherford, etc., and he considers that the appearance of longitudinal fibrillation in the sarcous elements is due to the presence in them of fine longitudinal canals or pores.

Rutherford has given a somewhat different account of the matter. According to him, each fibril is made up of a longitudinal row of segments of two kinds alternating with each other (Fig. 165): (1) 'Bowman's elements,' shaped like an elongated hour-glass, and containing a substance readily stained by various dyes; (2) an 'intermediate segment' of cylindrical shape, the general substance of which does not readily stain. The intermediate segments contains in its centre a globule (Dobie's globule), which is easily stained.* The fibrils are regularly arranged in bundles within the fibre. The apposition of Bowman's elements gives rise to the dim stripe; the apposition of the intermediate segments to the clear stripe; the apposition of the Dobie's globules to a line in the middle of the clear stripe (Dobie's line).

Changes during Contraction.—When a muscle contracts, according to Schäfer, the clear substance between the Krause's membrane and the sarcous element passes into the canals, which are open towards Krause's membrane, but closed towards Hensen's line. The sarcous element therefore swells up, and the sarcomere is shortened. In the extended muscle the clear substance leaves the pores of the sarcous element, and accumulates in the space between it and Krause's membrane. The sarcomere is thus lengthened and narrowed. While the existence of Schäfer's pores is not

* In the muscles of certain invertebrate animals, though not in those of vertebrates, the intermediate segment contains, in addition to Dobie's globule, two pear-shaped bodies (Flögel's elements), each of which occupies an intermediate position between Dobie's globule and the end of the adjoining Bowman's element. Flögel's elements also stain well, and are doubly refracting.

admitted by all observers, there is a pretty general agreement that in contraction a fluid does pass from the clear ends of the sarcomeres into the sarcous elements. According to Rutherford, during contraction the intermediate segment first shortens, so that the ends of Bowman's elements come close up to Dobie's globules. There is, apparently, no lateral bulging of the intermediate segments while this shortening is going on, so that the fluid in them must enter Bowman's elements. The Bowman's elements begin to shorten a little later than the intermediate segment. The easily-stainable substance in them passes to their ends, which swell and become dimmer, while their shafts become clear. The result of these changes is that in the fully contracted fibril the clear stripe occupies the middle of what was the dim stripe in the uncontracted fibril, and the dim stripe of the contracted fibril is made up of 'the swollen ends of Bowman's elements with the Dobie's globules and other tissue elements of the intermediate segments' (Rutherford). This phenomenon is known as the reversal of the stripes. It is not really a reversal in the sense of being a bodily exchange of the whole of the material of the dim and light stripes. Schäfer has explained it as due to the squeezing of sarcoplasm from between the sarcous elements into the position of the light stripe, when they bulge laterally in contraction. This accumulation of sarcoplasm in the stripes that were previously light makes them look darker in comparison with the true dim stripe.

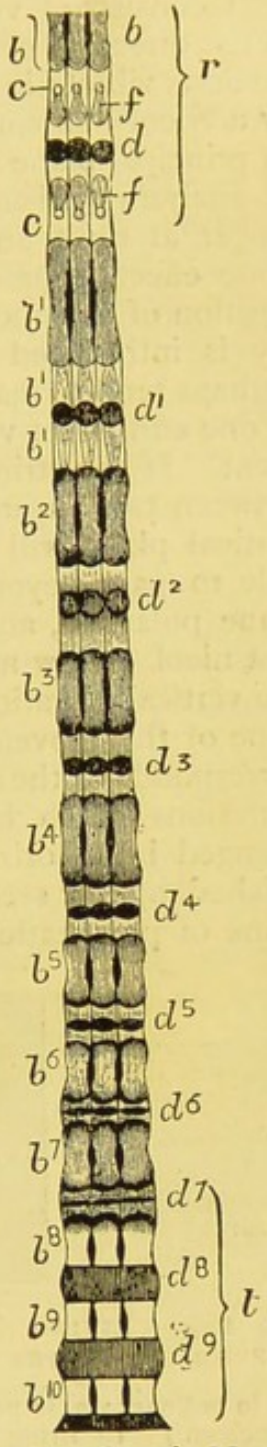


FIG. 165.—CRAB'S MUSCLE IN DIFFERENT STAGES OF CONTRACTION (after RUTHERFORD).

Three fibrillæ are shown: *r*, complete relaxation; *t*, complete contraction; *b*-*b*^{10}, sarcous elements; *d*-*d*^{9}, Dobie's granules; *f*, Flögel's granules.

Appearance of the Fibres in Polarized Light.—A ray of ordinary light consists of vibrations of the ether in all planes at right angles to the direction of the ray. In a ray of plane polarized light all the particles vibrate in one plane. A ray of light which has been polarized by a Nicol's prism cannot pass through another Nicol's prism with its principal plane at right angles to that of the first. If the second or analyzing prism be rotated so that the principal planes are no longer at right angles, some of the light will pass through. The same effect is produced if, without altering the original 'crossed' position of the nicols, a substance capable of rotating the polarized ray is introduced between the prisms. A rough illustration will perhaps tend to make this point clearer. Suppose that a string fixed at one end is set vibrating in various directions by a twisting movement. If the string has to pass through a narrow vertical slit, *e.g.*, between two fingers held vertically, all vibrations except those in the vertical plane will be extinguished; but vertical vibrations will be able to pass beyond the slit. The movement may be said to be plane polarized, and the effect of the slit corresponds to that of the first nicol. Now make the string pass also through a horizontal slit; the vertical vibrations will then be extinguished too; in other words, none of the movements will pass beyond the 'crossed' slits. This corresponds to the dark field of the crossed nicols. But if the vertical vibrations which have passed the first slit could be in any way changed into horizontal vibrations, they would no longer be extinguished by the second. This would correspond to rotation of the plane of polarization through 90°. A ray of light polarized by the first nicol will, if its plane of polarization be rotated through 90°, pass entirely (except for loss by ordinary reflection and absorption) through the second. If the angle of rotation is less than 90°, a portion will pass through.

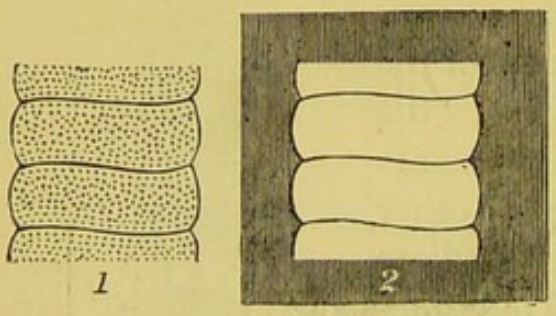


FIG. 166. — LIVING MUSCULAR FIBRE (FROM GEOTRUPES STERCORARIUS).

1, in ordinary; 2, in polarized light. (Van Gehuchten.) In living muscle (at least in fibres which are not extended) in contrast to dead muscle after treatment with reagents, the doubly refracting or anisotropous substance is present in the greater part of the fibre; and with crossed nicols the position of the singly refracting or isotropous material is indicated only by narrow transverse black lines or rows of dark dots.

The substance of the Bowman's element, and particularly the easily-stained material in it, is doubly refracting, and therefore rotates the plane of polarization. The same is true of the Dobie's globule, but the rest of the intermediate segment is singly refracting. When an uncontracted fibre is viewed with crossed nicols, the dim stripe accordingly appears bright in the otherwise dark field. In the contracted fibre the stripe that is dim in ordinary light is bright when looked at with crossed nicols, since the ends of the Bowman's elements, filled with the doubly refractive stainable material, and the doubly re-

fractive Dobie's globule are there approximated. The stripe which in the contracted fibre is the brighter of the two in ordinary light is the dimmer of the two in the field of the crossed nicols, although it is not absolutely dark, since the shafts of the Bowman's elements cause some rotation of the plane of polarization even in the absence of the stainable material (Rutherford).

Diffraction Spectrum of Muscle.—When a beam of white light passes through a striped muscle, it is broken up into its constituent colours, and a series of diffraction spectra are produced, just as happens when the light passes through a diffraction grating (a piece of glass on which are ruled a number of fine parallel equidistant lines). The nearer the lines are to each other, the greater is the displacement of a ray of light of any given wave-length. It has accordingly been found that when a muscular fibre contracts, the amount of displacement of the diffraction spectra increases. At the same time the whole fibre becomes more transparent.

(2) **Mechanical Phenomena.**—The muscular contraction may be graphically recorded by connecting a muscle with a lever which is moved either by its shortening or by its thickening. The lever writes on a blackened surface, which must travel at a uniform rate if the form and time-relations of the muscle-curve are to be studied, but may be at rest if only the height of the contraction is to be recorded. The whole arrangement for taking a muscle-tracing is called a myograph (Fig. 192). The duration of a 'twitch' or single contraction (including the relaxation) of a frog's muscle is usually given as about one-tenth of a second, but it may vary considerably with temperature, fatigue, and other circumstances. It is measured by the vibrations of a tuning-fork written immediately below or above the muscle curve. When the muscle is only slightly weighted, it but very gradually reaches its original length after contraction, a period of rapid relaxation being followed by a period of 'residual contraction,' during which the descent of the lever towards the base line becomes slower and slower, or stops altogether some distance above it.

Latent Period.—If the time of stimulation is marked on the tracing, it is found that the contraction does not begin simultaneously with it, but only after a certain interval, which is called the latent period.

This can be measured by means of the pendulum myograph or the spring myograph, in both of which the carrier

of the recording plate opens, at a definite point in its passage, a key in the primary coil of an induction machine, and so causes a shock to be sent through the muscle or nerve, which is connected with the secondary. The precise point at which the stimulus is thrown in can be marked on the tracing by carefully bringing the plate to the position in which the key is just opened, and allowing the lever to trace here a vertical line (or, rather, an arc of a circle). The portion of the time-tracing between this line and a parallel

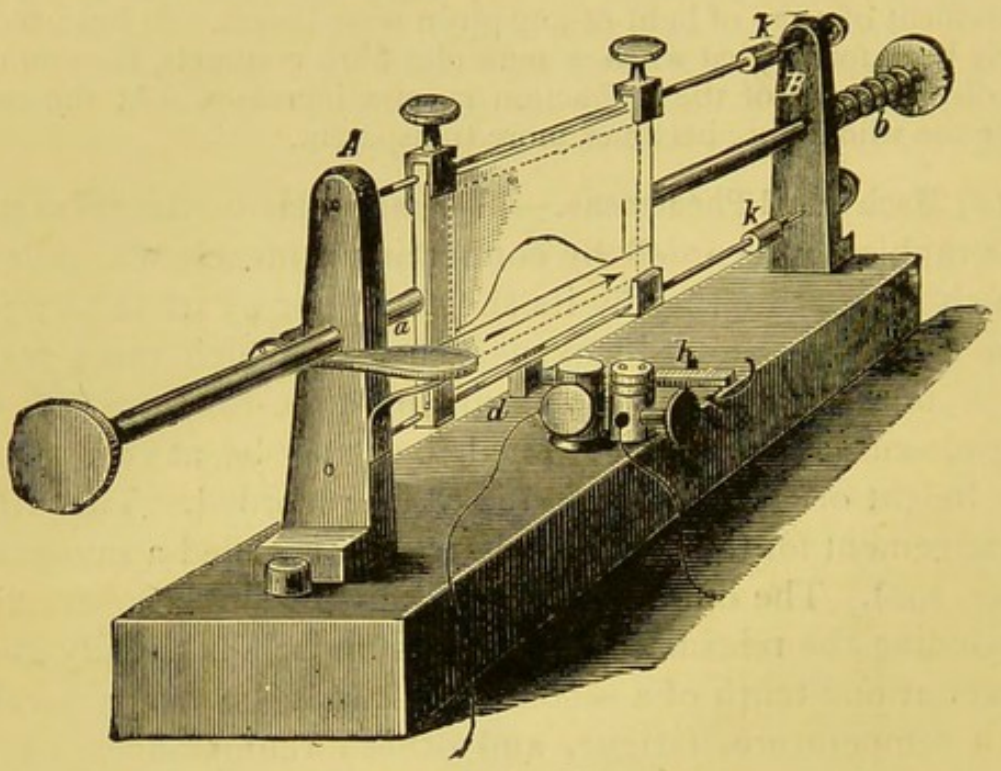


FIG. 167.—SPRING MYOGRAPH.

A, *B*, iron uprights, between which are stretched the guide-wires on which the travelling plate *a* runs; *k*, pieces of cork on the guides to gradually check the plate at the end of its excursion, and prevent jarring; *b*, spring, the release of which shoots the plate along; *h*, trigger-key, which is opened by the pin *d* on the frame of the plate.

line drawn through the point at which the contraction begins gives the latent period.

Helmholtz measured the length of the latent period by means of the principle of Pouillet, that the deflection of a magnet by a current of given strength and of very short duration is proportional to the time during which the current acts on the magnet. He arranged that at the moment of stimulation of the muscle a current should be sent through a galvanometer, and should be broken by the contraction of the muscle the moment it began. In this way he obtained

the value of $\frac{1}{100}$ second for the latent period of frog's muscle. The tendency of later observations has been to make the latent period shorter. Burdon Sanderson finds

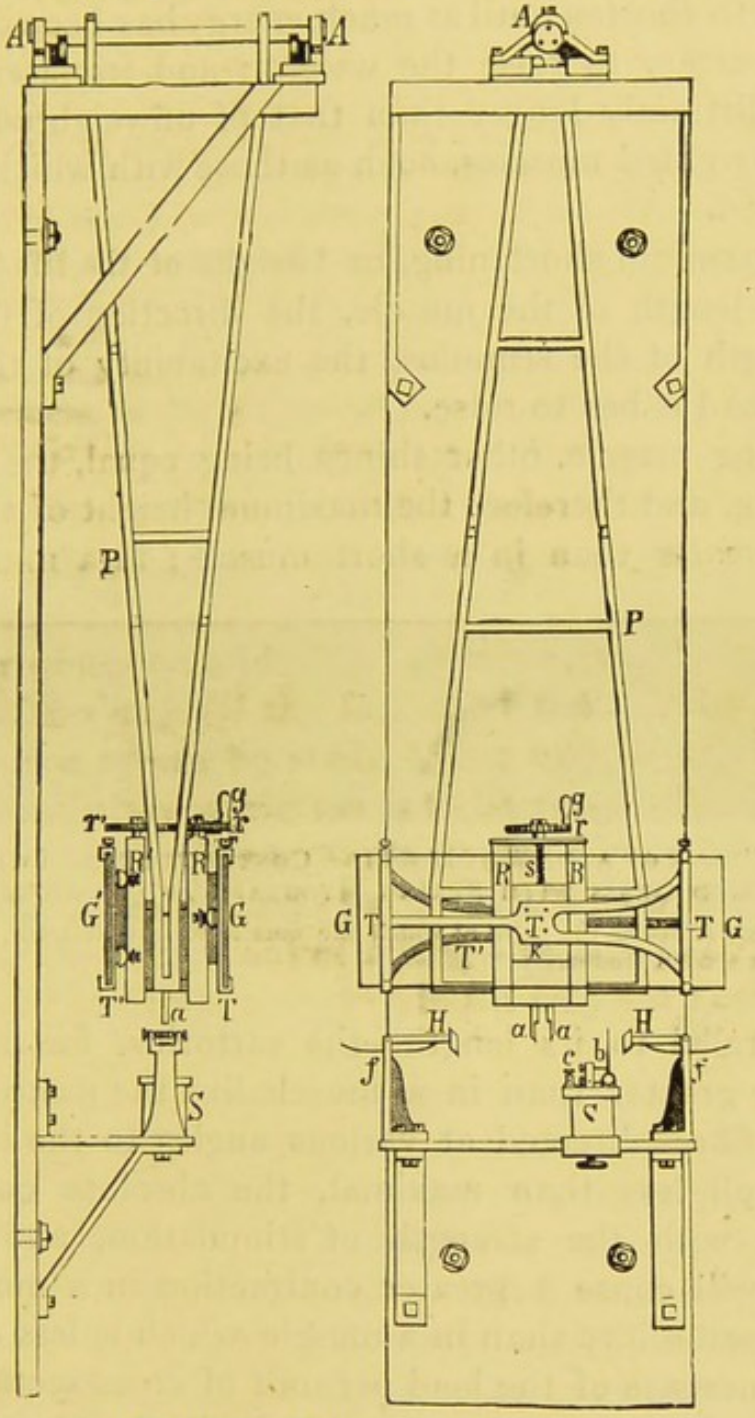


FIG. 168.—PENDULUM MYOGRAPH.

At the left as seen from the side, at the right as seen from the front. A, bearings on which the pendulum swings; P, pendulum; G, G', glass plates carried in the frames T, T'; *a*, pin which opens the trigger-key. The key, when closed, is in contact with *c*, and so completes the circuit of the primary coil.

that the change of form probably begins in muscle with direct stimulation in $\frac{4}{1000}$ second after, and the electrical change (p. 630) simultaneously with, the excitation. It is

known that the apparent latent period depends upon the resistance which the muscle has to overcome in beginning its contraction. A heavily-weighted muscle, for instance, cannot begin to shorten until as much energy has been developed as is necessary to raise the weight; and its latent period will be distinctly longer than that of unweighted or very slightly weighted muscles, such as those with which Sanderson worked.

The maximum shortening, or '**height of the lift**,' depends upon the length of the muscle, the direction of the fibres, the strength of the stimulus, the excitability of the tissue, and the load it has to raise.

In a long muscle, other things being equal, the absolute shortening, and therefore the maximum height of the curve, will be greater than in a short muscle; in a muscle with

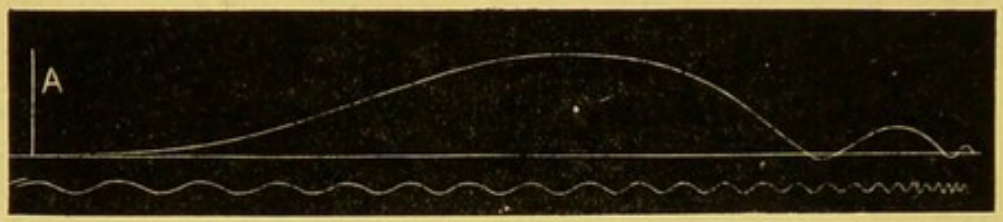


FIG. 169.—CURVE OF A SINGLE MUSCULAR CONTRACTION OR TWITCH TAKEN ON SMOKED GLASS WITH SPRING MYOGRAPH AND PHOTOGRAPHED.

Vertical line A marks the point at which the muscle was stimulated; time-tracing shows $\frac{1}{100}$ of a second (reduced).

fibres parallel to its length—the sartorius, for instance—it will be greater than in a muscle like the gastrocnemius, with the fibres directed at various angles to the long axis. For stimuli less than maximal, the absolute contraction increases with the strength of stimulation, and a given stimulus will cause a greater contraction in a muscle with a given excitability than in a muscle which is less excitable. Finally, increase of the load per unit of cross-section of the muscle diminishes above a certain limit the 'height of the lift,' although below that limit it may increase it.

Influences which affect the Time-relations of the Muscular Contraction.—Many circumstances affect the form of the muscle-curve and its time-relations.

(*a*) *Influence of the Load.*—The first effect of contraction is to suddenly stretch the muscle, and the more the muscle

is loaded the greater will this elongation be. So that at the beginning of the actual shortening part of the energy of contraction is already expended without visible effect, and has to be recovered from the elastic reaction during the ascent of the lever.

Then the inertia of the lever itself and of its load comes into play, and may carry the curve too high during the up-stroke and too low during the down-stroke. This can be minimized by making the lever very light, and attaching the weight close to the fulcrum, so that it has only a small range of movement, and never acquires more than a small velocity. The contraction of a muscle loaded by a weight which is not increased or diminished during the contraction is said to be *iso-tonic*, for here the tension of the muscle

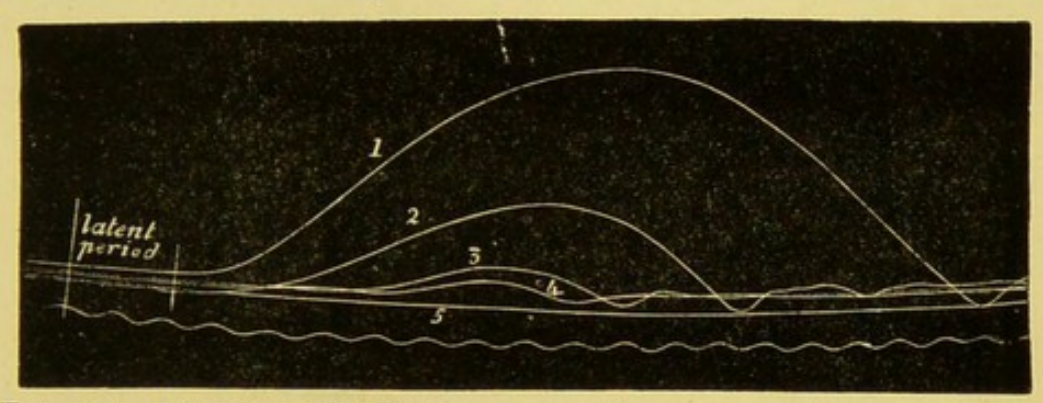


FIG. 170.—INFLUENCE OF LOAD ON THE FORM OF THE MUSCLE CURVE.

1, curve taken with unloaded lever; 2, 3, 4, weight successively increased; 5, abscissa line; time-trace $\frac{1}{100}$ sec. (reduced).

is the same throughout, and its length alters. When the muscle is attached very near the fulcrum of the lever, so that it acts upon a short arm, while the long arm carrying the writing-point is prevented from moving much by a spring, the muscle can only shorten itself very slightly; but the changes of tension in it will be related to those in the spring, and therefore to the curve traced by the writing-point. Such a curve is called *iso-metric*, since the length of the muscle remains almost unaltered.

The maximum of the iso-metric curve (the maximum tension with practically constant length) is sooner reached than that of the iso-tonic (the maximum contraction with constant tension). From this it has been concluded that during contraction the co-efficient of elasticity of the muscle continuously diminishes (Fick), or, what comes to the same thing, its extensibility continuously increases.

The work done by a muscle in raising a weight is equal to the product of the weight by the height to which it is raised. Beginning with no load at all, it is found that the weight can be increased up to a certain limit without diminishing the height of the contraction; perhaps the height may even increase. Up to this limit, then, the work evidently increases with the load. If the weight is made still greater, the contraction becomes less and less, but up to another limit the increase of weight more than compensates for the diminution of 'lift,' and the work still increases. Beyond this, further increase of weight can no longer make up for the lessening of the lift, and the work falls off till ultimately the muscle is unable to raise the weight at all.

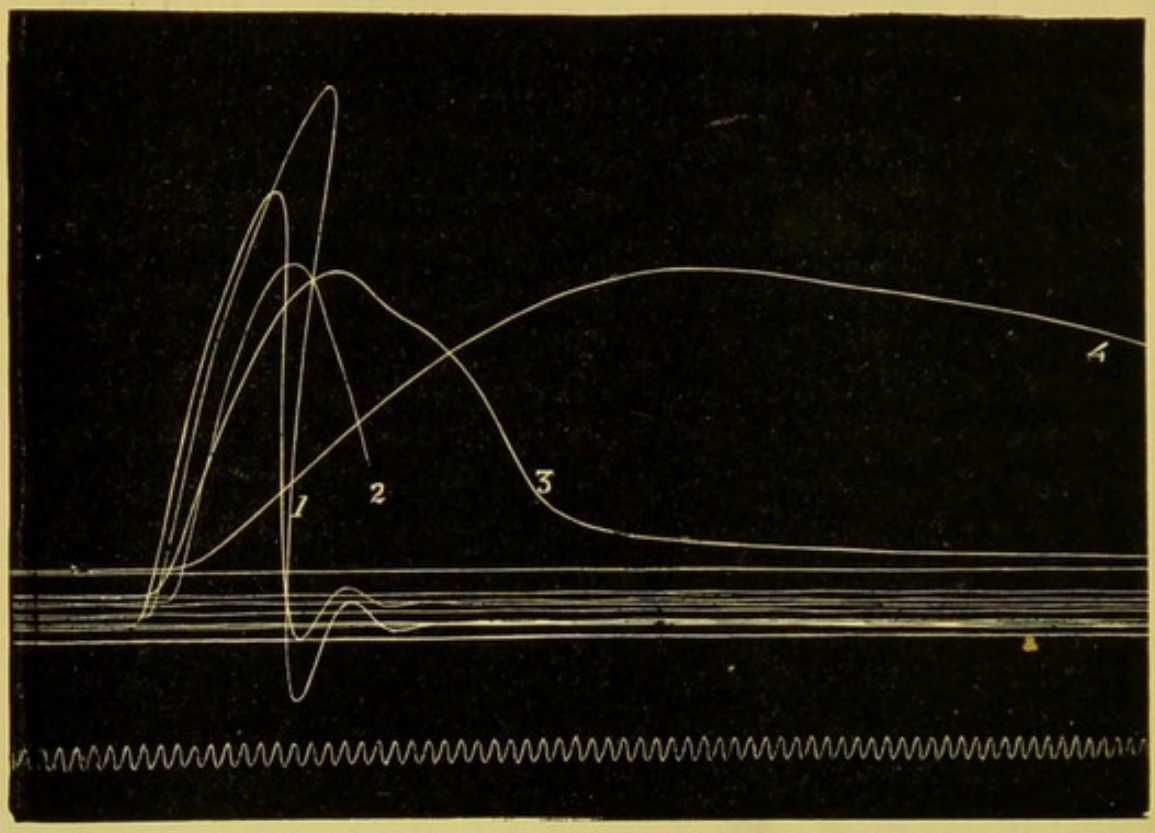


FIG. 171.—INFLUENCE OF TEMPERATURE ON THE MUSCLE CURVE.

2, air temperature; 1, 25°—30° C.; 3, 7°—10° C.; 4, ice in contact with muscle. The 5th curve was taken at a little above air temperature.

The manner of application of the weight has an influence on the work done by the muscle. If it is applied before the contraction begins, so that the muscle is already stretched at the moment of stimulation, a cause of error and uncertainty is introduced; for it is known that mere stretching of muscle affects its metabolism, and therefore its functional power. So that it is usual in experiments of this kind to after-load the muscle—that is, to support the lever and its load in such a way that the weight does not come upon the muscle till contraction has just begun. The '**absolute contractile force**' of an active muscle may be measured on this principle by determining the weight which, brought to bear upon the muscle at the instant of contraction, is just able to prevent shortening without

stretching the muscle. It, of course, depends, among other things, on the cross-section of the muscle. During the contraction the absolute force diminishes continually, so that a smaller and smaller weight is sufficient to stop any further contraction, the more the muscle has already shortened before it is applied. At the maximum of the contraction the absolute force is zero. Hence a muscle works under the most favourable conditions when the weight decreases as it is raised, and this is the case with many of the muscles of the body. During flexure of the forearm on the elbow, with the upper arm horizontal, a weight in the hand is felt less and less as it is raised, since its moment, which is proportional to its distance from a vertical line drawn through the lower end of the humerus, continually diminishes.

(*b*) *Influence of Temperature on the Muscular Contraction.*—Increase of temperature of the muscle up to a certain limit diminishes the latent period and the length of the curve, and increases the height of the contraction, but beyond this limit the contractions are lessened in height. Marked diminution of temperature causes, in general, an increase in the latent period and length, and a decrease in the height of the contraction. It is evident that much depends upon the normal temperature which we start from, and moderate cooling may increase the height of the curve. In the heart the effect of cold in strengthening the beat is often very marked.

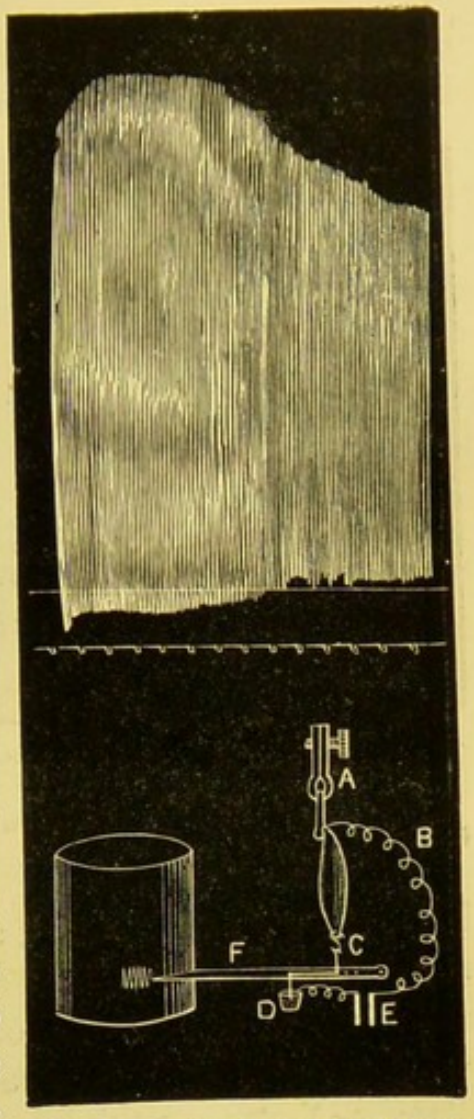


FIG. 172.—FATIGUE CURVE OF MUSCLE (FROG'S GASTROCNEMIUS).

Below is shown the arrangement with which the curve figured was obtained. A, femur with gastrocnemius attached, supported in clamp; C, metal hook with fine wire attached to lever F. The wire is continued along the lever and connected with a sewing-needle, the point of which just dips into the mercury cup D. A wire from one pole of the Daniell cell E dips permanently into the mercury; the wire B from the other pole is attached to the upper end of the muscle or the clamp. Or a wire on the lever may be made to close and open the primary circuit of an inductorium, the muscle or nerve being connected with the secondary. Every time the needle touches the mercury the muscle is stimulated automatically.

(*c*) *Influence of Previous Stimulation.*—If a muscle is stimu-

lated by a series of equal shocks thrown in at regular intervals, and the contractions recorded, it is seen that at first each curve overtops its predecessor by a small amount. This phenomenon, which is regularly seen in fresh skeletal muscle, although it was at one time supposed to be peculiarly a property of the muscle of the heart, is called the 'staircase,' and seems to indicate that within limits the muscle is benefited by contraction and its excitability increased for a new stimulus. Soon, however, in an isolated preparation, the contractions begin to decline in height, till the muscle is at length utterly exhausted, and reacts no longer to even the strongest stimulation.

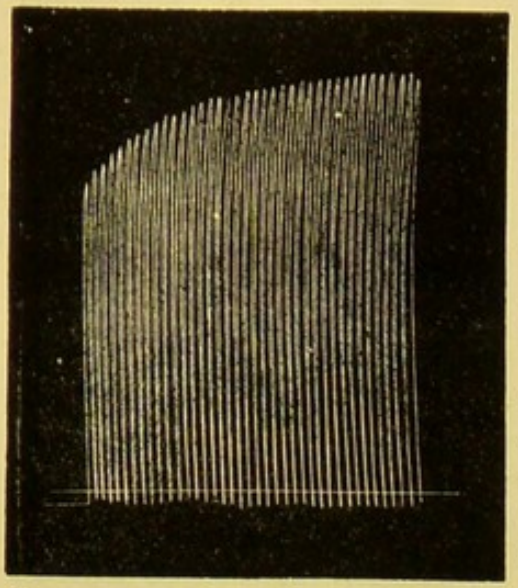


FIG. 173.—'STAIRCASE' IN SKELETAL MUSCLE (FROG).

Stimulation by arrangement shown in Fig. 172.

A conspicuous feature of the contraction-curves of fatigued muscle is the progressive lengthening, which is much more

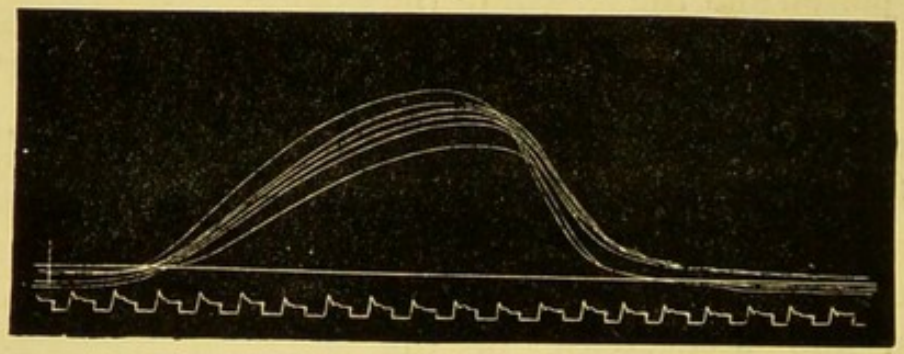


FIG. 174.—'STAIRCASE' IN CARDIAC MUSCLE.

Contractions recorded on a much more quickly moving drum than in Fig. 173. The contractions were caused by stimulating a heart reduced to standstill by the first Stannius' ligature (p. 175). The contractions gradually increase in height.

marked in the descending than in the ascending period; in other words, relaxation becomes more and more difficult and imperfect. It is by no means so easy to fatigue a muscle still in connection with the circulation as an isolated muscle. But even the latter, if left to itself, will to

some extent recover, and be again able to contract, although exhaustion is now more readily induced than at first.

What is the cause of **muscular fatigue?** An exact answer is not possible in the present state of our knowledge, but we may fairly conclude that in an isolated preparation it is twofold: (1) The material necessary for contraction breaks down more quickly than it can be reproduced or brought to the place where it is required; (2) waste products are

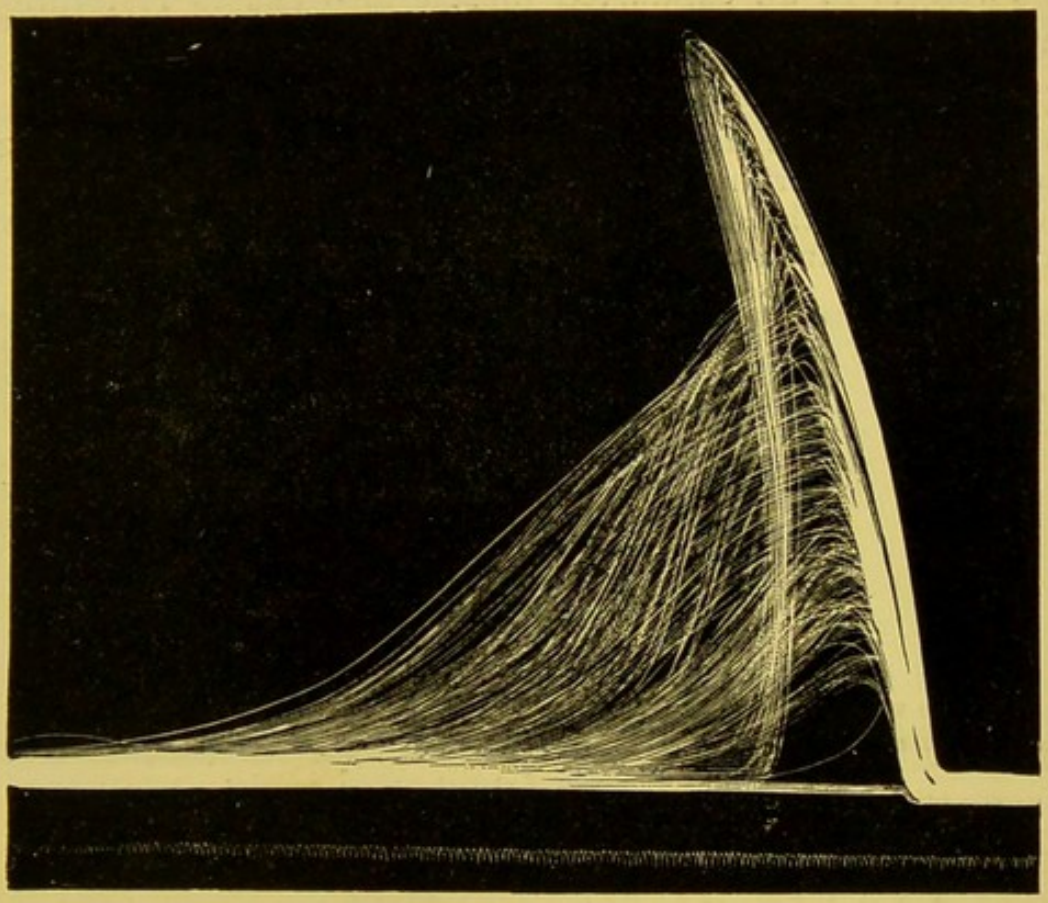


FIG. 175.—FATIGUE CURVE OF SKELETAL MUSCLE

(Gastrocnemius of frog, indirect stimulation), taken with arrangement shown in Fig. 192. Time-tracing, $\frac{1}{10}$ of a second.

formed by the active muscle faster than they can be removed. That even an isolated muscle has a certain store of the material needed for contraction which cannot be all exhausted at once, or which can to a certain extent be replenished by processes going on in the muscle, is shown by the beneficial effect of mere rest. That the accumulation of fatigue products has something to do with the exhaustion is shown by the fact that the muscles of a frog, exhausted in spite of the continuance of the circulation, can be restored by bleed-

ing the animal, or washing out the vessels with normal saline solution, while injection of a watery extract of exhausted muscle into the bloodvessels of a curarized muscle renders it less excitable (Ranke). This observer supposed that it was specially the removal of the acid products of contraction (sarcolactic acid and acid potassium phosphate) which restored the muscle. Injection of arterial blood, or even of an oxidizing agent like potassium permanganate, into the vessels of an exhausted muscle also causes restoration (Kronecker).

When a fatigued muscle responds no longer to indirect stimulation, it can still be directly excited. The **seat of exhaustion** must therefore be either the nerve-trunk or the nerve-endings. It is not the nerve-trunk which is first fatigued, for this still shows the negative variation on being excited. And if the two sciatic nerves of a frog

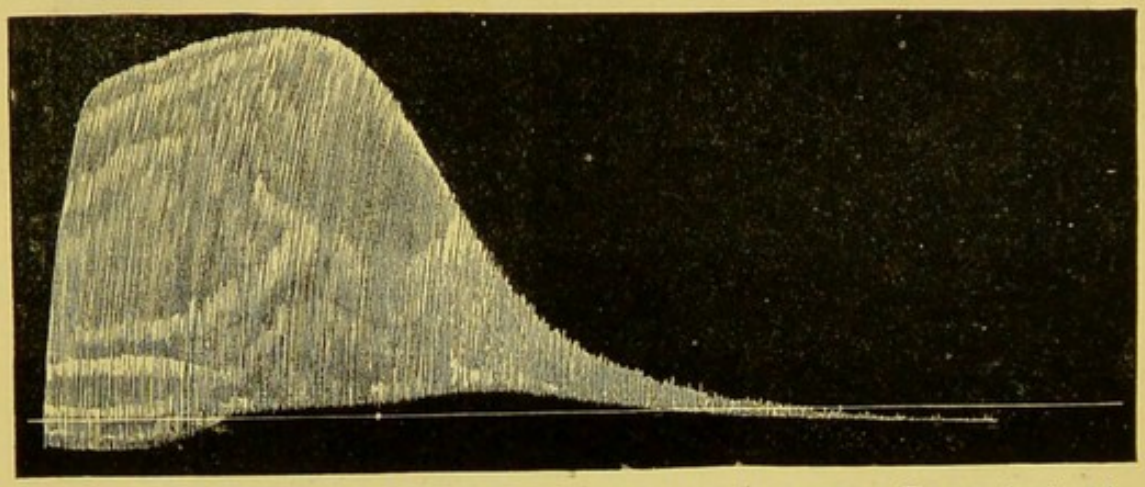


FIG. 176—FATIGUE CURVE TAKEN ON A SLOWLY MOVING DRUM (reduced to half).

Frog's gastrocnemius excited through the sciatic nerve by maximal shocks once in six seconds.

or rabbit be stimulated continuously with interrupted currents of equal strength, while the excitation is prevented from reaching the muscles of one limb till those of the other cease to contract, it will be found that when the 'block' is removed the corresponding muscles contract vigorously on stimulation of their nerve. The passage of a constant current through a portion of the nerve or the application of ether between the point of stimulation and the muscles may be used to prevent the excitation from passing down (p. 620).

The possible seats of **fatigue caused by voluntary muscular contraction** are (1) the muscle, (2) the nerve-endings, (3) the nerve-trunk, and (4) the path of the voluntary motor impulses in the central nervous system, which includes the pyramidal cells in the motor region of the cerebral cortex (p. 663), the fibres of the pyramidal tract, and the motor cells in the anterior horn of the spinal cord. Actual experiments (with an arrangement called an ergograph, by

means of which a record of the work done by one of the flexor muscles of a finger in raising a weight many times in succession can be obtained) (Mosso and Maggiora, Lombard) (p. 621) have shown that fatigue after voluntary effort is due to central changes, and not entirely to changes in the muscles and nerves themselves, for electrical stimulation, either of a 'tired' muscle or of its nerve, is readily responded to at a time when voluntary contraction is impossible. Now, there is no reason to suppose that the nerve-fibres in the central nervous system differ essentially from those of peripheral nerves, and therefore no reason for placing the seat of the fatigue anywhere in the pyramidal fibres, except perhaps in their terminal fibrils in the anterior horn, which correspond to the endings of the peripheral fibres in the muscles. The only other portions of the voluntary motor path besides these terminal fibrils that are likely to become easily fatigued are the nerve-cells of the cortex and the cord. These central structures we must consider the weakest links in the chain, the next weakest link being the motor endings in the muscles, and the strongest the nerve-fibres. The motor-endings do not, in general, break down in voluntary contraction, because the central apparatus becomes sooner fatigued. It is not inconsistent with these facts that a muscle, fatigued by direct electrical stimulation, can still be voluntarily contracted. For it has been shown that the voluntary excitation is more effective than any artificial stimulus.

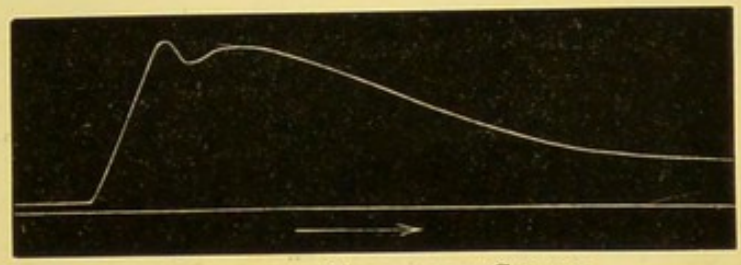


FIG. 177.—VERATRIA CURVE.

(Frog's gastrocnemius.) The curve shows a peak, the lever falling a little before the sustained contraction begins.

(*d*) *The Influence of Drugs on the Contraction of Muscle.*—The total work which a muscle can perform, its excitability and the absolute force of the contraction, may all be altered either in the plus or the minus sense by drugs. But in connection with our present subject those drugs which conspicuously alter the form and time-relations of the muscle-curve have most interest. Of these *veratria* is especially important. When a small quantity of this substance is injected below the skin of a frog, spasms of the voluntary muscles, well marked in the limbs, come on in a few minutes. These are attended with great stiffness of movement, for while the animal can contract the extensor muscles of its legs so as to make a spring, they relax very slowly, and some time elapses before it can spring again. If it be killed before the reflexes are completely gone, the peculiar altera-

tions in the form of the muscle-curve caused by veratria will be most marked. The poisoned muscle, stimulated directly or through its nerve, contracts as rapidly as a normal muscle, while the height of the curve is about the same, but the relaxation is enormously prolonged (Fig. 178). This effect seems to be to a considerable degree dependent on temperature, and it may temporarily disappear when the muscle is made to contract several times without pause. Barium salts, and in a less degree those of strontium and calcium, have an action on muscle similar to that of veratria. Sometimes the curve shows a peak (Fig. 177), due to a rapid descent of the lever for a certain distance. This is followed by a slow relaxation. The peak appears to be analogous to the initial contraction when a strong voltaic

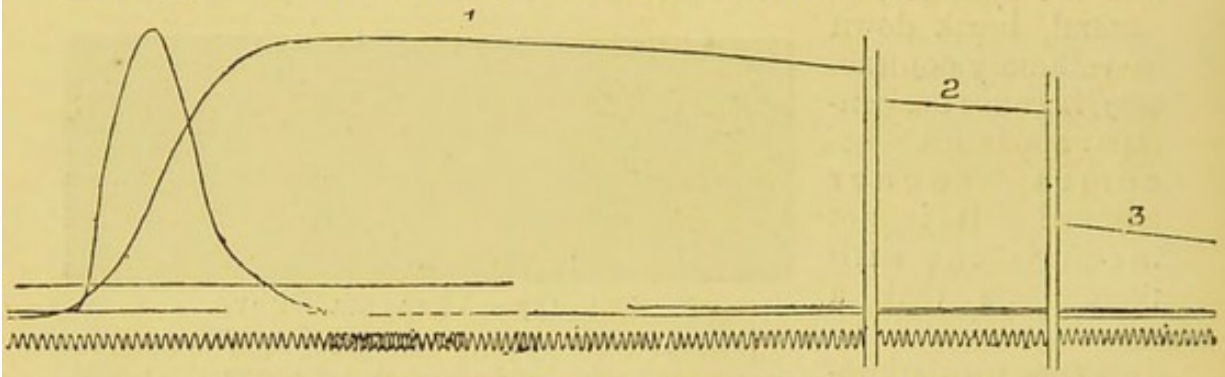


FIG. 178.—VERATRIA CURVE COMPARED WITH NORMAL.

(Frog's gastrocnemius.) The turning-fork marks hundredths of a second. Between 1 and 2 a portion of the tracing corresponding to one and a half seconds has been cut out, and between 2 and 3 a portion corresponding to one second. The veratria curve does not show a peak. At 3 it has not yet fallen to the base line.

current is passed through a muscle, and the rest of the curve to the tonic contraction.

(*e*) *The individuality of the muscle itself* has an influence on the muscle-curve. Not only do the muscles of different animals vary in the rapidity of contraction, but there are also differences in the skeletal muscles of the same animal. In the rabbit there are two kinds of striped muscle, the red and the pale (the semitendinosus is a red, and the adductor magnus a pale muscle), and the contraction of the former is markedly slower than that of the latter.

In many fishes and birds, and in some insects, a similar difference of colour and structure is present, although a physiological distinction has not here been worked out.

Even where there is no distinct histological difference,

there may be great variations in the length of contraction. In the frog, for instance, the hyoglossus muscle contracts much more slowly than the gastrocnemius. The wave of contraction, which in frogs' striped muscle lasts only about ·07 second at any point, may last a second in the forceps muscle of the crayfish, though only half as long in the muscles of the tail. In the muscles of the tortoise the contraction is also very slow. The muscles of the arm of man contract more quickly than those of the leg.

Summation of Stimuli and Superposition of Contractions.—Hitherto we have considered a single muscular contraction as arising from a single stimulus, and we have assumed that the muscle has completed its curve and come back to its original length before the next stimulus was thrown in. We have now to inquire what happens when a second stimulus acts upon the muscle during the contraction caused by a first stimulus, or during the latent period before the contraction has actually begun; and what happens when a whole series of rapidly-succeeding stimuli are thrown into the muscle.

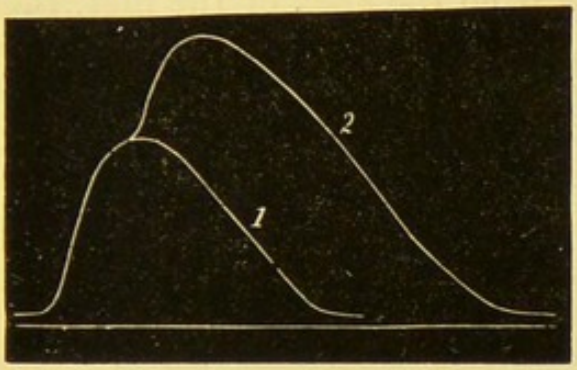


FIG. 179.—SUPERPOSITION OF CONTRACTIONS.

1 is the curve when only one stimulus is thrown in; 2, when a second stimulus acts at the time when curve 1 has nearly reached its maximum height.

First let us take two stimuli separated by a smaller interval than the latent period (p. 559). If they are both maximal (*i.e.*, if each by itself would produce the greatest amount of contraction of which the muscle is capable when excited by a single stimulus), the second has no effect whatever, the contraction is precisely the same as if it had never acted. But if they are less than maximal, the contraction, although it is a single contraction, is greater than would have been due to the first stimulus alone; in other words, the stimuli have been summed or added to each other during the latent period so as to produce a single result.

Next let us consider the case of two stimuli separated by

a greater interval than the latent period, so that the second falls into the muscle during the contraction produced by the first. The result here is very different: traces of two contractions appear upon the muscle-curve, the second curve being that which the second stimulus would have caused alone, but rising from the point which the first had reached at the moment of the second shock (Fig. 179). Although the first curve is cut short in this manner, the total height of the contraction is greater than it would have been had only the first stimulus acted; and this is true even when both stimuli are maximal. Under favourable circumstances, when the second curve rises from the apex of the first, the

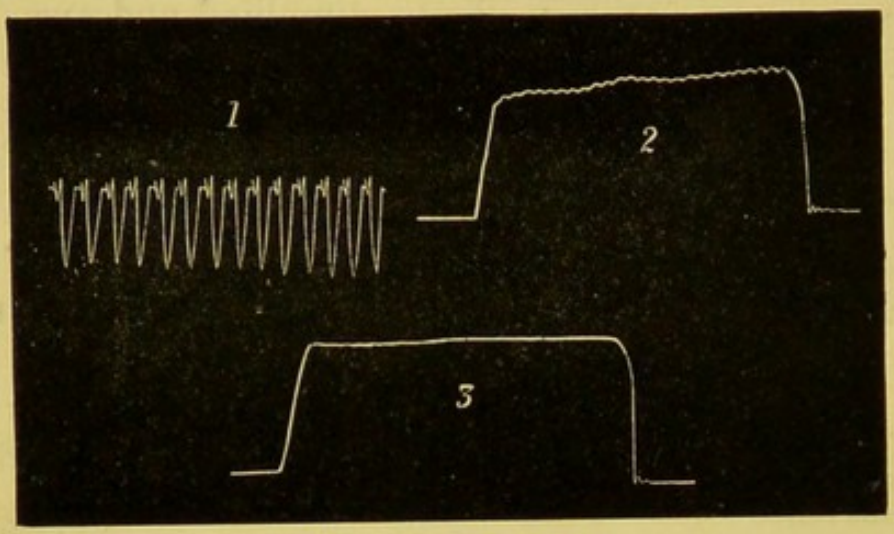


FIG. 180.—TETANUS.

1, 5 stimuli per second; 2, 15 per second; 3, 15 per second, when muscle was more exhausted than in 2.

total height may be twice as great as that of the contraction which one stimulus would have caused (p. 623).

Not only may we have superposition or fusion of two contractions, but of an indefinite number; and a series of rapidly following stimuli causes complete **tetanus** of the muscle, which remains contracted during the stimulation, or till it is exhausted (Fig. 180).

The meaning of a complete tetanus is readily grasped if, beginning with a series of shocks of such rapidity that the muscle can just completely relax in the intervals between successive stimuli, we gradually increase the frequency (p. 624). As this is done, the ripples on the curve become smaller and smaller, and at last fade out altogether. The

maximum height of the contraction is greater than that produced by the strongest single stimulus ; and even after complete fusion has been attained, a further increase of the frequency of stimulation may cause the curve still to rise.

It is evident from what has been said that the frequency of stimulation necessary for complete tetanus will depend upon the rapidity with which the muscle relaxes ; and everything which diminishes this rapidity will lessen the necessary frequency of stimulation. A fatigued muscle may be tetanized by a smaller number of stimuli per second than a fresh muscle, and a cooled by a smaller number than a heated muscle. The striped muscles of insects, which can contract a million times in an hour, require 300 stimuli per second for complete tetanus, those of birds 100, of man 40, the torpid muscles of the tortoise only 3. The pale muscles of the rabbit need 20 to 40 excitations a second, the red muscles only 10 to 20 ; the tail muscles of the crayfish 40, but the muscles of the claw only 6 in winter and 20 in summer. The gastrocnemius of the frog requires 30 stimuli a second, the hyoglossus muscle only half that number (Richet).

We see, then, that there is a lower limit of frequency of stimulation below which a given muscle cannot be completely tetanized, and the question arises whether there is also an upper limit beyond which a series of stimuli becomes too rapid to produce complete tetanus, or, indeed, to cause contraction at all. We may be certain that every stimulus requires a finite time to produce an effect, and it is possible that if the duration of each shock were reduced below a certain minimum, without lessening at the same time the interval between successive excitations, no contraction would be caused by any or all of the stimuli in the series. But above this minimum there apparently lies a frequency of stimulation—at least, when the interval between the stimuli is reduced exactly in the same proportion as the duration—at which an interrupted current comes to act like a constant current, causing a single twitch at its commencement or at its end, but no contraction during its passage.

As to this last limit, on the fixing of which much labour has been expended without any harmony of result, it undoubtedly does not depend upon the frequency of stimulation alone ; the intensity of the individual excitations, the temperature of the muscle, and probably other factors, affect it. For Bernstein found that with moderate strength of stimulus tetanus failed at about 250 per second, and was replaced by an initial contraction ; with strong stimuli at more than 1,700 per second, tetanus could still be obtained. Kronecker and Stirling, stimulating the muscle by a novel and ingenious method

(by induced currents set up in a coil by the longitudinal vibrations of a magnetized bar of iron), saw complete tetanus even at 24,000 stimuli a second; while v. Kries in a cooled muscle found tetanus replaced by the simple initial twitch at 100 stimuli per second, although in a muscle at 38° C. stimulation of ten times this frequency still caused tetanus. But it is doubtful whether the electrical method of stimulation is capable of solving the problem, because of the difficulty of being sure that the number of excitations is the same as the nominal number of shocks, all the more that even very short currents leave alterations of conductivity and excitability behind them (Sewall), which we shall have to discuss in another chapter (p. 596).

It is only while the actual shortening is taking place that a tetanized muscle can do external work. But although during the maintenance of the contraction no work is done, energy is nevertheless being expended, for the metabolism of a muscle during tetanus is greater than during rest. Among other changes, the carbon dioxide given off is increased, and lactic acid produced. And upon the whole a muscle is more quickly exhausted by tetanus than by successive single contractions, although there are great differences between different muscles. For example, the muscles which close the forceps of the crayfish or lobster have, as everyone knows, the power of most obstinate contraction. Richet tetanized one for over seventy minutes, and another for an hour and a half, before exhaustion came on, while a tetanus of a single minute exhausted the muscles of the crayfish's tail. The gastrocnemius of a summer frog kept up for twelve minutes, and a tortoise muscle for forty minutes.

Continuous stimulation is not always necessary for the production of continuous contraction; in some conditions a single stimulus is sufficient. A blow with a hard instrument may cause a dying or exhausted, and in thin persons even a fairly normal, muscle to pass into long-continued contraction. This so-called **'idio-muscular' contraction** seems to depend, in part at least, on the great intensity of the stimulus. It can sometimes be obtained in the frog's gastrocnemius, particularly in spring after the winter fast. It is not a tetanus and is not propagated along the muscular fibres, as an electrical tetanus is, but remains localized at the spot where it arises. Similar non-tetanic contractions have already been mentioned, such as the tonic contraction during the passage of a strong voltaic current and the sustained veratria contraction. Ammonia causes also a long but non-tetanic contraction, and this, too, does not spread when the sub-

stance has acted only on a portion of the muscle. The contraction force of all these tonic contractions, as measured by the resistance necessary to overcome or prevent them, is less than the contraction force in electrical tetanus (Schenck).

The rate at which the wave of muscular contraction travels may be measured by stimulating the muscle at one end, and recording, by means of levers, the movements of two points of its surface as far apart from each other as possible. Time is marked on the tracing by means of a tuning-fork, and the distance between the points at which the two curves begin to rise from the base-line divided by the time gives the velocity of the wave. Another method is founded upon the measurement of the rate at which the negative variation (p. 630) passes over the muscle, this being the same as the velocity of the contraction-wave. In frog's muscle it is about three metres a second, or six miles an hour. Rise of temperature increases, fall of temperature lessens it.

When a muscle is excited through its nerve, the contraction springs up first of all about the middle of each muscular fibre where the nerve-fibre enters it, and then sweeps out in both directions towards the ends. But so long is the wave, that all parts of the fibre are at the same time involved in some phase or other of the contraction. And this is the case even when the end of a long muscle like the sartorius is artificially stimulated.

The wave of contraction in unstriped muscle lasts a relatively long time at any given point, and in tubes like the intestines and ureters, the walls of which are largely composed of smooth muscle arranged in rings, the wave shows itself as a gradually-advancing constriction travelling from end to end of the organ. There is no evidence that the contraction of smooth muscular fibres is discontinuous—that is, composed of summated contractions like a tetanus; it appears to be a greatly-prolonged simple contraction of the kind called 'tonic.' An artificial stimulus, mechanical or electrical, causes, after a long latent period, a very definitely-localized contraction in a rabbit's ureter, which slowly spreads in a peristaltic wave in one or both directions along the muscular tube. Here, as in the cardiac muscle, the excitation passes from fibre to fibre, while in striped skeletal muscle only the fibres excited directly or through their nerves seem to contract. That the rhythmical contraction of the heart is not a tetanus has already been seen. It is a simple contraction, intermediate in its duration and other characters between the twitch of voluntary muscle and the tonic contraction of smooth muscle. The contraction both of unstriped and of cardiac muscle

is lengthened and made stronger by distension of the viscera in whose walls they occur, just as a skeletal muscle contracts more powerfully against resistance.

Voluntary Contraction.—It is often stated that the voluntary contraction is a tetanus, but in favour of this belief there is little direct evidence. One of the strongest buttresses of the theory of natural tetanus has been the **muscle-sound**, a low rumbling note which can be heard by listening with a stethoscope over the contracting biceps, or, when all is still, by stopping the ears with the fingers and strongly contracting the masseter and the other muscles concerned in closing the jaws.* Discovered about eighty years ago, first by Wollaston and then by Erman, half a century passed away before it was investigated more fully by Helmholtz. The latter observer, confirming the results of his predecessors, put down the pitch of the sound at 36 to 40 vibrations per second. He found, however, that little vibrating reeds with a rate of oscillation of about 19·5 per second, were more affected, when attached to muscle thrown into voluntary contraction, than those that vibrated at a smaller or a greater rate. He therefore concluded that the fundamental tone of the muscle corresponded to this frequency, although, since such a low note is not easily appreciated, the sound actually heard was really its octave or first harmonic (p. 263). The objection has been brought forward that the resonance tone of the ear also corresponds to a vibration frequency of 36 to 40 a second. In other words, this is the natural rate of swing of the elastic structures in the middle ear, the rate they will most easily fall into if set moving, and not compelled to vibrate at some other rate.

Now, this resonance tone might be elicited by a quivering muscle if, among many diverse rates of oscillation of different portions of its substance, the rate of 36 to 40 a second anywhere appeared, and the note corresponding to the real rate of vibration of the muscle as a whole might be overpowered. Or, even if there were no regular rate of vibration of the whole muscle, but, instead, a series of irregular tremors or pulls, waxing here, waning there, and flitting

* In order that a muscular sound may be produced there must be a certain abruptness in the contraction. Thus, the slowly-contracting smooth muscles do not produce a sound, nor the slowly-contracting heart-muscle of cold-blooded animals.

hither and thither along the muscle, the ear might from time to time pick out of the turmoil of feeble aerial waves those corresponding to its resonance tone, just as a tuning-fork or a piano-string attuned to a particular note would catch it up amid a thousand other sounds and strengthen it.

But while this renders it highly probable that the resonance of the ear contributes to the production of the muscle-sound, and shows that we cannot from the pitch of the muscle-sound alone deduce the rate at which the muscle-substance is vibrating, it does not invalidate Helmholtz's objective observations with the oscillating reeds. And several observers (Schäfer, Horsley, v. Kries) have noticed periodic oscillations, at the rate of 8 to 10 per second, in the curves taken from voluntarily contracted muscles, and from muscles excited

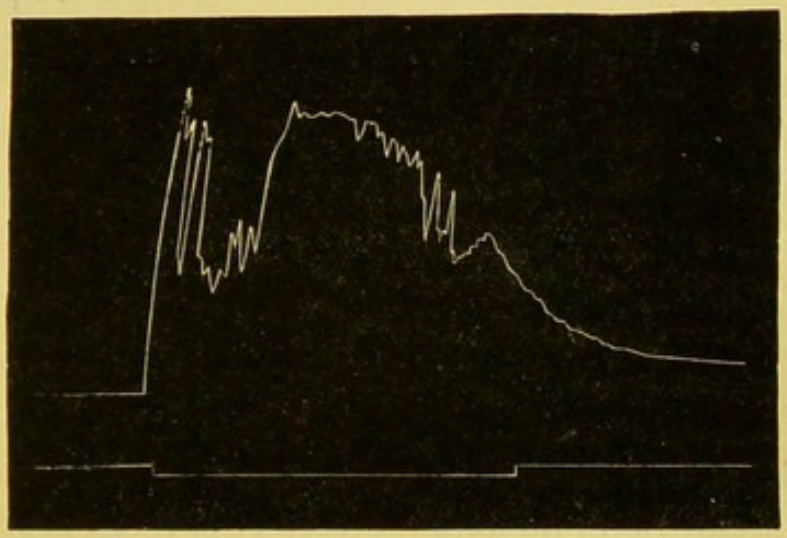


FIG. 181.—CONTRACTIONS CAUSED BY STIMULATION OF THE SPINAL CORD.

through stimulation of the motor areas of the surface of the brain. Since this rate remains the same whether the motor cortex, the corona radiata, or the spinal cord is excited, and, unlike the rate of response to excitation of peripheral nerves, is independent of the frequency of stimulation, it has been supposed to represent the rhythm with which impulses are discharged from the motor cells of the cord (Fig. 181). Other observers have seen a rhythm of 20 per second while Haycraft denies that regular oscillations occur at all, and thinks that irregularities in the contraction, connected with a want of co-ordination of all the fibres, cause the muscle-sound by drawing forth the resonance tone of the ear itself. Lovèn, however, found the rhythm of strychnia tetanus in

the frog about 8 to 10 per second, and asserted that by means of the capillary electrometer (p. 538) 8 electrical oscillations per second could be demonstrated in voluntarily contracted muscle. But they seem to differ in amplitude or abruptness from the electrical changes produced in experimental tetanus. For secondary tetanus (p. 644) is not caused by muscle in voluntary contraction, except (and even this is doubtful) just at the beginning. While, therefore, it cannot be denied that the voluntary contraction is discontinuous, in the sense that it is not a perfectly smooth and uniform tonic contraction, we still lack a decisive proof that it is maintained by a strictly intermittent outflow of nervous energy, and not by a continuous outflow causing a sustained contraction, which, it may be, remits and is reinforced at intervals. In this connection it is interesting that chemical stimulation, for example by ammonia, which certainly sets up a condition of sustained contraction, does not cause secondary tetanus. In any case, some voluntary contractions, namely, the shortest possible, do not seem to be tetanic. For a voluntary movement *can* be executed in $\frac{1}{10}$ to $\frac{1}{20}$ of a second, which, if we take the greatest frequency of discharge in natural tetanus that has been suggested, would allow time only for a single oscillation, caused by a single impulse.

(3) **Thermal Phenomena of the Muscular Contraction.**—When a muscle contracts its temperature rises; the production of heat in it is increased. This is most distinct when the muscle is tetanized, but has also been proved for single contractions. The change of temperature can be detected by a delicate mercury or air thermometer; and, indeed, a thermometer thrust among the thigh-muscles of a dog may rise as much as 1° to 2° C. when the muscles are thrown into tetanus. In the isolated muscles of cold-blooded animals the increase of temperature is much less; and electrical methods, which are the most delicate at present known, have generally been used for its detection and measurement.

They depend either upon the fundamental fact of thermo-electricity, that in a circuit composed of two metals a current is set up if the junctions of the metals are at different temperatures; or upon the fact that the electrical resistance of a metallic conductor varies with its temperature.

On the former principle the *thermopile* has been constructed (Fig. 182), on the latter the *bolometer*, or '*electrical-resistance thermometer*.'

Where no very fine differences of temperature are to be measured, a single thermo-junction of German silver and iron, or copper and iron, is inserted into a muscle or between two muscles. But the electromotive force, and therefore the strength of the thermo-electric current, is proportional for any given pair of metals to the number of junctions, and for delicate measurements it may be necessary to use several connected together in series. A thermopile of antimony-bismuth junctions gives a stronger current for a given difference of temperature than the same number of German silver-iron couples, but from its brittle nature is otherwise less convenient.

The direction of the current in the circuit is such that it passes through the heated junction from bismuth to antimony, and from copper or German silver to iron. Knowing this direction, we are aware of the changes of temperature which take place from the movements of the mirror of the galvanometer with which the pile is connected. The galvanometer must be of low resistance, since the electromotive force of the thermo-electric currents is small, and a high resistance would cut down their intensity too much.

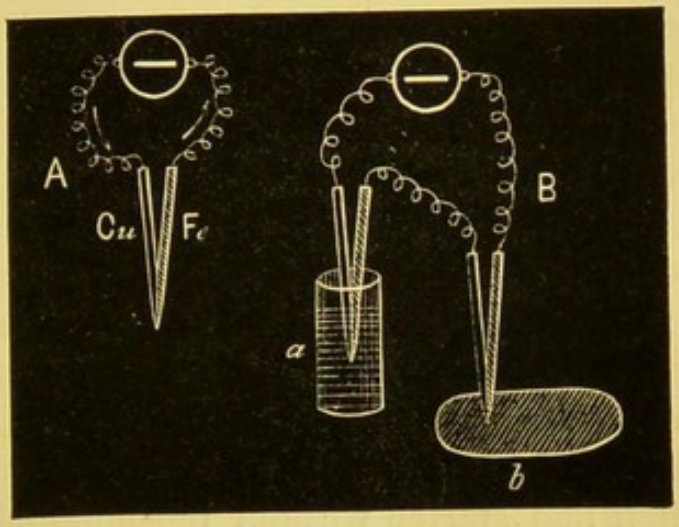


FIG. 182.

A, a single copper-iron thermo-electric couple; B, two pairs, one inserted into the tissue *b*, the other dipping into water in a beaker *a*. The temperature of the water may be adjusted so that the galvanometer shows no deflection. The temperature of the tissue is then the same as that of the water.

The muscle which is to be excited is brought into close contact with one junction or set of junctions, the other set being kept at constant temperature by immersing them in water, or covering them with muscle that is not to be stimulated. The image will now come to rest on the scale; and excitation of the muscle will cause a movement indicating an increase of temperature in it, the amount of which can be calculated from the deflection.

In this way Helmholtz observed a rise of temperature of

·14° to ·18° C. in excised frogs' muscles when tetanized for a couple of minutes.

Heidenhain, with a very delicate pile, found a rise of ·001° to ·005° C. for a single contraction of a frog's muscle. On the assumption that the pile had time to take on the temperature of the muscle before there was any appreciable loss of heat, this would be equal to the production by every gramme of muscle of a thousandth to five-thousandths of a small calorie (p. 493) of heat. From Fick's observations we may take about three-thousandths of a small calorie as the maximum production of a gramme of frog's muscle in a single contraction.

It is certain that when work is done by a muscle an equivalent amount is subtracted from its sum-total of energy, and we might therefore expect that the heat produced in contraction should diminish as the work increases. But experiment does not fulfil this expectation. The manner and the rate of its expenditure of energy depend upon the conditions under which the muscle is placed. A stretched muscle, when caused to contract, produces more heat than if it had started without tension, and still more heat when it is fixed so that it cannot shorten during stimulation. A muscle, starting without tension, produces more heat when it contracts isometrically than when it contracts isotonically. This fact does not, however, prove that the heat-production is greater when no work is done, because the tension increases during excitation when contraction is prevented, and, as has been said, increase of tension alone causes more heat to be given out by an active muscle.

When a muscle, excited by maximal stimuli, is made to lift continuously increasing weights, both the work done and the heat given out increase up to a certain limit. The muscle, as it were, burns the candle at both ends. This would be of itself enough to show that there is no fixed relation between the work and the heat-production; although the latter reaches its maximum somewhat sooner than the former.

We have already seen that when a muscle is cooled, or fatigued, or poisoned with veratria or with suprarenal extract,

the stress of the change falls chiefly upon the relaxation. This indicates that the relaxation is by no means a mere elastic recoil, but a physiological process as important as the contraction itself; and this conclusion is strengthened by the fact we have now to mention, that not only is heat produced during the actual shortening, but also during the relaxation. It is in accordance with this that as fatigue comes on the production of heat diminishes earlier than the height of the contraction. We must suppose that the diminution is related to the increasing slowness of the relaxation, and indicates that the chemical changes are less rapid when relaxation is more difficult.

The fraction of the total energy transformed which appears as muscular work varies with the conditions of the contraction. The greater the resistance,* the larger is the proportion of the energy which appears as work, the smaller the proportion which appears as heat; but even in the most favourable case, an excised frog's muscle never does work equal to more than $\frac{1}{4}$ of the heat given off. Generally the ratio is much less, and may sink as low as $\frac{1}{25}$. In the intact mammalian body the muscles work somewhat more economically than the excised frog's muscles at their best; for both experiment and calculation show (p. 501) that in a normal man under the most favourable conditions as much as one-third of the energy is converted into work. But in any case the heat-producing mechanism and the work-producing mechanism of muscle are certainly in some respects distinct, and a variation in the activity of the one is not necessarily associated with a corresponding variation in the activity of the other.

(4) **Chemical Phenomena of the Muscular Contraction.**—We as yet know but little regarding the chemical composition of living muscle, and are unlikely ever to know much, since most chemical operations cause the immediate death of the tissue. The *composition of dead mammalian muscle* may be stated, in round numbers, as follows, but there are considerable variations, even within the same species.

* This statement, based on experiments with excised frog's muscles is not, of course, inconsistent with the fact mentioned on p. 502, that in the intact body the fraction of the energy transformed into heat is greater in hard than in moderate work.

Water		75	per cent.
Proteids		20	"
Fats		2	"
Nitrogenous metabolites.	Kreatin, Xanthin, Hypoxanthin		
Carbohydrates.	Glycogen, Sarcolactic acid, Inosit ...	2	"

Salts, chiefly carbonate and phosphate of potassium, less than 1 per cent.

There is more water in the muscles of young than of old animals (v. Bibra), and more in tetanized than in rested muscle (Ranke). The fats probably belong to a small extent to the actual muscle-fibres. For even when the visible fat is separated with the utmost care, nearly 1 per cent. of fat still remains (Steil). In lean horse-flesh Pflüger found 0·35 per cent. of glycogen, but no sugar. The total nitrogen was 3·21 per cent. of the moist tissue.

It would be natural to expect that the proteids, which bulk so largely among the solids of the dead muscle, and which are so obviously important in the living muscle, should be affected by contraction. But up to the present time no quantitative difference in the proteids of resting and exhausted muscle has ever been made out. The following chemical changes, however, have been definitely established. In an active muscle—

(*a*) More carbon dioxide is produced.
(*b*) More oxygen is consumed.
(*c*) Sarcolactic acid is formed.
(*d*) Glycogen is used up.
(*e*) The substances soluble in water diminish in amount; those soluble in alcohol increase.

That the carbon dioxide is not formed by direct oxidation, but by the splitting up of a substance or substances with which the oxygen has previously combined, is, as has already been shown (pp. 247, 248), highly probable. For (to recapitulate) (*a*) no free oxygen exists in muscle. None can be pumped out. (*b*) A frog's muscle isolated from the body will go on contracting for a long time in an atmosphere devoid of oxygen, *e.g.*, in an atmosphere of hydrogen. (*c*) When artificial circulation is maintained through isolated muscles, the amount of carbon dioxide produced does not run parallel with the quantity of oxygen consumed. The

latter is dependent on the temperature of the muscle, being increased when the muscle is heated, diminished when it is cooled. The production of carbon dioxide, on the contrary, is, within a wide range, independent of the temperature.

Formation of Sarcolactic Acid—Reaction of Muscle.—To litmus paper fresh muscle is amphicroic; that is, it turns red litmus blue and blue litmus red. This is due, partly at least, to the phosphates. Monophosphate (tribasic phosphoric acid, H_3PO_4, in which one hydrogen atom is replaced, say by sodium or potassium) reddens blue litmus, while diphosphate (where two hydrogen atoms are replaced) turns red litmus blue. Litmoid (lacmoid) differs from litmus in not being affected by monophosphates. Diphosphates turn red litmoid blue, and so does fresh muscle, which has no effect on blue litmoid. A cross-section of fresh muscle is about neutral (sometimes faintly acid) to turmeric paper, which is turned yellow by monophosphates. A muscle which has entered into rigor or has been fatigued by prolonged stimulation is distinctly acid to blue litmus and to brown turmeric, reddening the former and turning the latter yellow, but does not affect blue litmoid. The sarcolactic acid produced in rigor and activity is at once neutralized, as is shown by the fact that blue litmoid paper is not reddened, as it would be by free sarcolactic acid. The neutralization takes place at the expense of the sodium carbonate and disodium phosphate, the latter being changed into monophosphate, which, in part at least, causes the acid reaction to turmeric (Röhmann).

Glycogen is the one solid constituent of muscle which has been definitely proved to diminish during activity. It accumulates in a resting muscle, especially in a muscle whose motor nerve has been cut; rapidly disappears from the muscles of an animal made to do work while food is withheld; or from the muscles of an animal poisoned by strychnia, which causes violent muscular contractions.

What substance is the sarcolactic acid formed from? From what we know of the production of lactic acid both outside the body and in the intestine from carbo-hydrates, it might seem a most plausible suggestion that in the active muscle it comes from glycogen. But the best evidence points the other way; *e.g.*, in rigor mortis sarcolactic acid is produced just as in muscular contraction. Not only so, but according to Ranke every isolated muscle has a certain maximum of acidity, which it reaches either through contraction, or through rigor, or through contraction followed by rigor. Yet in rigor mortis the quantity of glycogen is unaltered (Boehm). The probability is that the sarcolactic acid is formed from proteid.

Source of the Energy of Muscular Contraction.—The facts just mentioned show that glycogen may be one of the sources of muscular energy, but it cannot be the only source, for its amount is too small.

For example, the heart of an average man, which weighs 280 grammes, contains about 60 grammes of solids, and among these not more than 1·5 grammes of glycogen. In twenty-four hours it produces, even on a low estimate, at least 190,000 calories of heat (p. 503), equivalent to the complete combustion of a little more than 45 grammes of glycogen. To supply this amount, the whole store of glycogen in the heart would have to be used and replaced every 40 minutes. But the accumulation of glycogen is immensely slower in the muscles of a rabbit made glycogen-free by strychnia, and therefore we have to look around for some other source of energy to supplement the glycogen. We have already brought forward evidence (p. 468) that, under ordinary circumstances, not a great deal, at any rate, of the energy of muscular contraction comes from the proteids. Of carbohydrates, the only one except glycogen which is at all adequate to the task of supplying so much energy is the glucose of the blood. The quantity of blood passing through the coronary circulation has been estimated at 30 c.c. per 100 grammes of cardiac muscle per minute (Bohr and Henriques), which would be equivalent for an average man to about 120 litres in twenty-four hours. This quantity of blood will contain at least 150 grammes of glucose, and about 50 grammes will suffice to supply all the heat produced by the heart. Of proteids a little less than 45 grammes would be needed, of fat 20 grammes. We see, therefore, how intense must be the metabolism that goes on in an actively contracting muscle. On any probable assumption as to the source of muscular energy a quantity of material equal to two-thirds of its solids must be used up by the heart in twenty-four hours. Or, to put it in another way, the *heart requires not less than half its weight of ordinary solid food in a day*. The body as a whole requires $\frac{1}{50}$ to $\frac{1}{70}$ of its weight.

To sum up: It is universally admitted that carbohydrates can yield energy for muscular work. It has been demonstrated by Zuntz and his pupils and by others that fat can do so. The experiments of Pflüger, to which we have already alluded (p. 469), have shown than when an animal is fed on lean meat, the muscular work done is far too great to have come from non-proteid substances. We must conclude, therefore, that when carbohydrates and fats are plentiful in the food, the greater part of the energy of muscular contraction comes from them; it comes on the other hand from proteids, when the carbohydrates and the fats are restricted, and the proteids plentifully supplied. Not only so, but these three groups of food substances yield muscular energy in *isodynamic relation*. In other words, a

given amount of muscular work requires the expenditure of approximately the same quantity of chemical energy, whether it comes almost entirely from proteid, or chiefly from carbohydrates, or chiefly from fat. Some observers have stated that the taking of even a comparatively small quantity of sugar vastly increases the capacity for muscular work as measured by the ergograph (p. 621). But although it is not to be doubted that sugar is under normal circumstances one of the most important substances used up in muscular contraction, the claim that sugar is, *par excellence*, the food for muscular exertion has not yet been made out.

Rigor Mortis.—When a muscle is dying its excitability, after perhaps a temporary rise at the beginning, diminishes more and more until it ultimately responds to no stimulus, however strong. The loss of excitability is not in itself a sure mark of death, for, as we have seen, an inexcitable muscle may be partially or completely restored; but it is followed, or, where the death of the muscle takes place very rapidly, perhaps accompanied, by a more decisive event, the appearance of rigor. The muscle, which was before soft and at the same time elastic to the touch, becomes firm; but its elasticity is gone. The fibres are no longer translucent, but opaque and turbid. If shortening of the muscle has not been opposed, it may be somewhat contracted, although the absolute force of this contraction is small compared with that of a living muscle, and a slight resistance is enough to prevent it. The reaction is now distinctly acid to litmus. This is rigor mortis, the death-stiffening of muscle.

An insight into the real meaning of this singular and sometimes sudden change was first given by the experiments of Kühne. He took living frog's muscle, freed from blood, froze it, and minced it in the frozen state. The pieces were then rubbed up in a mortar with snow containing 1 per cent. of common salt, and a thick neutral or alkaline liquid, the muscle-plasma, was obtained by filtration. This clotted into a jelly when the temperature was allowed to rise, but at 0° C. remained fluid. The clotting was accompanied by a change of reaction, the liquid becoming acid. An equally

good, or better, method is to use pressure for the extraction of the plasma from the frozen fragments of muscle. A low temperature is essential, otherwise the plasma will coagulate rapidly within the injured muscle.

A similar plasma can be expressed from the skeletal muscles of warm-blooded animals (Halliburton), and with greater difficulty from the heart. Attempts to obtain it from smooth muscle have hitherto failed, possibly because of the unfavourable anatomical conditions.

When the muscle, after exhaustion with water, is covered with a solution of a neutral salt, a 5 per cent. solution of magnesium sulphate or 10 per cent. solution of ammonium chloride being the best, certain proteids are extracted which on dilution clot or are precipitated much in the same way as the muscle-plasma obtained by cold and pressure; and the process is hastened by keeping them at a temperature of 40° C.

In the extracts of mammalian muscle before coagulation has occurred three chief proteids are present: paramyosinogen, coagulated by heat at 47° to 50° C.; myosinogen, coagulating at 55° to 60° C. (usually about 56°); and serum-albumin, coagulating about 73°. In extracts of frog's muscle there is in addition a substance which coagulates at about 40°. Both the paramyosinogen and the myosinogen, but particularly the former, show a tendency, even at ordinary temperatures, to pass into an insoluble form—myosin. At body temperature this transformation occurs more quickly. The myosin precipitate, which rapidly forms in muscle-plasma, is sometimes called the muscle-clot, and the liquid which is left the muscle-serum. A similar myosin precipitate or clot is formed in the interior of the muscular fibres in natural rigor and in the rapid rigor produced by heating a muscle to a little above the body temperature. But in natural rigor this precipitate is either soluble in saline solutions or the whole of the paramyosinogen and myosinogen do not undergo the change, since a certain amount of these substances can as a rule be extracted from dead muscle by such solutions. Some have supposed that in the living muscle paramyosinogen and myosinogen exist as such. But this is not certain. They may simply be formed when the muscle dies.

It has been suggested that myosin (or its precursors), sarcolactic acid, and carbon dioxide are all products of some complex body which breaks up both at the death of the muscle and during contraction, and that, indeed, contraction is only a transient and removable rigor (Hermann). But it cannot be admitted that there is any fundamental connection between rigor and contraction, although there are some superficial resemblances. In both there is (1) shortening; (2) heat-production; (3) formation of fixed acid and carbon dioxide; (4) electrical changes. Another analogy might be forced into the list by anyone who was determined to see only rigor in

contraction : the rigor passes off as the contraction passes off, although the 'resolution' of a rigid muscle takes days, the relaxation of an active muscle a fraction of a second. The disappearance of rigor is not dependent on putrefaction ; it takes place when growth of bacteria is prevented (Hermann).

Why does coagulation of myosin occur at the death of the muscle? To this question no clear answer can be given. Some have looked on the process as analogous to the clotting of blood when it is shed, and it has even been suggested that just as a fibrin ferment is developed when the leucocytes begin to die, a myosin ferment, which aids coagulation, is developed in dead or dying muscle. But it is easy to make too much of the apparent analogy between the clotting of muscle and the clotting of blood, and there are differences as well as resemblances. For instance, the addition of potassium oxalate does not prevent coagulation of muscle extracts, as it does of blood and blood-plasma.

Various influences affect the onset of rigor. Fatigue hastens it ; heat has a similar effect ; the contact of caffeine, chloroform and other drugs causes most pronounced and immediate rigor. Blood applied to the cross-section of a muscle first stimulates the fibres with which it is in contact, and then renders them rigid. But it is to be remembered that normally the blood does not come into direct contact even with the sarcolemma, much less with its contents.

The effect of heat is of special interest. A skeletal muscle of a frog, like the gastrocnemius, if dipped into normal saline solution at 40° or 41° C. goes into rigor at once ; the frog's heart requires a temperature 3° or 4° higher ; the distended bulbus aortæ can withstand even a temperature of 48° for a short time. An excised mammalian muscle passes into immediate rigor at 45° to 50°. In heat rigor the reaction of the muscle becomes strongly acid owing to the formation of sarcolactic acid, and the production of carbon dioxide is also increased. Heat rigor resembles in these respects a greatly accelerated rigor mortis. A small quantity of heat is produced, and the temperature of the muscle may be raised as much as $\frac{1}{20}$° C. This is probably due chiefly to the increased chemical change, and only to a slight extent to the physical alteration in the myosin.

When muscle is at once raised to a temperature of 75° to 100° C., and all the proteids thus coagulated by heat, there is also an increase in the discharge of carbon dioxide (Fletcher), and the reaction becomes distinctly acid to blue litmus, although still alkaline to red. This is the easiest way of obtaining a maximum evolution of carbon dioxide from an excised muscle. It is highly improbable that a marked production of carbon dioxide should take place in heat-coagulated proteids. We must therefore suppose that the characteristic decomposition associated with rigor mortis can complete itself in the brief space that elapses between the application of the heat and the heat-coagulation of the proteids. This decomposition is wanting in the so-called rigor caused by water, which is not a true rigor, and causes no increase in the carbon dioxide given off. Chloroform, on the other hand, produces a marked increase in the carbon dioxide

production, and this is evidently related to its action in hastening the onset of rigor.

In a human body rigor generally appears not earlier than an hour, and not later than four or five hours, after death. In exceptional cases, however, it may come on at once, and the annals of war and crime contain instances where a man has been found after death still holding with a firm grip the weapon with which he had fought, or which had been thrust into his hand by his murderer. It is related that after one of the battles of the American Revolutionary War some of the dead were found with one eye open and the other closed as in the act of taking aim. A high temperature favours a rapid onset; a body wrapped up in bed will, other things being equal, become rigid sooner than a body lying stripped in a field. Muscular exhaustion, as we have said, is another favouring condition: hunted animals and the victims of wasting diseases go quickly into rigor. It is a rule, but not an invariable one, that rigor, when it comes on quickly, is short, and lasts longer when it comes on late. All the muscles of the body do not stiffen at the same time; the order is usually from above downwards, beginning at the jaws and neck, then reaching the arms, and finally the legs. After two or three days the rigor disappears in the same order. The position of the limbs in rigor is the same as at death; the muscles stiffen without any marked contraction. This can be strikingly shown on a newly-killed animal by cutting the tendons of the extensors of one foot and the flexors of the other; when natural rigor comes on the feet remain just as they were. If heat rigor, however, is caused, the one foot becomes rigid in flexion and the other in extension; and the contraction-force is considerable, although not so great as that of an electrical tetanus in a living muscle.

The Removability of Rigor.—It has been asserted that rigor can be removed and excitability restored. After interrupting the circulation in the hind-legs of rabbits by compression or ligation of the abdominal aorta (Stenson's experiment), and so causing the muscles to become rigid, Brown-Séquard saw them recover their irritability when the blood

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was again allowed to reach them. He performed a similar experiment with artificial circulation through the hand of an executed criminal, with a like result. But grave doubt has been cast upon these experiments by later observations, and it is now almost universally believed that no really rigid muscle has ever been restored, and that the apparent recovery which Brown-Séquard saw was due to the muscles not having been completely rigid. Heubel has, however, stated that the rhythmical contractions of the frog's heart can be restored by filling its cavity with blood, after rigor has been caused by heat and in other ways; and although we cannot transfer these results directly to skeletal muscle, they would show, if confirmed, that the question is not yet closed.

CHAPTER X.

NERVE.

THE voluntary movements are originated by efferent or outgoing impulses from the brain, which reach the muscles along their motor nerves. The involuntary movements and the secretions are in many cases able to go on in the absence of central connections, but are normally under central control. Afferent impulses are continually ascending to the cord and brain from the skin, joints, bones, muscles, and organs of special sense like the eye and the ear. Everywhere the connection between the nervous centres and the peripheral organs, and between different parts of the central nervous system, is made by nerve-fibres. Those which run outside the brain and cord are called peripheral nerve-fibres to distinguish them from the intracentral fibres of the central nervous system itself.

In this chapter we propose to consider certain of the general properties of nerve-fibres. Most of our knowledge of these properties has been derived from experiments on the peripheral, and particularly the peripheral motor nerves; but there is every reason to believe that the main results are true of all nerve-fibres, afferent and efferent, peripheral and central.

What we call nerve-fibres were known and named, and many important facts in their physiology discovered, long before their true morphological significance was recognised. The researches of recent years have shown that every nerve-fibre is, as regards its essential constituent the axis-cylinder, a process of a nerve-cell. The nerve-cells, each of which, including all its processes, may be conveniently termed a *neuron*, are the essential elements of the nervous system. The cell-bodies of most of the neurons are situated in, or in close relation to, the spinal cord and the brain, and therefore the detailed description of them will be reserved till we come to treat of the central nervous system (see p. 661 and Figs. 227 to 231). It is enough to say here that in general a nerve-cell gives off two kinds of processes: (1) one or more dendrites or protoplasmic processes, which repeatedly bifurcate like the branches of a tree into thinner and thinner twigs, and extend only for a relatively short distance from the cell-body; (2) an axis-cylinder process or axon, which as a rule runs for a considerable distance without altering its calibre, and either gives off no branches (as in the peripheral nerves) or only a comparatively small number of lateral twigs (collaterals). Ultimately

the axis-cylinder process and its collaterals, if it has any, end by breaking up into a brush, a plexus or a feltwork or basketwork of fibrils. The axons of different nerve-cells vary greatly in length. Some terminate within the grey matter of the brain or spinal cord not far from their origin; others run in the white tracts of the central nervous system or in the peripheral nerves for half the height of a man. All except the shortest axis-cylinder processes become clothed at a little distance from the cell-body with a protective covering, which continues to invest them (and their collaterals) throughout the rest of their course, disappearing only when they begin to break up at their terminations. An axis-cylinder process (spoken of simply as the axis-cylinder, when considered apart from the nerve-cell) constitutes, with its covering, a nerve-fibre.

An ordinary peripheral nerve like the sciatic is made up of a number of bundles of nerve-fibres. Connective tissue surrounds and separates the bundles, and also penetrates in fine septa within them and between the individual fibres, forming a framework for their support, and carrying the bloodvessels and lymphatics.

The great majority of the nerve-fibres of the sciatic consist of axis-cylinders covered by two sheaths. The axis-cylinders are processes of nerve-cells in the anterior horn of the spinal cord in the case of the motor fibres, and of nerve-cells in the spinal ganglia in the case of the sensory. The axis-cylinder is the essential conducting part of the fibre, for it is present in every nerve-fibre, running from end to end of it without break, and towards the periphery it is alone present. It is probably made up of fine longitudinal fibrils embedded in interstitial substance. Such a fibrillar structure is undoubtedly shown after treatment of the nerve-fibres with certain reagents, although it is not quite certain that it exists preformed in the living fibres. The innermost (Plate V. 1, and Fig. 231), and by far the thickest, of the sheaths is the medullary sheath, or white substance of Schwann, which is of fatty nature, and is blackened by osmic acid. It undergoes a kind of coagulation at death, loses its homogeneity, and shows a double contour. This sheath is not continuous, but is broken by constrictions of the outer sheath, called nodes of Ranvier, into numerous segments. The outer sheath, or neurilemma, is a thin, structureless envelope immediately external to the medulla. It invests the nerve-fibre, as the sarcolemma does the muscle-fibre. In each internodal segment immediately under the neurilemma lies a nucleus surrounded by a little protoplasm. Fibres with a medullary sheath such as those described are called medullated fibres. They are by far the most numerous in the cerebro-spinal nerves; but they are mixed with a few fibres which contain no white substance of Schwann, and are, therefore, called non-medullated (Plate V. 1). In these the axis-cylinder is covered only by the neurilemma. In the sympathetic system the non-medullated variety is present in greater abundance than the medullated. In the central nervous system the medullated fibres possess no neurilemma.

So far as we know, the only function of nerve-fibres is to conduct impulses from nerve-centres to peripheral organs,

or from peripheral organs to nerve-centres, or from one nerve-centre to another. And in the normal body these impulses never, or only very rarely, originate in the course of the nerve-fibres; they are set up either at their peripheral or at their central endings. By artificial stimulation, however, a nerve-impulse *may* be started at any part of a fibre, just as a telegram *may* be despatched by tapping any part of a telegraph wire, although it is usually sent from one fixed station to another.

The Nerve-impulse: its Initiation and Conduction.

What the nerve-impulse actually consists in we do not know. All we know is that a change of some kind, of which the only external token is an electrical change, passes over the nerve with a measurable velocity, and gives tidings of itself, if it is travelling along efferent fibres (that is, out from the central nervous system), by the contraction or inhibition of muscle or by secretion; if it is travelling along afferent fibres (that is, up to the central nervous system), by sensation, or by reflex muscular or glandular effects.

Whether the wave which passes along the nerve is a wave of chemical change (such, for example, as runs along a train of gunpowder when it is fired at one end), or a wave of mechanical change, a peculiar and most delicate molecular shiver, if we may so phrase it, there is no definite experimental evidence to decide, although the former is the most probable view.

That chemical changes go on in living nerve, we need not hesitate to assume; and, indeed, if the circulation through a limb of a warm-blooded animal be stopped for a short time, the nerves lose their excitability. But the metabolism appears to be very slight compared with that in muscle or gland. Even in active nerve no measurable production of carbon dioxide has ever been observed, nor, in fact, has any chemical or physical difference between the excited and the resting state ever been unequivocally made out. Neither in cold-blooded nor in mammalian nerves does there seem to be any sensible rise of temperature during stimulation.

Stimulation of Nerve.—With some differences, the same stimuli are effective for nerve as for muscle (p. 549); but *chemical stimulation* is not in general so easily obtained.

In fact, it is doubtful whether any great reliance should be placed on many of the observations hitherto made with this mode of excitation. For it has been shown that the current of rest of the nerve (p. 629), when a short-circuit is formed for it by a drop of any conducting liquid applied to a fresh cross-section (the usual method of experimenting on chemical stimulation), may of itself cause excitation (Hering).

Grützner uses equimolecular solutions for experiments on chemical stimulation — *i.e.*, solutions which contain an equal number of molecules of the substances to be tested in a given volume of water. He has found that for motor nerves the halogen salts have a stimulating power in the order of their molecular weights; *e.g.*, sodium iodide (NaI) is stronger than sodium bromide (NaBr), and sodium bromide than sodium chloride (NaCl). Sensory nerves are much less susceptible to chemical stimulation. Bile or bile salts, for example, which stimulate motor nerves, have no effect on sensory.* A sugar solution, which excites motor nerves, does not alter the rate of respiration when applied to the central end of the vagus, which, however, is excited by potassium chloride (p. 214). In non-narcotized animals reflex secretion of saliva is caused by stimulation of the central end of the lingual with sodium chloride (Wertheimer).

Mechanical stimulation has been carried to great perfection by Heidenhain, and especially by Tigerstedt. By means of an instrument invented by the latter, not only may a regular tetanus be obtained, but the strength of the stimulus (fall of a weight) can be graduated with fair accuracy within a considerable range. He found that the smallest amount of work spent on a frog's nerve which would suffice to excite it was a little less than a gramme-millimetre—that is, the work done by a gramme falling through a distance of a millimetre, or (taking an erg as equivalent to $\frac{1}{1000}$ gramme-centimetre) about 100 ergs. No doubt a great part of this is wasted, as a much smaller quantity of work done by a beam of light on the retina or by an electrical current on an isolated nerve, both of which may be supposed to act more directly on the excitable constituents, suffices to cause stimulation. Thus, the work done by the minimal, *natural or specific*, stimulus for the retina in the form of green light may be as little as $\frac{1}{10^8}$ erg (S. P. Langley), or only one-ten-thousand-millionth part of the minimum work necessary for mechanical stimulation. Again, with electrical stimulation (closure of a voltaic current, or condenser discharges) it has been shown that an amount of work equal to $\frac{1}{10^4}$ erg may be enough to cause excitation of a frog's nerve.

* It would be more correct to say that the sensory *mechanisms* are not affected by these chemical stimuli than that the sensory *nerves* are not affected. For there is no proof that the absence of response is due to inexcitability of the nerve-fibres and not to inexcitability of the centres connected with them.

This is ten thousand times as great as the minimal luminous stimulus, but a million times less than the minimal mechanical stimulus.

The laws of *electrical stimulation* for nerve are essentially the same as those we have already discussed for muscle (p. 553). The voltaic current stimulates a nerve, as it does a muscle, at closure and opening. During the flow of the current, so long as its intensity remains constant, there is, as a rule, no excitation, or at least none which is propagated along the nerve, so that the muscles supplied by it remain uncontracted. But under certain conditions—for example, when the nerve is more excitable than usual (as is the case with nerves taken from frogs which have been long kept in the cold) —a closing tetanus may be seen while the current continues to pass through the nerve, and an opening tetanus after it has ceased to flow, just as when the current is led directly through the muscle. Sensory nerve-fibres, too, are stimulated by a voltaic current during the whole time of flow. Induction shocks are relatively more powerful stimuli for nerve than the make or break of a voltaic current. The opposite, as we have seen, is true of muscle; and, upon the whole, we may say that muscle is more sluggish in its response to stimuli, and is excited less easily by very brief currents, than nerve is. An apparent illustration of this difference is the fact that the nervous excitation has no measurable latent period, while muscular excitation has. But it is quite possible that, if the conditions of experiment were as favourable in nerve as in muscle, a sensible latent period might be found here too.

In nerve as in muscle, strength of stimulus and intensity of response correspond within a fairly wide range, when we take the height of the muscular contraction or the amount of the negative variation (p. 630) as the measure of the nervous excitation. Superposition of stimuli, superposition of contractions, and complete tetanus, are caused by stimulating a muscle through its nerve, just as by stimulating the muscle itself (p. 571).

The **excitability** of nerve, as measured by the muscular response to stimulation, is increased, for induction shocks or voltaic currents of short duration, by rise of temperature up to about 30° C., and diminished by fall of temperature. It has been suggested that this increase of excitability is only apparent, and due to the strengthening of the current by diminution of the resistance, since the resistance of all animal tissues, like that of electrolytic conductors in general, diminishes as the temperature rises (Gotch). Cooling of the nerve, even to 5° C., increases the excitability for currents of long duration (several hundredths of a second). The **conductivity** for the nervous impulse—that is, the power of a portion of the nerve to conduct an impulse set up elsewhere —is undoubtedly increased by heat and diminished by cold.

Drying of a nerve at first increases its excitability; and the same is true of separation of a nerve from its centre. In the latter case the increase of irritability begins at the proximal end of the nerve, and travels towards the periphery. As time goes on, the excitability diminishes, and ultimately disappears in the same order (Ritter-Valli Law). At a certain stage it may be found that a given stimulus causes a smaller and smaller contraction the farther down the nerve—that is, the nearer to the muscle—it is applied. On this was based the now abandoned 'avalanche theory,' according to which the impulse continually unlocked new energy as it passed along the nerve, and so gathered strength in its course like an avalanche. It is now known that no material change takes place in the intensity of the excitation while it is being propagated along a normal uninjured nerve. For instance, experiments on the phrenic nerve, in its natural position, and with all its connections intact, have shown that with a given strength of stimulus the amount of contraction of the diaphragm is the same whether the nerve be excited in the upper, middle or lower portion of its course. In the above experiment on the isolated, and therefore injured nerve, the contraction varies in height with the distance of the point of stimulation from the muscle, not because the excitation grows as it travels, but because it is already greater at the moment when it sets out from a point near the central end of the nerve than at the moment when it sets out from a point near the muscle.

Electrotonus.—Although the constant current does not, unless it is very strong or the nerve very irritable, cause stimulation during its passage, it modifies profoundly the excitability and conductivity of the nerve. In the neighbourhood of the kathode the excitability is increased (condition of katelectrotonus), while around the anode it is diminished (anelectrotonous). Immediately after the opening of the current these relations are for a brief time reversed, the excitability of the post-kathodic area (area which was at the kathode during the flow) being diminished, and that of the post-anodic increased. In the intrapolar area there is one point the

excitability of which is not altered. This indifferent point, as it is called, shifts its position when the intensity of the current is varied.

These statements have been made on the strength of experiments in which the height of the muscular contraction was taken as the index solely of the *excitability* of the nerve at any given point. But it is now known, partly from observations on muscular contraction in which changes of excitability of the nerve were eliminated by proper choice of the point of stimulation, and partly from observations on the action stream (p. 642), that very striking alterations of *conductivity* are also produced by the constant current, which even outlast its flow. For all currents except the weakest the conductivity at the kathode and in its immediate neighbourhood is diminished, and with currents still only moderately strong ($\frac{1}{100000}$ ampère, *e.g.*) the block deepens into utter impassability. The conductivity at the anode is, during all this stage, but little affected, and is at any rate much higher than at the kathode, so that at the time of full kathodic block the nerve-impulse still freely passes through the region around the positive pole. With still stronger currents the conduc-

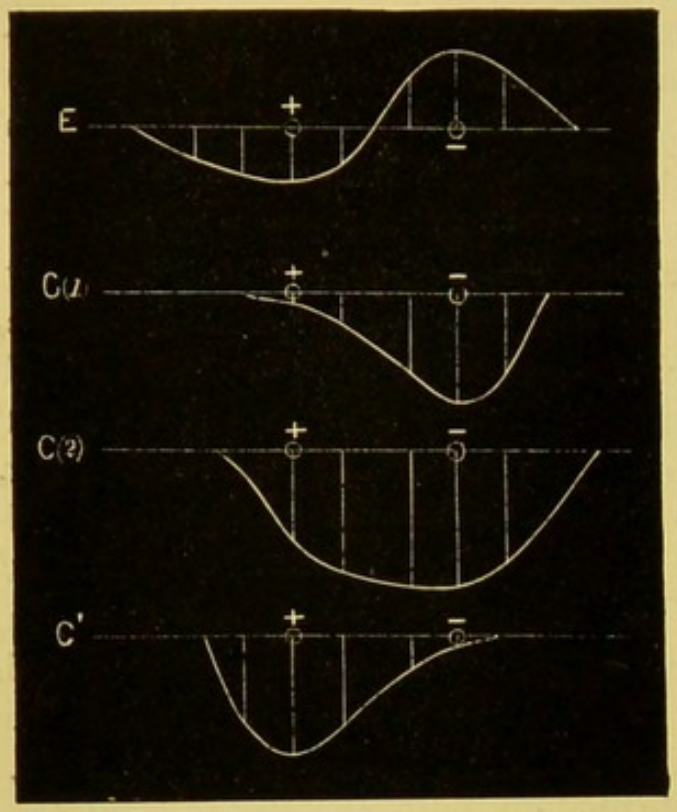


FIG. 183.—DIAGRAM OF CHANGES OF EXCITABILITY AND CONDUCTIVITY PRODUCED IN A NERVE BY A VOLTAIC CURRENT.

E, changes of excitability during the flow of the current, according to Pflüger. The ordinates drawn from the abscissa axis to cut the curve represent the amount of the change. C(1), changes of conductivity during the flow of a moderately strong current. Conductivity greatly reduced around kathode; little affected at anode. C(2), changes of conductivity during flow of a very strong current. Conductivity reduced both in anodic and kathodic regions, but less in the former. C', changes of conductivity just after opening a moderately strong current. Conductivity greatly reduced in region which was formerly anodic; little affected in region formerly kathodic.

tivity here, too, begins to diminish, until at last the anode is also blocked; but this is to be looked upon as merely an extension of the defect of conductivity which has been creeping along the intrapolar area from the kathode. After the opening of the current, the relation between kathodic and anodic conductivity is reversed, for now the post-kathodic region conducts the nerve-impulse relatively better than the post-anodic.

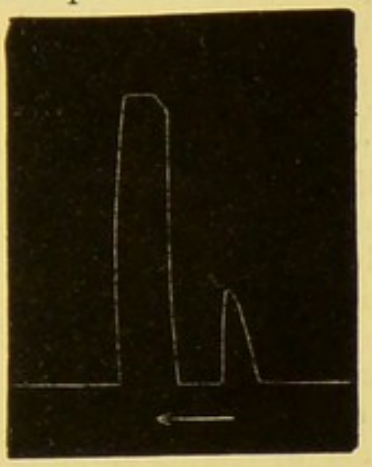


FIG. 184.—KATELECTROTONUS.

Weak tetanus of muscle (the right-hand elevation), greatly intensified in katelectrotonus of the motor nerve (the left-hand elevation).

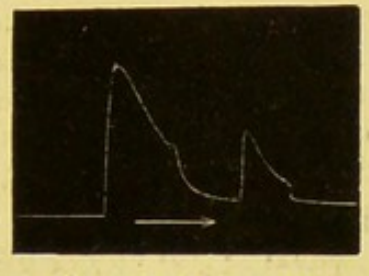


FIG. 185.—ANELECTROTONUS.

Strong tetanus of muscle (left-hand elevation), lessened in strength by an-electrotonic condition of the motor nerve (right-hand elevation).

The above facts serve to explain the manner in which the effects of stimulation of a nerve with the constant current vary with the strength and direction of the stream. These effects, so far as the contraction of the muscles supplied by the nerve is concerned, have been formulated in what has been somewhat loosely termed the **law of contraction.** In this formula the direction of the current in the nerve is commonly distinguished by a thoroughly bad but now ingrained phraseology, as *ascending* when the anode is next the muscle, and *descending* when the kathode is next the muscle.

Law of Contraction.

Current.	Ascending.		Descending.	
	M.	B.	M.	B.
Weak -	C	—	C	—
Medium -	C	C	C	C
Strong -	—	C	C	—

Here M means 'make,' B, 'break,' of the current; C means 'contraction follows.'

The explanation generally given of the facts summed up in the 'law of contraction' is as follows: Wherever there is an increase of excitability sufficiently rapid and sufficiently large, stimulation is supposed to take place; where there is a fall of excitability, stimulation does not occur. Accordingly, at closure the kathode stimulates—the anode does not; while at opening, the anode, at which the depressed excitability jumps up to normal or more, is the stimulating pole; the kathode, at which it declines to normal or under it, is inactive.

With a *weak current*, (1) contraction only occurs at make, and (2) the direction of the current is indifferent. The explanation of the first fact is that the make is a stronger stimulus than the break, and when the current is weak enough the break is less than a minimal stimulus. No sensible change of conductivity is caused by weak currents, which suffices to explain (2).

With a '*medium*' *current*, contraction occurs at make and break with both directions. Here the break excitation is effective as well as the make. With anode next the muscle (ascending current), there is of course nothing to prevent the opening excitation, which starts at the anode, from passing down the nerve and causing contraction; and since there is no block around the anode or in the intrapolar region with 'medium' currents, there is nothing to keep the closing (kathodic) excitation from reaching the muscle too. With the kathode next the muscle (descending current), the closing excitation, which starts from the kathode, has no region of diminished conductivity to pass through, nor has the opening (anodic) excitation, for the kathodic block, caused by moderately strong currents, is removed as soon as the current is broken.

With 'strong' currents there are only two cases of contraction out of the four, just as with 'weak,' but for very different reasons. There is a break-contraction with ascending, and a make-contraction with descending current. With ascending current the anode is next the muscle, and the break-excitation starting there has nothing to hinder its course. The make-excitation, although as strong or stronger, has to pass through the whole intrapolar region and over the anode, and here the conductivity is depressed and the nerve-impulse blocked. With descending current the kathode is next the muscle, and there is no hindrance to the passage of the make excitation. The break-excitation, however, has to traverse the intrapolar region, and the anodic end of this area has a smaller conductivity immediately after opening than during the flow, while the kathodic end does not at once, after a strong current, become passable. The break-excitation, accordingly, cannot get through to the muscle.

In all these cases of complete or partial block, during or after the flow of a constant current, the progress of the nerve-impulse, its

gradual weakening, and final extinction can be very well shown by means of the action stream (p. 630).

The above formula can only be verified upon isolated nerves, and, even for these, exceptional results are apt to be obtained as soon as the nerves begin to die.

A formula similar to the law of contraction has been shown to hold for the inhibitory fibres of the vagus (Donders), 'inhibition' being substituted for 'contraction.' There is also some evidence that a similar law obtains for sensory nerves.

The Law of Contraction for Nerves 'in Situ.'—When a nerve is stimulated without previous isolation—in the human body, for instance, through electrodes laid on the skin—the current will not enter and leave it through definite small portions of its sheath, nor will it be possible to make the lines of flow nearly parallel to each other and to the long axis of the nerve, as is the case in a slender strip of tissue when there is a considerable distance between the electrodes.

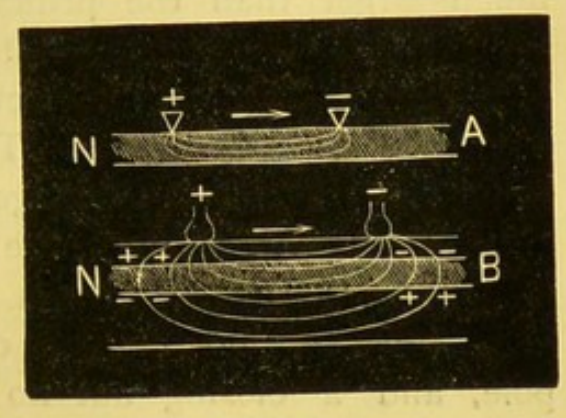


FIG. 186.—DIAGRAM OF LINES OF FLOW OF A CURRENT PASSING THROUGH A NERVE.

A, an isolated nerve; B, a nerve *in situ*. Secondary anodes (+) are formed where the current re-enters the nerve below the negative electrode after passing through the tissues in which it is embedded, and secondary kathodes (−) where the current passes out of the nerve into the surrounding tissues below the positive electrode.

On the contrary, when, as is usually the case in electro-therapeutical treatment, a single electrode—say, the positive—is placed over the position of the nerve, and the other at a distance on some convenient part of the body, the current will enter the nerve by a broad fan of stream-lines cutting it more or less obliquely, and pass out again into the surrounding tissues; so that both an anode (surface of entrance) and a kathode (still larger surface of exit) will correspond to the single positive pole. Similarly, the single negative electrode will correspond to an anodic surface where the now narrowing sheaf of lines of flow enters the nerve, and a smaller kathodic surface, where they emerge. Even if the two electrodes were on the course of the nerve, the stream-lines would still cut it in such a way that each electrode would correspond both to anode and kathode (Fig. 186).

It is impossible under these circumstances to take account of the *direction* of a current in a nerve, or to connect *direction* with any specific effect. When we place one of the electrodes over the nerve and the other at a distance, the law of contraction only appears in a disguised form; for since a kathode and an anode exist at each pole, there is, with a current of sufficient strength ('strong current'), excitation at each both at make and break. The negative make-contraction is, however, stronger than the positive, for the excitation corresponding to the latter arises at the secondary kathodic surface, where the sheaf of current-lines spreading from the positive electrode passes out of the nerve. Now, this is much larger than the primary kathodic surface, through which the narrow wedge of stream-lines passes to reach the negative electrode, and the current density at the latter is accordingly much greater. The positive break-contraction is, for a similar reason, stronger than the negative.

With a 'weak' current, the only contraction is a closing one at the kathode; with a 'medium' current there are both opening and closing contractions at the positive pole, and a closing but no opening contraction at the negative.

The **conductivity of the nerve**, as we have seen in various examples, is not necessarily altered in the same sense as the excitability. In the neighbourhood of the kathode it is easier to cause excitation than in the normal nerve (increased excitability), but it is less easy for an excitation set up elsewhere to pass through (diminished conductivity). Change of temperature seems also, for stimuli of not very short duration, to act in the opposite way on these two properties of nerve. Carbon dioxide appears to depress the excitability without affecting the conductivity, and alcohol to have the contrary effect (Gad and Sawyer). Munk found that in a dying sciatic nerve certain points may be quite inexcitable to the strongest stimuli, while weak stimulation of points lying nearer the central end may cause muscular contraction. These facts seem to show that the process by which the nerve-impulse is propagated is not the same as that by which it is originated and therefore is not

merely an excitation of each nerve-element by the one next it, as some have supposed.

Double Conduction.—When a nerve (or muscle) is stimulated artificially, the excitation runs along it in both directions from the point of stimulation; so that nerve-fibres which in the intact body are afferent *can* conduct impulses towards the periphery, and efferent fibres can conduct impulses away from the periphery. In the normal state, however, double conduction must seldom occur, for efferent fibres are connected centrally, and afferent fibres peripherally, with the structures in which their natural stimuli arise. In general, too, an impulse, if it did pass centrifugally along an afferent fibre, would not give any token of its existence, for the peripheral organ would not be able to respond to it; and we have no reason to believe that the central mechanisms connected with afferent fibres are better fitted to answer such foreign and unaccustomed calls as impulses reaching them along normally efferent nerves. There is some evidence that muscular excitation is not carried over to the motor nerve-fibres; in other words, the wave of action flows from the nerve to the muscle, but cannot be got to flow backwards. Whether such an organ as the retina can be excited by impulses reaching it 'the wrong way' along the optic nerve we do not know, although the point might possibly be decided by means of the retinal currents to be mentioned later on (p. 647). We shall see that a nutritive influence is exerted over the afferent fibres of the spinal nerves by the ganglion cells of the posterior root ganglia (p. 607), an influence which must spread along these fibres in the opposite direction to that of the normal excitation; but from this we cannot deduce anything as to the behaviour of ordinary nerve-impulses.

The best proofs of double conduction in nerves, with artificial stimulation, are: (1) The propagation of the negative variation or action current in both directions. This holds for sensory as well as for motor fibres, as du Bois-Reymond showed on the posterior roots of the spinal nerves of the frog and the optic nerves of fishes. (2) Stimulation of the posterior free end of the electrical nerve of Malap-

terurus (p. 649) causes discharge of the electric organ, although the nerve-impulse travels normally in the opposite direction. (3) If the lower end of the frog's sartorius is split into two, gentle stimulation of one of the tongues causes contraction of individual fibres in the other. This is supposed to be due to conduction of the nerve-impulse up a twig of a nerve-fibre distributed to the one tongue, and down another twig of the same fibre going to the other tongue. A similar experiment can be done on the gracilis of the frog. This muscle is divided by a tendinous inscription into two parts, each supplied by a branch of a nerve which divides after entering the muscle. Stimulation of either twig is followed by contraction of both parts of the muscle (Kühne).

Bert's much-quoted experiment on the rat is valueless as a proof of double conduction. He caused union of the point of the tail with the tissues of the back, then divided the tail at the root, and found that stimulation of what was now the distal end caused pain. From this he concluded that the sensory fibres of the 'transposed' tail conducted in the direction from root to tip. But the conclusion is not warranted, for sensation disappeared in the tail after the section, and did not return till some months later, when the nerve-fibres, after degenerating, would have been replaced by new sensory fibres growing down from the dorsal nerves (Ranvier). For a similar reason the so-called union of the peripheral end of the cut hypoglossal nerve (motor) with the central end of the cut lingual (sensory) proves nothing as to double conduction, nor as to the possibility of motor nerves taking on a sensory function. For while sensation is after a time restored in the affected portion of the tongue, this is due to the growth of sensory fibres from the central stump of the lingual down through the degenerated hypoglossal and not to the conduction upwards of sensory impulses by the motor fibres of the latter.

Every fibre of a nerve is physiologically isolated from the rest, so that an impulse set up in a fibre runs its course within it, and does not pass laterally into others (**law of isolated conduction**). In connection with this physiological fact there is the anatomical fact that nerve-fibres do not branch in the trunk of a peripheral nerve. It has, however, been shown recently that bifurcation of nerve-fibres may occur in the spinal cord (Sherrington). The axis-cylinder of a peripheral nerve-fibre only begins to branch where isolation of function is no longer required, as within a muscle. The experiment of Kühne on double con-

duction, mentioned above, seems to show that an excitation set up in one twig or one fibril of an axis cylinder which has branched can spread to the rest.

Velocity of the Nerve-impulse.—We have said that the nerve-impulse travels with a measurable velocity. It is now time to describe how this has been ascertained (p. 624). For *motor fibres* the simplest method is to stimulate a nerve successively at two points, one near its muscle, the other as far away from it as possible, and to record the contractions on a rapidly-moving surface (pendulum or spring myograph) (p. 561). The apparent latent period of the curve corresponding to the nearer point will be less than that of the curve corresponding to the point which is more remote, by the time which the impulse takes to pass between the two points. The distance between these points being measured, the velocity is known. Helmholtz found the velocity for frog's nerves at the ordinary temperature of the air to be a little under, and for human nerves, cooled so as to approximate to the ordinary temperature, a little over 30 metres per second. For observations on man the contraction curves of the flexors of one of the fingers or of the thumb may be recorded, first with stimulation of the brachial plexus at the axilla, and then with stimulation of the median or ulnar nerve at the elbow. Probably at the same temperature there is little difference in the rate of transmission in the nerves of warm-blooded and cold-blooded animals, but temperature has an enormous influence.

By cooling a frog's nerve Helmholtz reduced the rate to $\frac{1}{10}$ of its value at the ordinary temperature, and in the human arm it may vary from 30 to 90 metres per second, according to the temperature, 50 metres being about the normal rate. This is greater than the speed of the fastest train in the world.

The passage of a voltaic current through an isolated nerve also affects the velocity of the nerve-impulse. When the current is weak, the velocity is increased in the neighbourhood of the kathode, but diminished near the anode; when it is stronger, the velocity is diminished, not only around both poles, but in the whole intrapolar area. This agrees with what we have already seen as to the effect of the constant current on the conductivity of nerve.

The velocity with which the negative variation is propagated (p. 634) is the same as that of the nerve-impulse.

In *sensory nerves* there is no reason to believe that the velocity of the nerve-impulse differs from that in motor nerves, but experiments really free from objection are as yet wanting.

The usual method is to stimulate the skin first at a point distant from the brain, and then at a much nearer point. The person experimented on, as soon as he feels the stimulation, makes a signal, say, by closing or opening with the hand a current connected with an electric time-marker, writing on a moving surface. There is, of course, a measurable interval between the excitation and the signal, and this being in general longer the more remote the point of stimulation is from the brain, it is assumed that the excess represents the time taken by the nerve-impulse to pass over a length of sensory nerve equal to the difference in the length of the path. But there is this difficulty, that the propagation of the impulse from the point of stimulation to the brain is only one link in the chain of events of which the signal marks the end. The impulse has first to be transformed into a sensation, and then the will has to be called into action, and an impulse sent down the motor nerves to the hand. And while the time taken by the excitation in travelling up and down the peripheral nerve-fibres is, perhaps, fairly constant, the time spent in the intermediate psychical processes is very variable.

Chemistry of Nerve.—Our knowledge of this subject is scanty in the extreme; and most of what we do know has been obtained from analyses, not of the peripheral nerves, but of the white matter of the central nervous system.

Proteids are present, especially in the axis cylinder. They include a globulin and a nucleo-proteid.

Substances soluble in ether include *cholesterin*, *lecithin*, and *cerebrin*. The cholesterin and lecithin, at least, belong chiefly to the medullary sheath, which further contains a kind of network of a peculiar resistant substance called neurokeratin (Kühne).

The *neurilemma* consists of substances insoluble in dilute sodium hydrate.

Gelatin is obtained from the connective tissue which binds the nerve-fibres together. There may also be ordinary fat in the meshes of the epineurium connecting the bundles. Small quantities of xanthin, hypoxanthin, and other extractives, can also be obtained from nerve.

The composition of the white matter of the brain is as follows:

Water		68 per cent.	
Solids	Proteids	8	32 per cent.
	Cholesterin	16	
	Lecithin	3	
	Cerebrin	3	
	Salts	0·5	
	Other substances	1·5	

An analysis of the sciatic nerve of man gave in round numbers :

Water			66 per cent.
Solids	Cerebrin, lecithin, cholesterin, and fatty acids	17	34 per cent.
	Proteids and glutin	16	
	Other substances	1	

The only difference between living and dead nerve which has been made out with any degree of certainty is that the former is neutral or faintly alkaline, and the latter acid, in reaction.

Degeneration and Regeneration of Nerve.—Nerve-fibres are 'bound in the bundle of life' with the nerve-cells from which their axis-cylinders arise; the connection between cell and axon once severed, the nerve-fibre dies inevitably. We shall see later on that changes also occur in the nerve-cell whose axon has been divided from it, although they are of a different nature (rather a slow atrophy than an acute degeneration), and do not necessarily lead to the absolute destruction of the cell. Thus, we must regard the neuron not only as a morphological unit, a single cell from nucleus to remotest end-brush, but also as a functional and nutritive unit, the fortune of any portion of which is not indifferent to the rest. The acute changes that occur in severed nerve-fibres are most conveniently studied in the peripheral nerves, although

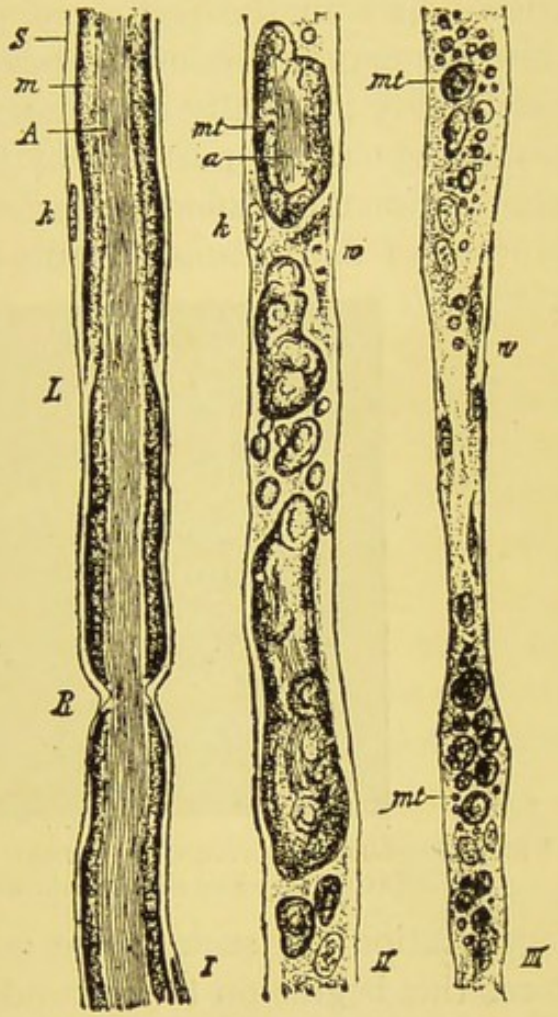


FIG. 187.—DEGENERATION OF NERVE-FIBRES AFTER SECTION (BARKER, after THOMA).

I, normal fibre; II, degenerating fibre; III, further stage of degeneration; S, neurilemma; *m*, medullary sheath; A, axis-cylinder; L, incisure; R, node; *mt*, drops of myelin; *a*, remains of axis-cylinder; *w*, proliferating cells of neurilemma.

essentially similar phenomena take place also in the fibres of the central nervous system.

A spinal nerve is composed of efferent fibres whose cells of origin are in the grey matter of the anterior horn, and afferent fibres whose cells of origin are in the posterior root ganglion. When such a nerve is cut below the junction of its roots, muscular paralysis and impairment of sensation at once follow in the region supplied by the nerve; but for a time the nerve remains excitable to direct stimulation. The excitability gradually diminishes, and in a few days is completely gone. If portions of the nerve distal to the lesion are examined at different periods after section, a remarkable process of *degeneration* (commonly spoken of as Wallerian

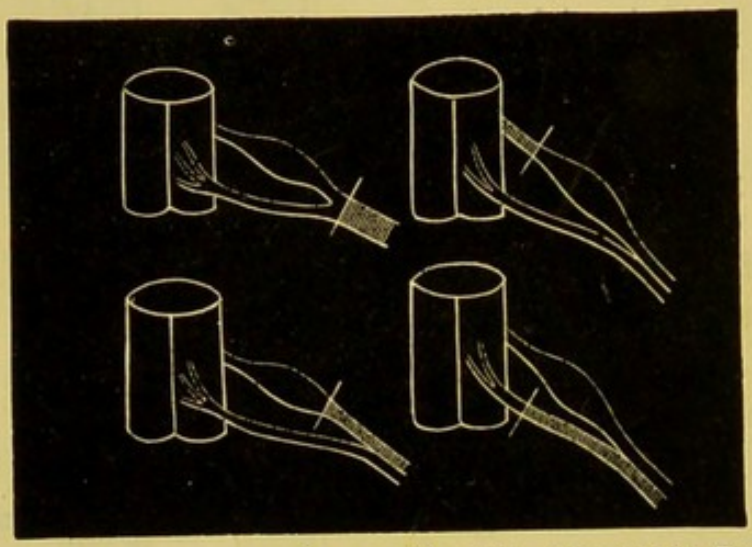


FIG. 188.—DEGENERATION OF SPINAL NERVES AND THEIR ROOTS AFTER SECTION.—The shading shows the degenerated portions.

degeneration) is seen to be going on. In the medullated fibres this begins on the second or third day with a swelling of the axis-cylinder, which breaks up into detached pieces (fragmentation). The medullary sheath also separates into clumps and droplets of myelin. The nuclei under the neurilemma proliferate and insinuate themselves between the fragments of the medullary sheath and axis-cylinder, which ultimately disappear, leaving the nerve-fibre represented only by a kind of mummy of connective tissue, in which the neurilemma with its abnormally numerous nuclei can still be recognised. This process goes on simultaneously along the whole nerve, from the cut end to the periphery, and more rapidly in warm than in cold-blooded animals. In a

mammal it is far advanced in a fortnight, although the last remnants of the myelin may not be absorbed for months.

In the degenerated nerve the substances soluble in ether are relatively increased, owing in part to fatty degeneration of the axis-cylinder. The percentage of phosphorus is markedly diminished (Mott and Barratt). In the portion of the nerve-fibre still connected with the nerve-cell the degeneration only extends as far back as the next node of Ranvier, and seems to be due to the direct effect of the injury. In non-medullated fibres, such as the fibres arising from the cells of the superior cervical ganglion (Tuckett) the degeneration is confined to the axis-cylinders. It begins in about twenty-four hours after section, and the loss of excitability and conductivity is complete by the fortieth hour.

It follows from what has been said as to the position of the cells of origin of the root fibres of the spinal nerves that section of the anterior root causes degeneration on the peripheral, but not on the central side of the lesion.* Only the anterior root fibres in the mixed nerve degenerate.

Section of the posterior root above the ganglion causes degeneration of the central stump, but not of the portion still connected with the ganglion, nor of the posterior root fibres below the ganglion or in the mixed nerve.

Section of the posterior root below the ganglion causes degeneration of the fibres of the root below the section and in the mixed nerve, but not above it.

Degeneration of the nerve is followed, if its divided ends are not kept artificially apart, by a process of regeneration, already distinct under favourable conditions in from three to four weeks after the section, and indeed in some cases commencing as early as the second week. This consists in the outgrowth of new axis cylinders, in the form of fine fibres, from the ends of the divided axis cylinders of the central stump of the nerve. These push their way into and along the degenerated fibres, ultimately acquire a medullary

* A few fibres in the peripheral stump of the anterior root do not degenerate, and a few fibres in the central stump do. These are the 'recurrent fibres,' whose course is described on p. 699.

sheath, and develop into complete nerve-fibres, restoring first sensation, and later on voluntary motion, to the paralyzed part. The process needs several months for its completion, even in warm-blooded animals. It takes place under the influence of the nucleated portion of the neuron (the cell-body), and never occurs if the peripheral and central portions of the nerve are permanently separated by a substance through which the new axis-cylinders cannot grow or by a gap too wide for them to bridge over. When the cut ends of the nerve are carefully sutured together, the conditions for complete and speedy regeneration are rendered more favourable, a fact which finds its application in the surgical treatment of injured nerves.

It is not as yet well understood how the regenerating fibres are directed in their growth, so that they join their appropriate end-organs without mistake. Doubtless the old nerve-sheaths serve to some extent as guides by offering to the new axones a path of least resistance. That this is the case is clearly shown by the results of cross-suturing such nerves as the median and ulnar, *i.e.*, of uniting the central end of the one with the peripheral end of the other. Howell and Huber found that after this operation in the dog, both co-ordinated voluntary motion and sensation returned in large measure in the parts supplied by the nerves. Here the motor fibres of the median nerve must of course have made connection with muscles previously supplied by the ulnar, being guided to them along the nerve-sheaths of the latter. That there is something more, however, seems evident from the experiments of Langley on regeneration of the cervical sympathetic in the cat after section below the superior cervical ganglion. The nerve contains fibres of various functions which reach it from the upper thoracic nerves. The anterior roots of the first and third thoracic nerves supply the cervical sympathetic mainly with fibres which end in the ganglion around cells that give off dilator fibres for the pupil. The fibres connected with the cells in the ganglion which send vaso-motor fibres to the vessels of the ear are for the most part contained in the anterior roots of the second and fifth thoracic nerves; and the fibres connected with the cells that give origin to the pilomotor fibres for the hairs of the face and neck in the anterior roots of the fourth to the seventh. Stimulation of any one of the upper thoracic roots accordingly causes a specific effect, which, according to Langley, is in general the same after regeneration as before section of the cervical sympathetic. We must assume, therefore, that each regenerating fibre seeks out either the ganglion cell with which it was originally connected, or one belonging to the same class. But under certain conditions these pre-ganglionic nerve-fibres can form connections with nerve-cells of a different class, *e.g.*, pupillo-

dilators with cells whose axons end in the erector muscles of the hairs. Further, after section of the sympathetic above the superior cervical ganglion, the post-ganglionic nerve fibres (*i.e.*, the fibres coming off from the cells of the ganglion) may also, if the opportunity be favourable during regeneration, exchange their old end-organs for new ones; pilomotor fibres, for instance, finding their way into the iris and becoming pupillo-dilators.

It is a remarkable and as yet unexplained fact that regeneration of the fibres of the central nervous system either does not in general occur, or is exceedingly difficult to realize. It has, however, been shown that regeneration of the fibres which proceed from the cells of the spinal ganglia along the posterior roots into the cord may take place after the roots have been cut.

Experimental section or, in man, traumatic division or compression of a nerve leads not only to its degeneration, but ultimately, if regeneration of the nerve does not take place, to degeneration of the muscles supplied by it as well. The muscle-fibres dwindle to a quarter of their normal diameter; the stripes disappear; the longitudinal fibrillation fades out; and at length only hyaline moulds of the fibres are left, filled and separated by fatty granules and globules, and surrounded by engorged capillaries. Amidst the general decay, the muscular fibres of the terminal 'spindles,' with which the afferent nerves of muscles are connected, alone remain unchanged (Sherrington). Certain diseases of the cord which interfere with the cells of the anterior horn cause degeneration of motor nerves, and ultimately of muscles.

Muscles whose motor nerves have been separated from their trophic centres show, when a certain stage in degeneration has been reached, a peculiar behaviour to electrical stimulation, called the '**reaction of degeneration.**' To the constant current the muscles are more excitable, and the contraction slower and more prolonged than normal. When a current, either constant or induced, is passed through a normal muscle, the muscular fibres may be stimulated either directly or indirectly through the intra-muscular nerves. Under ordinary conditions the nerves respond more readily than the muscular fibres, especially to momentary stimuli like induction shocks, and therefore the so-called direct stimulation of uncurarized muscle is as a rule an indirect stimula-

tion. When the muscle is curarized and the nerves thus eliminated the excitability to induced currents is found to be diminished. The same is the case in a muscle which exhibits the reaction of degeneration after section of its motor nerve, only the loss of excitability to induced currents is greater, and may even be complete. The closing anodic contraction is stronger than the closing kathodic — the opposite of the ordinary law. The nerves are inexcitable either to constant or induced currents. The reaction of degeneration is only obtained from paralyzed muscles when the paralyzing lesion is situated in the cells of the anterior horn from which the motor nerves take origin, or below that level. Accordingly, it is sometimes of use in localizing the position of a lesion. For instance, a group of muscles might be paralyzed by a lesion in the grey matter of the brain or in the nerve-fibres connecting this with the grey matter of the anterior horn of the cord, or in the grey matter of the anterior horn itself, or in the peripheral nerve-fibres leading from this to the muscles. In the first two cases the reaction of degeneration would be absent, although the muscles, if the lesion was of long standing, would be atrophied to some extent; in the last two there would be acute atrophy of the muscles and the reaction of degeneration would be obtained.

Trophic Nerves. — The fact that the proper nutrition of nerve-fibres is dependent on their connection with nerve-cells has been by some writers generalized into the doctrine that all tissues are provided with 'trophic' nerves, which, apart from any influence on functional activity, regulate the nutrition of the organs they supply. But the evidence for this view, when weighed in the balance, is found wanting; and it may be said that up to the present *no unequivocal proof, experimental or clinical, has ever been given of the existence of specific trophic nerves.*

It is true that division of the trigeminus nerve within the skull is sometimes followed by cloudiness of the cornea, going on to ulceration, and ultimately inflammation and destruction of the eyeball. Ulcers also form on the lips and on the mucous membrane of the mouth and gums; and the nasal mucous membrane on the side corresponding to the

divided nerve becomes inflamed. But in this case the sensibility of the eye is lost, and reflex closure of the eyelids ceases to prevent the entrance of foreign bodies. The animal is no longer aware of the contact of particles of dust or bits of straw or accumulated secretion with the conjunctiva, and makes no effort to remove them. The lips, being also without sensation, are hurt by the teeth, particularly as the muscles of mastication on the side of the divided nerve are paralyzed, and decomposed food, collecting in the mouth, and inhaled dust in the nose, will tend still further to irritate the mucous membranes. There is thus no more need to assume the loss of unknown trophic influences in order to explain the occurrence of the ulcerative changes than there is to explain the production of ordinary bed-sores, bunions or corns on parts peculiarly liable to pressure. And, as a matter of fact, if the eye be artificially protected, after section of the trigeminal nerve, the ophthalmia either does not occur or is much delayed.

In man, too, a case has been recorded in which both the fifth and the third nerves were paralyzed. The eye was still shielded by the contraction of the orbicularis oculi supplied by the seventh nerve, as well as by the drooping of the upper eyelid that accompanies paralysis of the third. It remained perfectly sound for many months, till at length the tumour at the base of the brain which had affected the other nerves involved the seventh too. The eye was now no longer completely closed; inflammation came on, and vision was soon permanently lost (Shaw). In another case a patient lived for seven years with complete paralysis of the fifth nerve, yet the eye remained free from disease and sight was unimpaired (Gowers).

The so-called 'trophic' effects following division of both vagi we have already discussed (p. 221) so far as they are concerned with the respiratory system. The degenerative changes sometimes seen in the heart are perhaps due to its being overworked in the absence of nervous restraint on its functional activity. The nutritive alterations in muscles and salivary glands after section of motor and secretory nerves seem to depend in part on functional and vaso-motor

changes. In the paralyzed muscles nutrition is not only interfered with in consequence of their inactivity, as would be the case even if the paralysis were due to a lesion above the level of the anterior cornual cells, but the already poorly nourished fibres are continually pressed upon by the capillaries, which are dilated owing to the division of the vaso-motor nerves. The degeneration must also be in part ascribed to the loss of a tonic influence exerted on the muscles by the motor cells of the spinal cord, through the ordinary motor nerves (p. 713).

Section of the cervical sympathetic in young rabbits and dogs is said to increase the growth of the ear and of the hair on the same side; but it is impossible to separate these consequences from the vaso-motor paralysis; and the same is true of the hypertrophy following section of the vaso-motor nerves of the cock's comb and of the nerves of bones. The statement has been made that on section of the superior laryngeal nerve in the horse the laryngeal muscles on the corresponding side undergo rapid atrophy. Since the nerve in this animal is destitute of motor fibres this seemed to indicate either that the nerve contains efferent 'trophic' fibres for the muscles, or that the activity of its afferent fibres has a profound influence on their nutrition. But by means of the laryngoscope it has been shown that after section of the superior laryngeal the vocal cord on the side of the section is at once rendered motionless, and remains so. The atrophy of the muscles is therefore due to their inaction in the absence of the sensory impulses by which the centre controlling them is normally roused to activity. And Mott and Sherrington have found that, although section of the posterior roots in monkeys is followed after a time (three weeks to three months) by ulceration over certain portions of the foot, no corresponding lesions occur in the hand. They believe, therefore, that the lesions are not due to the withdrawal of a reflex trophic tone, but are accidental injuries in positions specially exposed to mechanical or microbic insults.

Omitting the group of 'trophic' nerves, and the even more problematical 'thermogenic' fibres (which some have

supposed to preside over the production of heat, and therefore to assist in the regulation of the temperature of the body, but of whose existence as distinct and specific nerve-fibres with no other function there is not the slightest proof), peripheral nerves may be classified as follows :

- Centripetal or afferent fibres
  - 1. Nerves of special sensation
    - Smell.
    - Taste.
    - Hearing.
    - Sight.
  - 2. Nerves of general sensation
    - Tactile sensation (perhaps including the nerves of muscular sense).
    - Temperature.
    - Pain.
  - 3.* Possibly nerves other than those included under 1 and 2, concerned in reflex changes in
    - Calibre of small arteries (pressor, depressor).
    - Action of heart.
    - Visceral movements.
    - Respiratory movements.
    - Glandular secretion.
    - Ordinary skeletal muscles.
- Centrifugal or efferent fibres
  - 1. Motor nerves for
    - Skeletal muscles.
    - Visceral ,,
    - Vascular ,,
      - Vaso-constrictor.
      - Cardio-augmentor.
    - Erector muscles of hairs (pilo-motor fibres).
  - 2. Inhibitory nerves for
    - Visceral muscles.
    - Vascular ,,
      - Vaso-dilator.
      - Cardio-inhibitory.
  - 3. Secretory nerves.

* It is not known whether the afferent portion of a reflex arc is *always* composed of fibres included in the first two categories, although undoubtedly in some cases it is.

PRACTICAL EXERCISES ON CHAPTERS IX. AND X.

1. **Difference of Make and Break Shocks from an Induction Machine.**—Connect a Daniell or other cell B (p. 173) with the two upper binding-screws of the primary coil P, and interpose a spring key K in the circuit. Connect a pair of electrodes with the binding-screws of the secondary coil (Fig. 189).

Electrodes can be very simply made by pushing copper wires through two glass tubes, filling the ends of the tubes with sealing-wax, and binding them together with waxed thread. The projecting points may be filed, and the nerve laid directly on them, or they may be tipped with small pieces of platinum wire soldered on.

(*a*) Push the secondary away from the primary, until no shock can be felt on the tongue when the current from the battery is made or broken with the key. Then bring the secondary gradually up towards

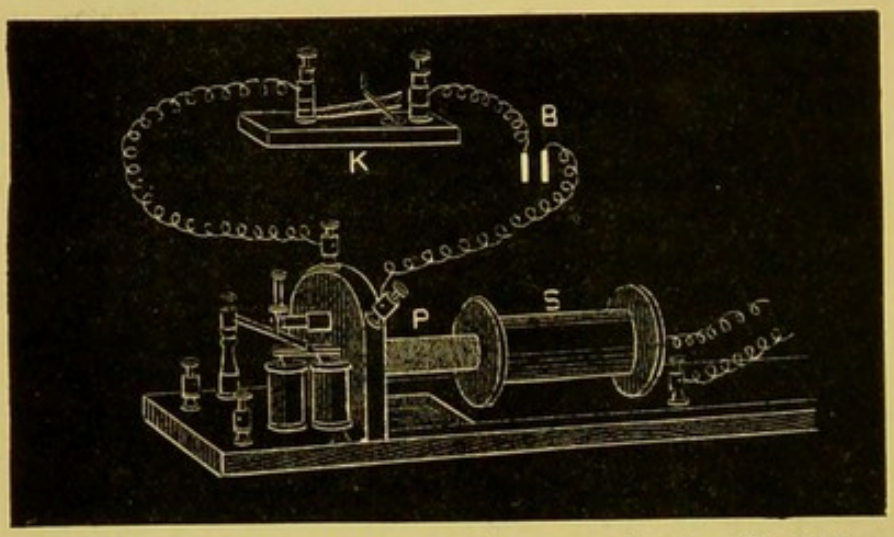


FIG. 189.—ARRANGEMENT OF COIL FOR SINGLE SHOCKS.

the primary, testing at every new position whether the shock is perceptible. It will be felt first at break. If the secondary is pushed still further up, a shock will be felt both at make and at break. From this we learn that for sensory nerves the break shock is stronger than the make. The same can easily be demonstrated for motor nerves and for muscle.

(*b*) Smoke a drum and arrange a myograph, as shown in Fig. 192. But omit the brass piece F, and do not connect the primary through the drum, as there shown, but connect it as in Fig. 189. Pith a frog (brain and cord), and make a muscle-nerve preparation.

To make a Muscle-Nerve Preparation.—Hold the frog by the hind-legs back upwards; the front part of the body will hang down, making an angle with the posterior portion. With strong scissors divide the backbone anterior to this angle, and cut away all the front portion of the body, which will fall down of its own weight. Make a circular incision at the level of the tendo Achillis, and another at the lower end of the femur, through the skin. The sciatic nerve must now be dis-

sected out, as follows : Remove the skin from the thigh, and, holding the leg in the left hand, slit up the fascia which connects the external and internal groups of muscles on the back of the thigh. Complete the separation with the two thumbs. Cut through the iliac bone, taking care that the blade of the scissors is well pressed against the bone, otherwise there is danger of severing the sciatic plexus. Now divide in the middle line the part of the spinal column which remains above the urostyle. A piece of bone is thus obtained by means of which the nerve can be manipulated without injury. Seize this piece of bone with the forceps, and carefully free the sciatic plexus and nerve from their attachments right down to the gastrocnemius muscle, taking care not to drag upon the nerve. The muscles of the thigh will contract, as the branches going to them are cut. This is an instance of mechanical stimulation. Now pass a thread under the tendo Achillis, tie it, and divide the tendon below it. Strip up the tube of skin that covers the gastrocnemius, as if the finger of a glove were being taken off. Tear through the loose connective tissue between the muscle and the bones of the leg, and divide the latter with scissors just below the knee. Cut across the thigh at its middle.

Fix the preparation on the cork plate of the myograph by a pin passed through the cartilaginous lower end of the femur, and attach the thread to the upright arm of the lever by one of the holes in it. Hang not far from the axis by means of a hook a small leaden weight (5 to 10 grammes) on the arm of the lever which carries the writing-point, and move the myograph plate or the muscle-nerve preparation until this arm is just horizontal. Fasten the electrodes from the secondary coil on the cork plate with an indiarubber band ; lay the nerve on them ; and cover both muscle and nerve with an arch of blotting-paper moistened with normal saline, taking care that the blotting-paper does not touch the thread. Adjust the writing-point to the drum. Begin with such a distance between the coils that a break contraction is just obtained on opening the key in the primary circuit, but no make contraction. The lever will trace a vertical line on the stationary drum. Read off on the scale of the induction machine the distance between the coils, and mark this on the drum. Now allow the drum to move a little, still keeping the writing-point in contact with it ; then push up the secondary coil 1 centimetre nearer the primary, and close the key. If there is a contraction, let the drum move a little before opening the key again, so that the lines corresponding to make and break may be separated from each other. If there is still no contraction at make, go on moving the secondary up, a centimetre (or less) at a time, till a make contraction appears. When the coils are still further approximated, the make may become equal in height to the break contraction, both being maximal, *i.e.*, as great as the muscle can give with any single shock (Fig. 190).

(*c*) Attach a thin insulated copper wire to each terminal of the secondary. Loop the bared end of one of the wires through the tendo Achillis, and coil the other round the pin in the femur, so that the shocks will pass through the whole length of the muscle. Repeat the experiment of (*b*), with direct stimulation of the muscle.

2. **Stimulation of Nerve and Muscle by the Voltaic Current.**—(*a*) Connect a Daniell cell through a key with a pair of electrodes on which the nerve of a muscle-nerve preparation lies. Observe that the muscle contracts when the current is closed or broken, but not during its passage.

Connect the cell with a simple rheocord, as shown in Fig. 191, so

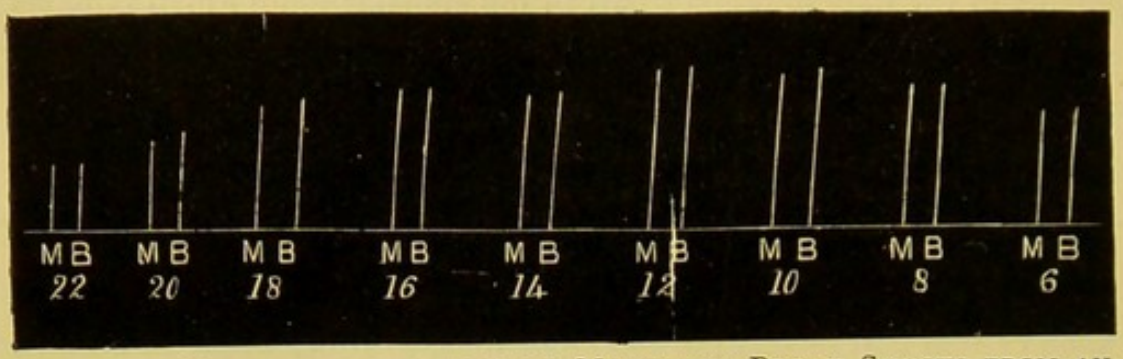


FIG. 190.—CONTRACTIONS CAUSED BY MAKE AND BREAK SHOCKS FROM AN INDUCTION MACHINE.

M, make, B, break, contractions. The numbers give the distance between the primary and secondary coils in centimetres.

that a twig of the current of any desired strength may be sent through the nerve. As the strength of the current is decreased by moving the slider S, it will be found that it first becomes impossible to obtain a contraction at break. The current must be still further reduced before the make contraction disappears, for the closing of a galvanic stream is a stronger stimulus than the breaking of it. The break or make contraction obtained by stimulating a nerve with an in-

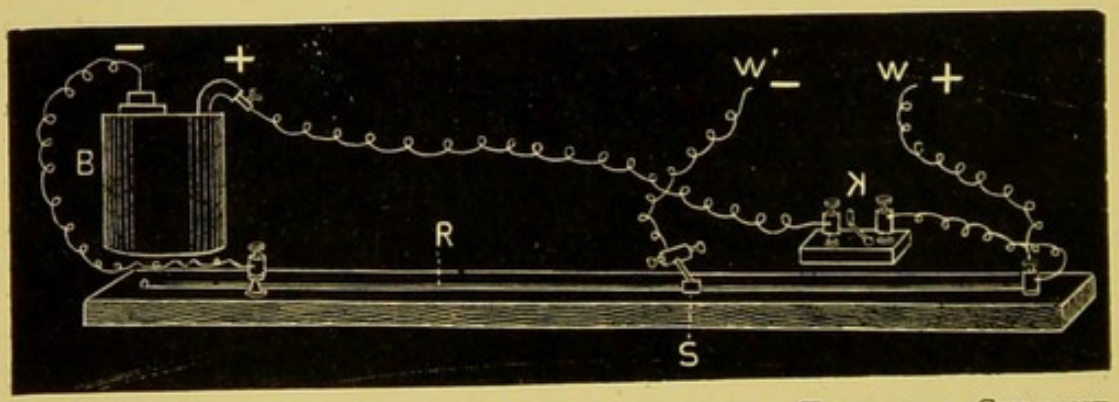


FIG. 191.—SIMPLE RHEOCORD ARRANGED TO SEND A TWIG OF A CURRENT THROUGH A MUSCLE OR NERVE.

B, battery: R, rheocord wire (German silver); S, slider formed of a short piece of thick indiarubber tubing filled with mercury; K, spring key; W, W', wires connected with electrodes.

duction-machine must not be confused with the break or make contractions caused by the voltaic current. In the case of the induction-machine, the break or make applies merely to what is done in the primary circuit, not to what happens to the current actually passing through the nerve. The current induced in the secondary at make of the primary circuit is, of course, both made and broken in

the nerve—made when it begins to flow, broken when the flow is over; the shock induced at break of the primary is also made and broken in the nerve. And although make and break of the actual stimulating current come very close together, the real make, here, too, is a stronger stimulus than the real break.

(*b*) Repeat (*a*) with the muscle directly connected by thin copper wires, or, better, unpolarizable electrodes (p. 542), to the cell.

3. **Mechanical Stimulation.**—Pith a frog. Cut away the anterior portion of the body, dissect out one sciatic nerve, and separate the leg to which it belongs from the other. Pinch the end of the nerve or prick the muscles, and they contract.

4. **Thermal Stimulation.**—Touch the nerve of the same preparation with a hot wire; the muscle contracts. The nerve is killed at the point of contact, but can be again stimulated by touching it with the wire lower down.

5. **Chemical Stimulation.**—(*a*) Cut off the injured portion of the nerve used in 3 and 4. Apply to the cut end a crystal of common salt, or let the nerve dip into a watch-glass containing a saturated solution of salt. In a short time the muscles supplied by the nerve begin to twitch, and soon enter into irregular tetanus. Take a tracing of the contractions. Cut off the piece of nerve in contact with the salt, and the tetanus stops. This shows that the seat of irritation is the portion of the nerve into which the salt has penetrated, and from which water has been withdrawn by osmosis. Contraction can also be caused by applying the salt directly to the muscles.

(*b*) Wrap the leg in blotting-paper moistened with normal saline, and expose the nerve to the vapour of strong ammonia; it will be killed, but not stimulated, for the muscles will not contract. Expose the muscles themselves to the ammonia, and contraction will occur. Accordingly muscle is stimulated by ammonia, while nerve is not.

6. **Ciliary Motion.**—Cut away the lower jaw of the same frog, and place a small piece of cork moistened with normal saline on the ciliated surface of the mucous membrane covering the roof of the mouth. It will be moved by the cilia down towards the gullet. Lay a small rule, divided into millimetres, over the mucous membrane, and measure with the stop-watch the time the piece of cork takes to travel over 10 millimetres. Then pour normal saline heated to 30° C. on the ciliary surface, rapidly swab with blotting-paper, and repeat the observation. The piece of cork will now be moved more quickly than before, unless the normal saline has been so hot as to injure the cilia.

7. **Direct Excitability of Muscle**—*Action of Curara.*—Pith the brain of a frog, and prevent bleeding by inserting a piece of match. Expose the sciatic nerve in the thigh on one side. Carefully separate it, for a length of half an inch, from the tissues in which it lies. Pass a strong thread under the nerve, and tie it tightly round the limb, excluding the nerve. Now inject into the dorsal or ventral lymph-sac a few drops of a 1 per cent. curara solution. As soon as paralysis is complete, make two muscle-nerve preparations, isolating the sciatic

nerves right up to the vertebral column. Lay their upper ends on electrodes and stimulate; the muscle of the ligatured limb will contract. This proves that the nerve-trunks are not paralyzed by curara, since the poison has been circulating in them above the ligature. The muscle of the leg which was not ligatured will contract if it be stimulated directly, although stimulation of its nerve has no effect. The muscular fibres, accordingly, are not paralyzed. The seat of paralysis must therefore be some structures physiologically intermediate between the nerve-trunk and the muscular fibres (p. 551).

8. **Graphic Record of a Single Muscular Contraction or Twitch.**—Pith a frog (brain and cord), make a muscle-nerve preparation, and arrange it on the myograph plate, as in 1 (*b*). Lay the nerve on electrodes connected with the secondary coil of an induction machine arranged for single shocks. Introduce a short-circuiting key (Fig. 158) between the electrodes and the secondary coil, and a spring key in the primary circuit. Close the short-circuiting key, and then press down the spring key with the finger. Let the drum off (fast speed); the writing-point will trace a horizontal abscissa line. Open the short-circuiting key, and then remove the finger from the spring-key. The nerve receives an opening shock, and the muscle traces a curve. Now adjust the writing-point of an electrical tuning-fork (Fig. 192), vibrating, say, 100 times a second, to the drum, and take a time-tracing below the muscle-curve. Stop the drum, or take off the writing-point, the moment the time-tracing has completed one circumference of the drum, so that the trace may not run over on itself. Cut off the drum-paper, write on it a brief description of the experiment, with the time-value of each vibration of the fork, the date, and the name of the maker of the tracing, and then varnish it. An exactly similar tracing can be obtained by directly stimulating the muscle (curarized or not).

9. **Influence of Temperature on the Muscle-curve.**—Pith a frog (brain and cord), make a muscle-nerve preparation, and arrange it on a myograph. Lay the nerve on electrodes connected through a short-circuiting key with the secondary coil of an induction-machine, or connect the muscle directly with the key by thin copper wires. Take a Daniell cell, connect one pole through a simple key with one of the upper binding-screws of the primary coil, and the other pole with the metal of the drum. A wire, insulated from the drum, but clamped on the vertical part of its support, and with its bare end projecting so as to make contact with a strip of brass fastened on the spindle, is connected with the other upper terminal of the primary (Fig. 192). At each revolution of the drum the primary circuit is made and broken once as the strip of brass brushes the projecting end of the wire. The object of this arrangement is to ensure that when the writing-point of the myograph lever has been once adjusted to the drum, successive stimuli will cause contractions, the curves of which all rise from the same point. Close the key in the primary, set the drum off (fast speed), open the short-circuiting key, and as soon as the muscle has contracted once, close it again.

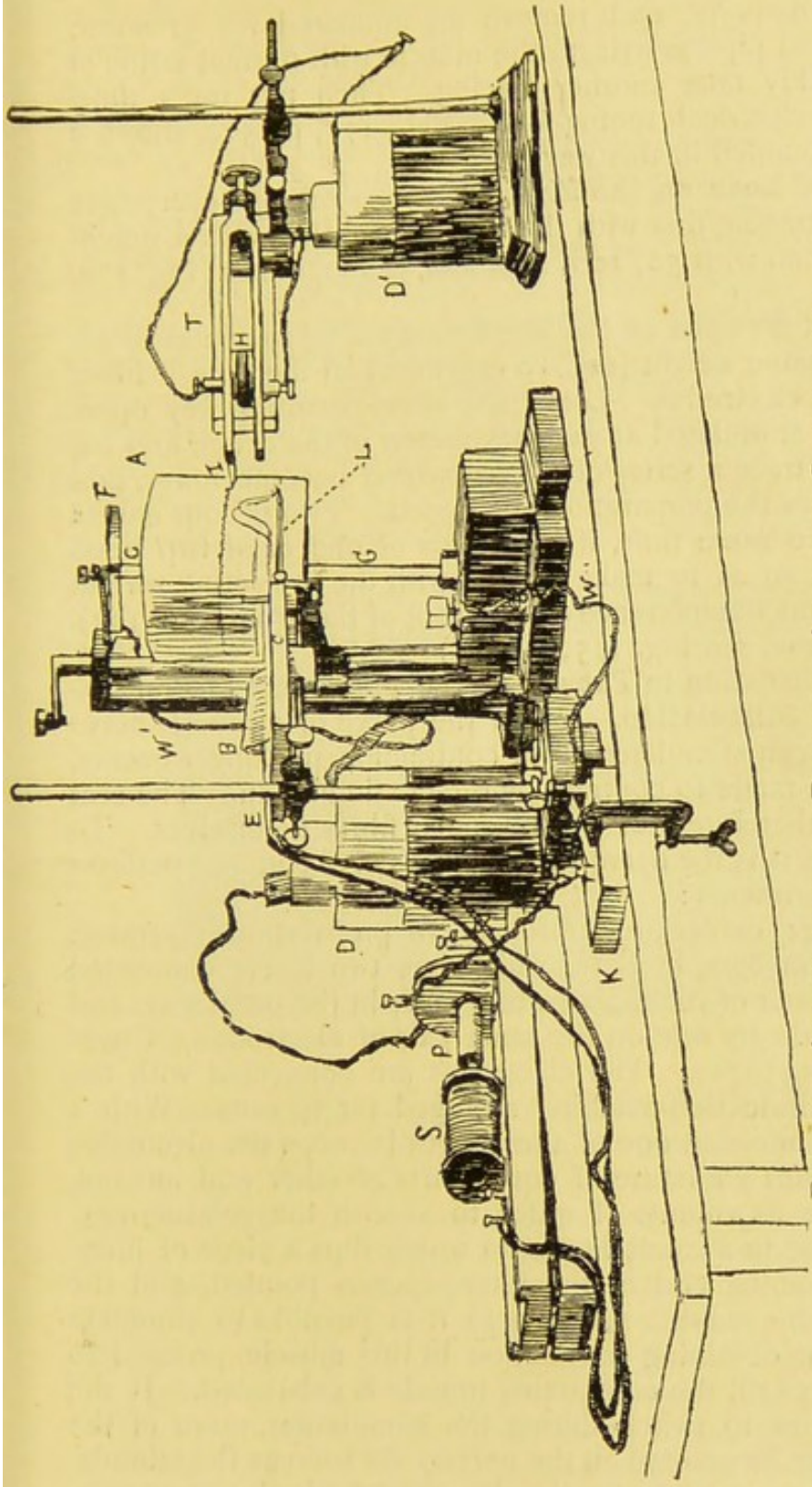


FIG. 192.—ARRANGEMENT OF DRUM FOR AUTOMATIC STIMULATION.

D, Daniell cell in circuit of primary coil P. S, secondary coil; E, electrodes. B, tent of moist blotting-paper covering muscle-nerve preparation, which lies on the myograph plate C. The lever L, connected with the muscle, writes on the drum, A. One wire W connects the metal of the foot of the drum, through the spring key K, with the primary coil. The wire W is insulated from the drum, but projects so as to touch the metal tongue F, which is fixed on the spindle G, twice in each revolution of the drum. The primary circuit is made for an instant when F touches G, and in this way the muscle-nerve preparation is stimulated twice in each revolution, and two fatigue curves are obtained. T is a tuning-fork kept in vibration by the electro-magnet H. The current of the Daniell cell D' is made and broken at each vibration of the fork. When it is made, H is magnetized, and pulls the prongs of the fork towards itself, thus drawing a small contact connected with one prong (not shown in the figure) away from a platinum point. The circuit is thus broken, H is demagnetized, the prongs of the fork again fly out and complete the circuit, and so the fork is kept continuously vibrating. I is a writing-point on one prong, by means of which the vibrations are recorded.

Now stop the drum, mark with a pencil the position of the feet of the stand carrying the myograph plate, take the writing-point off the drum, and surround the muscle with pounded ice or snow. After a couple of minutes brush away any ice which would hinder the movement of the muscle, rapidly replace the stand in exactly its original position, with the writing-point on the drum, and take another tracing. Again

take off the writing-point, and remove all unmelted ice or snow. With a fine-pointed pipette irrigate the muscle with normal saline at 30° C., and quickly take another tracing. Then put on a time-tracing with the electrical tuning-fork. Fig. 171, p. 564, shows a series of curves obtained in this way.

10. **Influence of Load on the Muscle-curve.**—Arrange everything as in 9. Take a tracing first with the lever alone, then with a weight of 10 grammes, then with 50, 100, 200, and 500 grammes (Fig. 170, p. 563).

11. **Influence of Fatigue on the Muscle-curve.**—Arrange as in 10, but leave on the same weight (say, 10 grammes) all the time. Place the nerve on the electrodes. Leave the short-circuiting key open. The nerve will be stimulated at each revolution of the drum, and the writing-point will trace a series of curves, which become lower, and especially longer, as the preparation is fatigued. Two or four curves can be taken at the same time, if both ends of one or of two brass slips be arranged so as to make contact with the projecting wire at an interval of a semicircumference or quadrant of the drum (Fig. 192). (For specimen curve, see Fig. 175, p. 567.)

12. **Seat of Exhaustion in Fatigue of the Muscle-nerve Preparation for Indirect Stimulation.**—When the nerve of a muscle-nerve preparation has been stimulated until contraction no longer occurs, the muscle can be made to contract by direct stimulation. The seat of exhaustion is, therefore, not the muscular fibres themselves. To determine whether it is the nerve-fibres or the nerve-endings, perform the following experiments:

(*a*) Pith a frog; make two muscle-nerve preparations; arrange them both on a myograph plate, which has two levers connected with it. Attach each of the muscles to a lever in the usual way, and lay both nerves side by side on the same pair of electrodes. Cover with moist blotting-paper. The electrodes are connected with the secondary of an induction-machine arranged for tetanus. With a camel's-hair brush moisten one of the nerves between the electrodes and the muscle with a mixture of equal parts of ether and alcohol, diluted with twice its volume of water, to abolish the conductivity. Or put the mixture in a small bottle, in which dips a piece of filter-paper. The projecting end of the filter-paper is pointed, and the nerve is laid on the point. As soon as it is possible to stimulate the nerves without obtaining contraction in this muscle, proceed to tetanize both nerves till the contracting muscle is exhausted. If the other muscle begins to twitch during the stimulation, more of the ether mixture must be painted on the nerve. As soon as the stimulation ceases to cause contraction in the non-etherized preparation, wash off the mixture from the other nerve with normal saline, and soon contraction may be seen to take place in the muscle of this preparation. This shows that the nerve-trunk is still excitable. Now, both nerves have been equally stimulated, and therefore the exhaustion in the non-etherized preparation was not due to fatigue of the nerve-fibres, but of the nerve-endings.

(*b*) Inject $\frac{3}{4}$ gramme chloral hydrate into the rectum of a rabbit,

and put a pair of bulldog forceps on the anus. Fix the animal on a holder as soon as the chloral has taken effect. Clip the hair from the front of the neck and insert a tracheal cannula (p. 177). Now inject subcutaneously enough of a 1 per cent. solution of curara to just paralyze the skeletal muscles. As soon as symptoms of paralysis of the muscles of respiration have appeared, connect the tracheal cannula with the artificial respiration apparatus. Now expose the sciatic nerve (p. 186) on one side, put on a ligature, and divide it above the ligature. Lay the nerve on electrodes connected with the secondary coil of an induction machine arranged for tetanus, and stimulate it. If the muscles supplied by the nerve contract, curara must be injected till contraction is no longer obtained. Then the nerve is continuously stimulated for a long time. After some hours the curara action will begin to wear off, and it may be seen that the muscles of the leg again contract. This shows that even a very prolonged stimulation is not sufficient to exhaust the extra-muscular nerve-fibres (Bowditch).

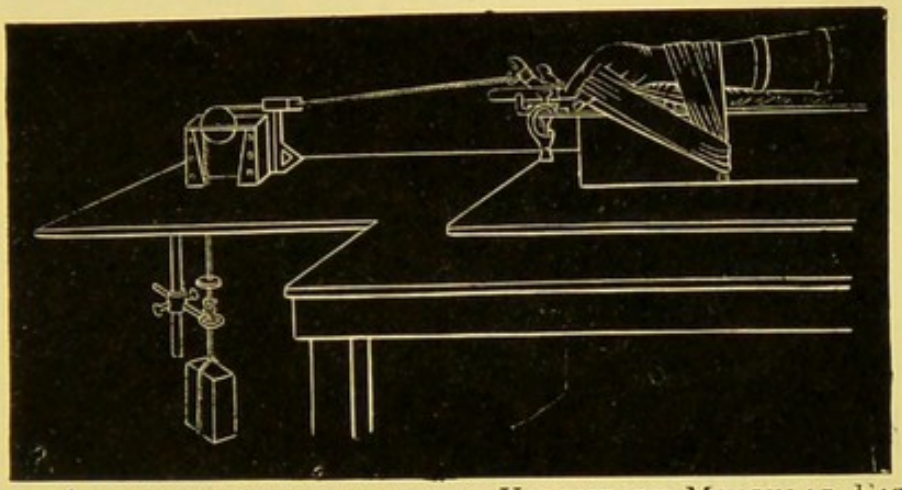


FIG. 193.—ARRANGEMENT FOR STUDYING VOLUNTARY MUSCULAR FATIGUE.

13. **Seat of Exhaustion in Fatigue for Voluntary Muscular Contraction.**—Support the arm, extensor surface downwards, on a rest such as that shown in Fig. 193, and connect the middle finger of one hand, by means of a string passing over a pulley on the edge of a table, with a weight of 3 or 4 kilos. The string is attached to the finger by a leather collar surrounding the second phalanx of the finger, but allowing free movements of the joints. The extent of the vertical movements of the string (and therefore the work done) may be registered on a drum by a writing-point connected with it, the whole arrangement forming what is called an *ergograph*. Two collar electrodes (strips of copper covered with cotton-wool soaked in salt solution, and bent to a circular form) are placed on the forearm, and connected through a short-circuiting key with the secondary coil of an induction machine arranged for tetanus (p. 175), and having a battery of four or five Daniell cells, coupled in series,* in its primary circuit. The middle finger is now made to raise the weight repeatedly by vigorous contractions of the flexor muscles until at length a failure

* *I.e.*, the copper of one cell connected with the zinc of the next.

occurs. At this moment the short-circuiting key is opened, and the flexor muscles stimulated electrically. They again contract and raise the weight, therefore the seat of exhaustion in voluntary muscular effort is not in the muscles. That it is not usually in the nerve-endings nor in the nerves may be shown by inducing fatigue of the finger for voluntary contraction in the same way, and then stimulating the median nerve at the bend of the elbow by sponge electrodes. The usual seat of fatigue for voluntary muscular contraction must therefore be in the spinal cord or brain, and as we have no reason to believe that the nerve-fibres of the central nervous system are essentially different from peripheral nerve-fibres, we conclude that the fatigue is in the nerve-cells or the network of fibrils around them (p. 662).

14. **Influence of Veratria on Muscular Contraction.**—Arrange a drum as in Fig. 192 Pith a frog (brain only), expose the sciatic nerve in one thigh, and isolate it for ½ inch from the surrounding tissues. Pass under it a strong thread, and ligature everything except the nerve. Now inject into the dorsal or ventral lymph-sac a few drops of 0·1 per cent. solution of sulphate of veratria. In a few minutes make two muscle-nerve preparations from the posterior limbs. First put the preparation from the unligatured limb on the myograph plate. Lay the nerve on electrodes connected through a short-circuiting key with the secondary of an induction machine arranged as in Fig. 192. Put the writing-point on the drum and set it off (fast speed). Open the short-circuiting key till the nerve has been once stimulated, then close it again. The curve obtained differs from a normal curve, in that the period of descent (relaxation) is exceedingly prolonged. Now connect the preparation from the ligatured limb with the lever, and take a tracing of a single contraction. Put on a time-tracing with the electrical tuning-fork (see Figs. 177, 178).

15. **Effect of Suprarenal Extract on Muscular Contraction.**—Proceed as in 14, but instead of veratria inject a watery solution of the suprarenal capsules (calf, sheep, dog, etc.). The curve of the gastrocnemius acted upon by the extract is prolonged as in veratria poisoning, although not to such a great extent. (For the action of suprarenal extract on the smooth muscle of the bloodvessels, see p. 189.)

16. **Measurement of the Latent Period of Muscular Contraction.**—Use the spring myograph (Fig. 167, p. 560), raising it on blocks of wood. Smoke the glass plate over a paraffin flame, or cover it with paper, and smoke the paper. Connect the knock-over key of the myograph with the primary circuit of an induction coil. Pith a frog, and make a muscle-nerve preparation. Arrange it on the myograph plate. Place electrodes below the nerve as near the muscle as possible, and connect by a short-circuiting key with the secondary. Bring the writing-point in contact with the smoked surface of the spring myograph, so as to get the proper pressure. See that the writing-point of the tuning-fork is in the right position for tracing time. Then push up the plate so as to compress the spring, till the rod connected with the frame which carries the plate is held by the catch.

With the short-circuiting key closed, press the release and allow an abscissa line to be traced. Again shove back the frame till it is caught. Push home the rod by means of which the prongs of the tuning-fork are separated, and rotate it through 90°. Close the knock-over key, open the short-circuiting key, shoot the plate again, and a muscle-curve and time-tracing will be recorded. Again close the short-circuiting key, withdraw the writing-point of the tuning-fork, push back the plate, close the trigger-key, then open the short-circuiting key, and holding the travelling frame with the hand, allow it just to open the knock-over and stimulate the nerve. The writing-point now records a vertical line (or, rather, an arc of a circle), which marks on the tracing the moment of stimulation. The latent period is obtained by drawing a parallel line (or arc) through the point of the muscle-curve where it just begins to diverge from the abscissa line. The value of the portion of the time-tracing between these two lines can be readily determined, and is the latent period.

17. **Summation of Stimuli.**—Arrange two knock-over keys on the spring myograph at such a distance from each other that the plate travels from one to the other in a time less than the latent period. Connect each key with the primary circuit of a separate induction coil having a couple of Daniells in it. Join two of the binding-screws of the secondaries together; connect the other two through a short-circuiting key with electrodes, on which the nerve of a muscle-nerve preparation is arranged. Push up the secondaries till the break shocks obtained on opening the two knock-over keys are maximal. Then shoot the plate as described in 16, first with one trigger key closed, and then with both. The curves obtained should be of the same height in the two cases, as a second maximal stimulus falling within the latent period is ignored by the nerve or muscle. Repeat the experiment with submaximal stimuli, *i.e.*, with such a distance of the coils that opening of either trigger key does not cause as strong a contraction as is caused when the coils are closer. The curve will now be higher when the two shocks are thrown in successively than when the nerve is only once stimulated. This shows that (submaximal) stimuli can be summed in the nerve. The same could be demonstrated for muscle (p. 571).

18. **Superposition of Contractions.**—Smoke a drum arranged for automatic stimulation as in Fig. 192. Adjust the brass points with a distance of, say, one centimetre between them, so that a second stimulus may be thrown into the nerve at an interval greater than the latent period of muscle. Put two Daniells in the primary circuit. Lay the nerve of a muscle-nerve preparation on electrodes connected through a short-circuiting key with the secondary. Allow the drum to revolve (fast speed); open the short-circuiting key till both brass points have passed the projecting wire, then close it. Now bend back the second brass point, and take a tracing in which the first curve is allowed to complete itself. This will not rise as high as the second curve obtained when the two stimuli were thrown in. Repeat the experiment with varying intervals between the brass points—that is, between the two successive stimuli. Put on a time-tracing

with the electrical tuning-fork. (For specimen curve see Fig. 179, p. 571.)

19. **Composition of Tetanus.**—(*a*) Adjust a muscle-nerve preparation on a myograph plate, the nerve being laid on electrodes connected through a short-circuiting key with the secondary of an induction machine, the primary circuit of which contains a Daniell cell and is arranged for an interrupted current (Fig. 65, p. 175). The lever should be shorter than that used for the previous experiments, or the thread should be tied in a hole farther from the axis of rotation, so as to give less magnification of the contraction. Set the Neef's hammer going, let the drum revolve (slow speed), and open the key in the secondary. The writing-point at once rises, and traces a horizontal or perhaps slightly-ascending line. Close the short-circuiting key, and the lever sinks down again to the abscissa line. If it does not quite return, it should be loaded with a small weight. This is an example of complete tetanus.

(*b*) Connect the spring shown in Fig. 194 with one of the upper terminals of the primary coil, and the mercury cup with the other. Fasten the end of the spring in one of the notches in the upright piece of wood by means of a wedge, so that its whole length can be made to vibrate. Let the drum off, set the spring vibrating by depressing it with the finger, then open the key in the secondary. The muscle is thrown into incomplete tetanus, and the writing-point traces a wavy curve at a higher level than the abscissa line. Close the short-circuiting key, and the lever falls to the horizontal. Repeat the experiment with the spring fastened, so that only $\frac{3}{4}$, $\frac{1}{2}$, $\frac{1}{4}$, $\frac{1}{8}$ of its length is free to vibrate. The rate of interruption of the primary circuit increases in proportion to the shortening of the spring, and the tetanus becomes more and more complete till ultimately the writing-point marks an unbroken straight line. Put on a time-tracing by means of an electro-magnetic marker connected with a metronome beating seconds or half-seconds (Fig. 60, p. 170). (For specimen curves see Fig. 180, p. 572.)

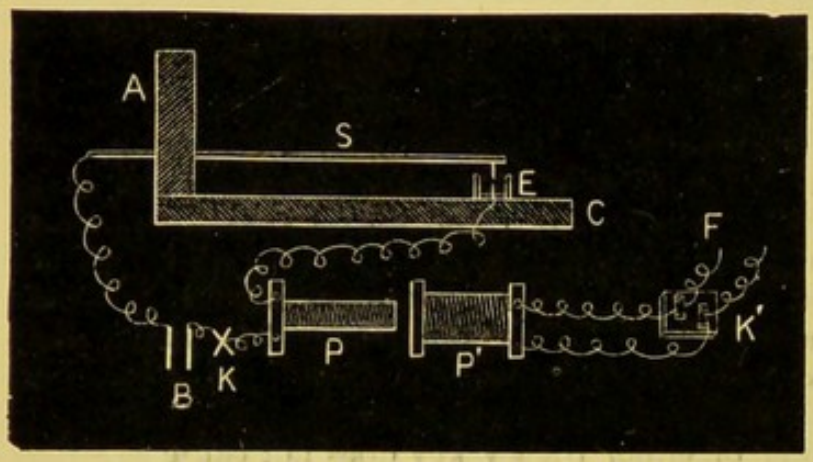


FIG. 194.—ARRANGEMENT FOR TETANUS.

A, upright with notches, in which the spring S is fastened (shown in section); C, horizontal board to which A is attached, and in a groove in which the mercury-cup E slides. The primary coil P is connected with E, and through a simple key, K, with the battery B, the other pole of which is connected with the end of the spring. The wires from the secondary coil, P′, go to a short-circuiting key, K′, from which the wires F go off to the electrodes.

19. **Velocity of the Nerve-impulse.**—Use the spring myograph

(Fig. 167, p. 560). Make a muscle-nerve preparation from a large frog (preferably a bull-frog), so that the sciatic nerve may be as long as possible. Connect the knock-over key with the primary circuit of an induction machine, which should contain a single Daniell cell. Arrange two pairs of fine electrodes under the nerve on the myograph plate, one near the muscle, the other at the central end. Connect the electrodes with a Pohl's commutator (without cross-wires), the side-cups of which are joined to the terminals of the secondary coil, as shown in Fig. 195. By tilting the bridge of the commutator the nerve may be stimulated at either point. Great care must be taken to keep the nerve in a moist atmosphere by means of wet blotting-paper; but at the same time it must not lie in a pool of normal saline, as twigs of the stimulating current would in this case spread down the nerve, and we could never be sure that the apparent was always the real point of stimulation. The writing-points of the lever and tuning-fork having been adjusted to the smoked plate, as in 16, the bridge of the Pohl's commutator is arranged for stimulation of the distal point of the nerve, the plate is shot with the short-circuit-

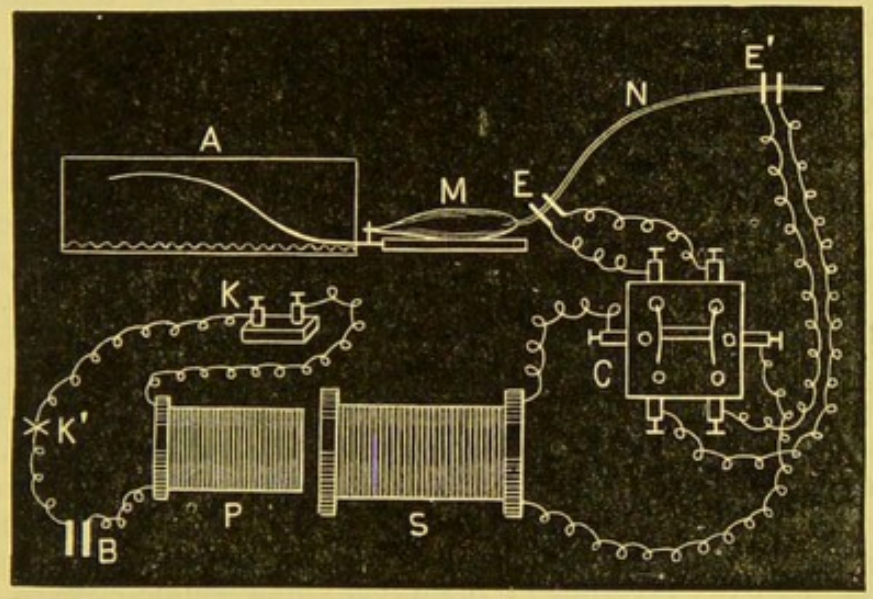


FIG. 195.—ARRANGEMENT FOR MEASURING THE VELOCITY OF THE NERVE-IMPULSE.

A, travelling plate of spring myograph; M, muscle lying on a myograph plate; N, nerve, lying on two pairs of electrodes, E and E'; C, Pohl's commutator without cross wires; K, knock-over key of spring myograph (only the binding-screws shown); K', simple key in primary circuit; B, battery; P, primary coil; S, secondary coil.

ing key in the secondary closed, and an abscissa line and time-curve traced. Then the writing-point of the fork is removed and the plate again shot with the key in the secondary open, and a muscle-curve is obtained. The commutator is now arranged for stimulation of the central end of the nerve, and another muscle-curve taken. Vertical lines are drawn through the points where the two curves just begin to separate out from the abscissa line. The interval between these lines corresponds to the time taken by the nerve-impulse to travel along the nerve from the central to the distal pair

of electrodes. Its value in time is given by the tracing of the tuning-fork. The length of the nerve between the two pairs of electrodes is now carefully measured with a scale divided in millimetres, and the velocity calculated (p. 603).

21. **Chemistry of Muscle.**—Mince up some muscle from the hind-legs of a dog or rabbit (used in some of the other experiments), of which the bloodvessels have been washed out by injecting normal saline solution through a cannula tied into the abdominal aorta until the washings are no longer tinged with blood. To some of the minced muscle add twenty times its bulk of distilled water, to another portion ten times its bulk of a 5 per cent. solution of magnesium sulphate. Let stand, with frequent stirring, for twenty-four hours. Then strain through several folds of linen, press out the residue, and filter through paper. (1) With the filtrate of the watery extract make the following observations :

(*a*) *Reaction.*—To litmus paper acid.

(*b*) Determine the temperatures, at which coagulation of the various proteids in the extract takes place, according to the method described on p. 21.* Put some of the watery extract in the test-tube, and heat the bath, stirring the water in the beakers occasionally with a feather. Note at what temperature a coagulum first forms. It will be about 47° C. Filter this off, and again heat ; another coagulum will form at 56° to 58°. Filter, and heat the filtrate ; a third slight coagulum may be formed at 60° to 65° C. A fourth precipitate (of serum-albumin) will come down at 70° to 73°. Saturate some of the watery extract with magnesium sulphate ; a large precipitate will be formed, showing the presence of a considerable amount of globulin. Filter off the precipitate and heat the filtrate ; coagulation will again occur at very much the same temperatures as before, although the total amount of precipitate will be less. Note in particular that there is still some precipitate at 47° to 50°. Paramyosinogen possesses some of the characters of both globulins and albumins, for it is partially but not entirely precipitated by saturation with magnesium sulphate, and is not precipitated by sodium chloride.

(2) (*a*) Test the reaction of the magnesium sulphate extract. It will usually be faintly acid to litmus.

(*b*) Heat some of it. Precipitates will be obtained at the same temperatures as in (1) (*b*), but those at 47° to 50° and 56° to 58° will be more abundant. Of the two, that at 47° to 50° will usually be the larger when time is given for it to come down and the heating is gradual.

(*c*) Dilute some of the magnesium sulphate extract with three

* It should be remembered that the temperature of heat-coagulation of any substance is by no means an absolute constant. It depends on the reaction, the proportion and kind of neutral salts present, perhaps on the strength of the proteid solution and the manner of heating. A solution of egg-albumin, *e.g.*, can be coagulated at a temperature much below 70° when it is heated for a week. Small differences in the temperature of heat-coagulation, unless supported by well-marked chemical reactions, are not enough to characterize proteid substances as chemical individuals.

times, another portion with four times, and another with five times, its volume of water in a test-tube, and put in a bath at 40° C. Coagulation will occur in one or all of these test-tubes. To another test-tube of the extract diluted in the proportion which has given the best 'muscle-clot' add a few drops of a dilute solution of potassium oxalate, and place in the bath at 40°. Coagulation occurs as before. Filter off the clot from all the test-tubes. The filtrate is the 'muscle-serum,' and yields a precipitate of serum-albumin at 70° to 73° C.

(3) *Myosinogen*, like other globulins, is insoluble in distilled water, but soluble in weak saline solutions. Saturation with neutral salts like sodium chloride and magnesium sulphate precipitates myosinogen, but not albumin, from its solutions; saturation with ammonium sulphate precipitates both. Myosinogen is said to be dissolved without change in very weak acids. Stronger acids precipitate it. Verify the following reactions of myosinogen, using the original magnesium sulphate extract of the muscle.

(*a*) Dropped into water, it is precipitated in flakes, which can be redissolved by a weak solution of a neutral salt (say 5 per cent. magnesium sulphate).

(*b*) When a solution of myosinogen is dialysed, it is precipitated on the inside of the dialyser as the salts pass out.

(*c*) If a piece of rock-salt is suspended in a solution, the myosin gradually gathers upon it, diffusion of the salt out through the precipitated myosin always keeping a saturated layer around it.

(*d*) Saturate a solution containing myosinogen with crystals of magnesium sulphate, stirring or shaking at frequent intervals. The myosinogen is precipitated.

(*e*) Without adding any salt, simply shake a myosinogen solution vigorously; a certain amount of the myosinogen will be precipitated, and the solution will become turbid. This reaction can also be obtained with solutions of other proteids, such as albumin (Ramsden).

Extracts in all essentials similar to those obtained from the muscles of a freshly-killed animal can be got from muscles that have entered into rigor.

22. **Reaction of Muscle in Rest, Activity, and Rigor Mortis.**—(*a*) Take a frog's muscle, cut it across, and press a piece of red litmus paper on the cut end; it is turned blue. Yellow turmeric paper is not affected.

(*b*) Immerse another muscle in normal saline solution at 40° to 42° C. It becomes rigid. The reaction becomes acid to litmus paper, and also turns brown turmeric paper yellow.

(*c*) Plunge another muscle into boiling normal saline solution. It becomes harder than in (*b*), and its reaction becomes acid to litmus paper.

(*d*) Stimulate another muscle with an interrupted current from an induction machine (Fig. 65, p. 175), till it no longer contracts. The reaction is now acid to litmus paper. Brown turmeric paper may also be turned yellow.

CHAPTER XI.

ELECTRO-PHYSIOLOGY.

A LITTLE more than a hundred years ago the foundation both of electro-physiology and of the vast science of voltaic electricity was laid by a chance observation of a professor of anatomy in an Italian garden. It is indeed true that long before this electrical fishes were not only popularly known, but the shock of the torpedo had been to a certain extent scientifically studied. But it was with the discovery of Galvani of Bologna that the epoch of fruitful work in electro-physiology began. Engaged in experiments on the effect of static and atmospheric electricity in stimulating animal tissues, he happened one day to notice that some frogs' legs, suspended by copper hooks on an iron railing, twitched whenever the wind brought them into contact with one of the bars (p. 651). He concluded that electrical charges were developed in the animal tissues themselves, and discharged when the circuit was completed. Volta, professor of physics at Pavia, fixing his attention on the fact that in Galvani's experiment the metallic part of the circuit was composed of *two* metals, maintained that the contact of these was the real origin of the current, and that the tissues served merely as moist conductors to complete the circuit; and after a controversy lasting for more than a decade, he finally clinched his argument by constructing the voltaic pile, a series of copper and zinc discs, every two pairs of which were separated by a disc of wet cloth. The pile yielded a continuous current of electricity. 'So,' said Volta, 'it is clear that the tissue in Galvani's experiment only acts the part of the cloth.' Galvani, however, had shown in the meantime that *contraction without metals* could be obtained by dropping the nerve of a preparation on to the muscle (p. 651); and it soon began to be recognised that both Galvani and Volta were in part right, that two brilliant discoveries had been made instead of one; in short, that the tissues produce electricity, and that the contact of different metals does so too. Although it is curious to note how completely the growth of that science of which Volta's discovery was the germ has overshadowed the parent tree planted by the hand of Galvani, yet animal electricity has been deeply studied by a large number of observers, and many interesting and important facts have been brought to light.

Since it is in muscle and nerve that the phenomena of electro-physiology are seen in their simplest expression, and have been chiefly studied, we shall develop the fundamental laws with reference to muscle and nerve alone, and afterwards apply them to other excitable tissues.

1. *All points of an uninjured resting muscle are approximately at the same potential* (*or iso-electric*). In other words, if any two points are connected with a galvanometer by means of unpolarizable electrodes, little or no current is indicated. (Although it is scarcely possible to isolate a muscle without its showing some current, the more carefully the isolation is performed the feebler is the current; and between two points of the inactive, uninjured ventricle of the frog no electrical difference has been found.)

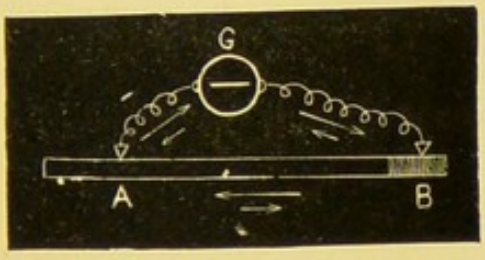


FIG. 196.—A, uninjured, B, injured, portion of nerve; G, galvanometer. The large arrows show direction of demarcation current or current of rest, the small arrows direction of negative variation or action current.

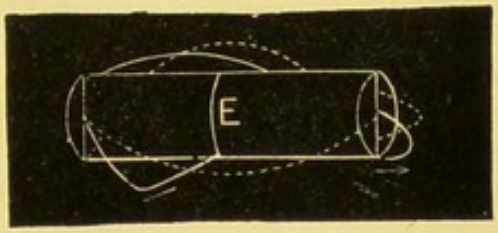


FIG. 197.—DIAGRAM OF CURRENTS OF REST IN A REGULAR MUSCLE, OR MUSCLE CYLINDER.

E, equator. The dotted lines join points at the same potential, between which there is no current.

2. *Any uninjured point of a resting muscle or nerve is at a higher potential than any injured point;* so that a current will pass through the galvanometer from uninjured to injured point, and in the tissue from the latter to the former (current of rest or demarcation current—Fig. 196).

3. *Any unexcited point of a muscle or nerve is at a higher potential than any excited point, and any less excited point is at a higher potential than any more excited point.*

The injured or excited muscle may thus be compared to a Daniell cell, the injured or active tissue corresponding to the zinc, which is connected with the negative pole of the battery, and the uninjured or inactive tissue to the copper, which is connected with the positive pole. The best object for experiments on the demarcation current is a straight-fibred muscle like the frog's sartorius. If this muscle be taken, and the ends cut off perpendicularly to the surface, a muscle-prism or muscle-cylinder is obtained (Fig. 197). The

strongest current is got when one electrode is placed on the middle of either cross-section and the other on the 'equator'—that is, on a line passing round the longitudinal surface midway between the ends. The direction of this current is from the cross-section towards the equator in the muscle. If the electrodes are placed on symmetrical points on each side of the equator, there is no current.

A particular case of this symmetrical or 'streamless' arrangement is where the middle points of the two cross-sections are led off to the galvanometer; here, if the sections are similar, their potential is the same, and the needle remains at zero. Between two points of the longitudinal surface at unequal distances from the equator there is a current in the galvanometer from the nearer to the more distant point, the potential of a longitudinal point nearer a cross-section being lower than that of one more remote. Between two points on the same cross-section there is a current if they are not symmetrically placed with reference to its centre, the direction in the muscle being from more central to more peripheral point.

The above may be taken as applying to nerve also, with the proviso that less is known as to electrical differences between points on the same cross-section, since ordinary cold-blooded nerves are too small for such experiments, and that two parallel cross-sections of a nerve are not iso-electric, so that a current (the so-called axial stream) passes between them when they are connected with the galvanometer.

Current of Action, or Negative Variation.—When a muscle or nerve is excited, a wave of diminished potential (negativity) sweeps over it. Suppose two points, A and B (Fig. 198), on the longitudinal surface of a muscle to be connected with a capillary electrometer (p. 538), the movements of the mercury being photographed on a travelling surface, for example, a pendulum carrying a sensitive plate. Let the muscle be excited at the end, so that the wave of excitation will be propagated in the direction of the arrow. The wave will reach A first, and while it has not yet reached B, A will become negative to B. If there is a resting difference of potential between A and B, this will be altered, the new and transitory difference adding itself algebraically to the old. When the wave reaches B, it may already have passed over A altogether, and B now becoming negative to A, there will be a movement of the meniscus of the electrometer in the opposite direction. This is called the diphasic current of action. If the wave has not passed over A before it reaches B, as would in general be the case in an actual experiment, there will be first a period during which A is more negative than B (first phase); this will end as soon as B has become equally negative with A, and will

be succeeded by a period during which B is more negative than A (second phase). Since the wave takes time to reach its maximum, it is evident that a well-marked first phase will be favoured when the interval between its arrival at A and B is long, for in this case A will have a chance of becoming strongly negative while B is still normal. Similarly, if A has again become normal, or nearly normal, before the maximum negativity has passed over B, a strong second phase will be favoured. The heart-muscle, accordingly, where the wave of contraction, and its accompanying electrical change, move with comparative slowness, is better

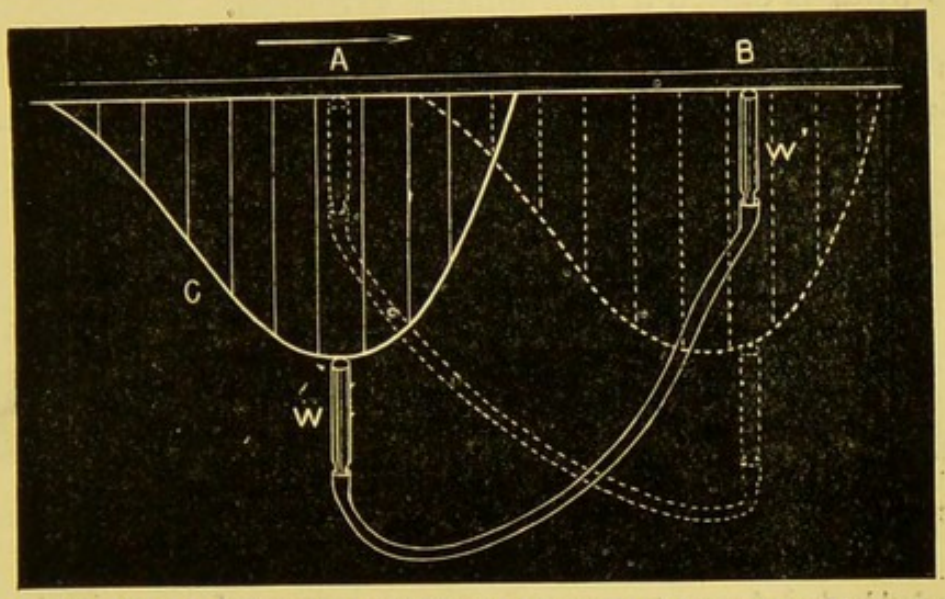


FIG. 198.—DIAGRAM TO ILLUSTRATE PROPAGATION OF THE NEGATIVE CHANGE ALONG AN ACTIVE MUSCLE OR NERVE.

Suppose A B to be a horizontal bar representing the muscle or nerve. Let C be a curved piece of wood representing the curve of the electrical change at any point. Let W W′ be two glass cylinders connected by a flexible tube, the whole being filled with water. Suppose the rims of the cylinders originally to touch A B at the points A and B, and let them be movable only in the vertical direction. The level of the water being the same in both, there is no tendency for it to flow from one to the other. This represents the resting state of the tissue when A and B are symmetrical points. Now let C be moved along the bar at a uniform rate. The cylinder W, being free to move down, but not horizontally, will be displaced by C, and, if it is kept always in contact with its curved margin, will, after describing the curve of the electrical variation, come again to rest in its old position at A. B will do the same when C reaches it. But since C reaches A before B, the level of the water in B will at first be higher than that in A, and water will flow from B to A. This will correspond to the time during which the point of the tissue represented by A would be negative to a point represented by B. Later on, when C has reached the position shown by the dotted lines, the level of the water in A will be higher than that in B, and a flow will take place in the opposite direction to the first flow This corresponds to a second phase of the negative variation.

suited for showing a well-marked diphasic variation than skeletal muscle, and still better suited than nerve. In the gastrocnemius muscle of the frog, when excited through its

nerve, the electrical response begins about $\frac{4}{1000}$ second, and the change of form of the muscle about $\frac{8}{1000}$ second after the stimulation. It is believed that in a muscle directly excited the electrical change begins in less than $\frac{1}{1000}$ second, and the mechanical change in $\frac{4}{1000}$ second (Burdon Sanderson). (Figs. 199-204.)

When one electrode is placed on an injured part, the wave of action and of electrical change diminishes as it reaches the injured tissue; and if the tissue is killed at this part, it diminishes to zero; so that here the second phase may be greatly weakened or may disappear altogether, and we then have what is called a monophasic variation.

In this case the current of action can be demonstrated, even for a single excitation, but still better for a tetanus, with the galvano-

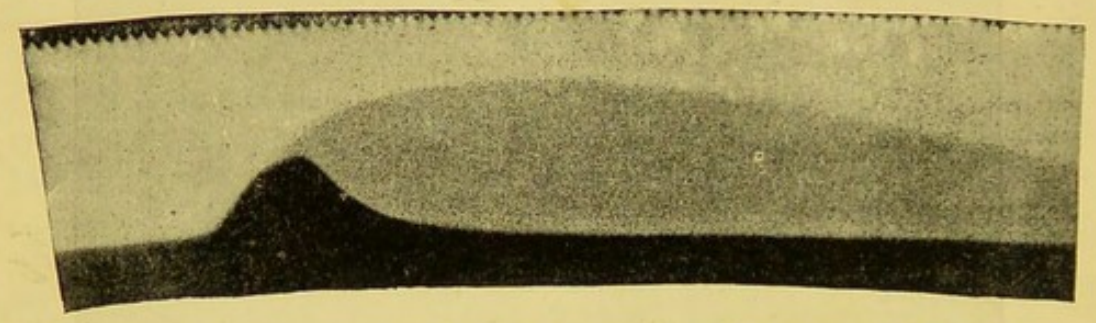
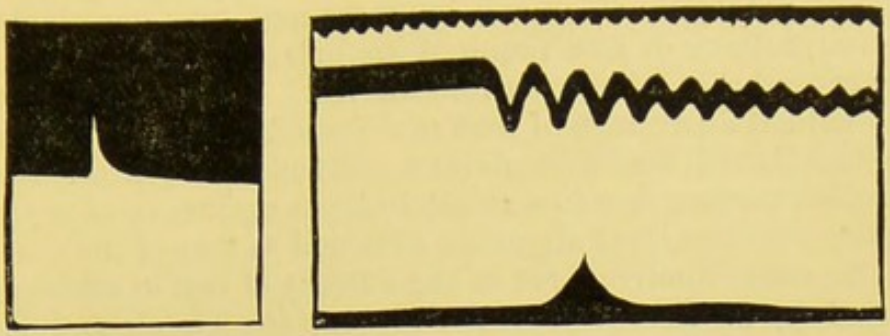


FIG. 199.—PHOTOGRAPHIC ELECTROMETER CURVES FROM SARTORIUS MUSCLE (SANDERSON).

The darkly-shaded curve represents the diphasic variation of the uninjured muscle; the lightly-shaded curve the monophasic variation of the muscle after injury of one end. The toothed curve at the top is the time-tracing registered by photographing the prong of a tuning-fork vibrating five hundred times a second.

meter, which in general is not quick enough to analyze a diphasic variation with equal phases, and gives, therefore, only their algebraic sum—that is, zero. When the muscle or nerve is tetanized, the negative variation appears, while stimulation is kept up, as a permanent deflection representing the 'sum' of the separate effects. It is in the opposite direction to the current of rest, since the injured tissue, being less affected by the excitation, and therefore undergoing a smaller negative change than the uninjured, becomes relatively to the latter less negative.

When the current of rest is compensated by a branch of an external current just sufficient to balance it and bring the galvanometer image back to zero, the action current appears alone in undiminished strength. This shows that the latter is not due to a change of electrical resistance during excitation, since such a change would equally affect current of rest and compensating current, and they would still balance each other. The action current is really due to



A. B.

FIG. 200.—'SPIKE' (DIPHASIC VARIATION) OF UNINJURED GASTROCNEMIUS (SANDERSON).

A photographed on slow, B on fast-moving plate.

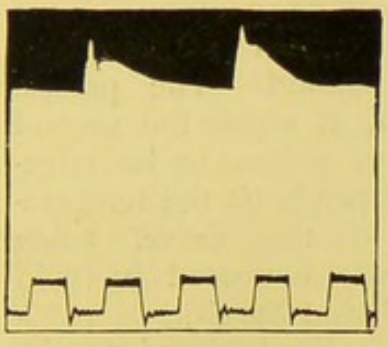


FIG. 201.—VARIATION OF INJURED GASTROCNEMIUS (SANDERSON).

A 'spike' followed by a 'hump.'

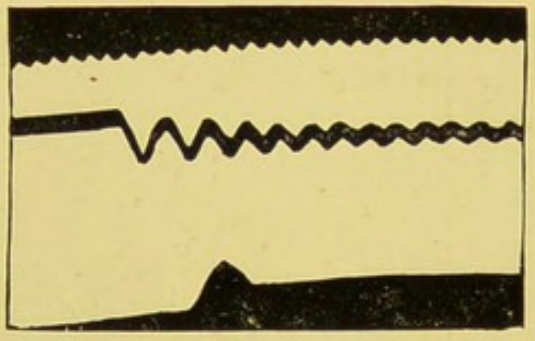


FIG. 202.—VARIATION OF INJURED GASTROCNEMIUS (SANDERSON).

The plate was moving ten times faster than in Fig. 201.

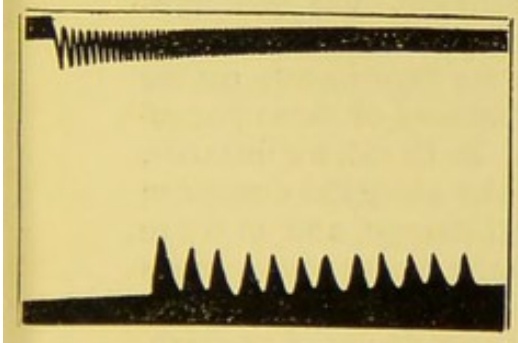


FIG. 203.—VARIATION OF UNINJURED MUSCLE EXCITED EIGHTY-FOUR TIMES A SECOND (SANDERSON).

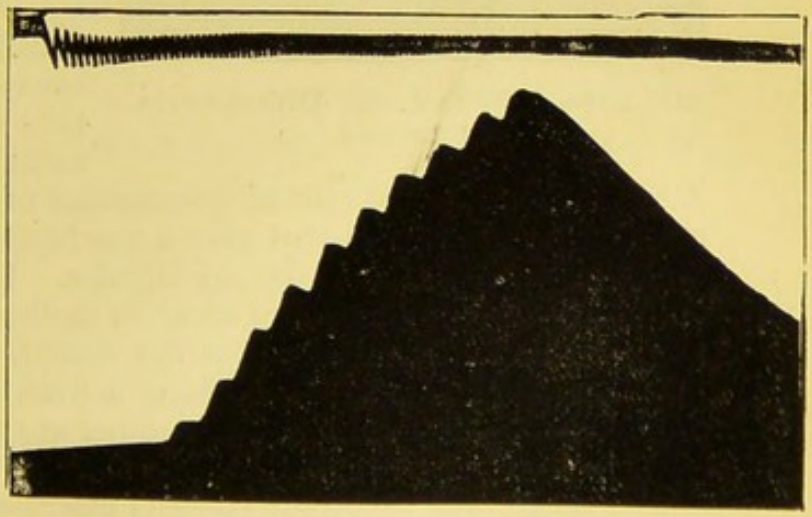


FIG. 204.—CURVE OF AN INJURED MUSCLE EXCITED SIXTY TIMES A SECOND (SANDERSON).

a change of potential, which can be measured by determining what electromotive force is just required to balance it, and which may actually exceed that of the current of rest. Thus, Sanderson and Gotch obtained an average of 0·08 of a Daniell cell (the electromotive force of the Daniell would be about a volt) as the electromotive force of the action current due to a single indirect excitation of a vigorous frog's gastrocnemius, and about 0·04 Daniell as that of the current of rest. The electromotive force of the current of rest in rabbit's nerve was found by du Bois-Reymond to be 0·026; Gotch and Horsley found the average for the cat 0·01, and for the monkey only 0·005.

That the fusion of the successive variations of a tetanized muscle, as seen with the galvanometer, is only apparent has been shown by means of the capillary electrometer. Even with a frequency of stimulation far beyond what is necessary for complete tetanus, each stimulus is answered by a movement of the meniscus (Figs. 203, 204). In nerve, also, as has been recently demonstrated, each of two successive stimuli causes its appropriate electrical change when they are separated by an interval longer than a certain small fraction of a second. The precise interval at which the second stimulus ceases to be effective depends on the temperature of the nerve, being markedly increased by cold (Gotch and Burch).

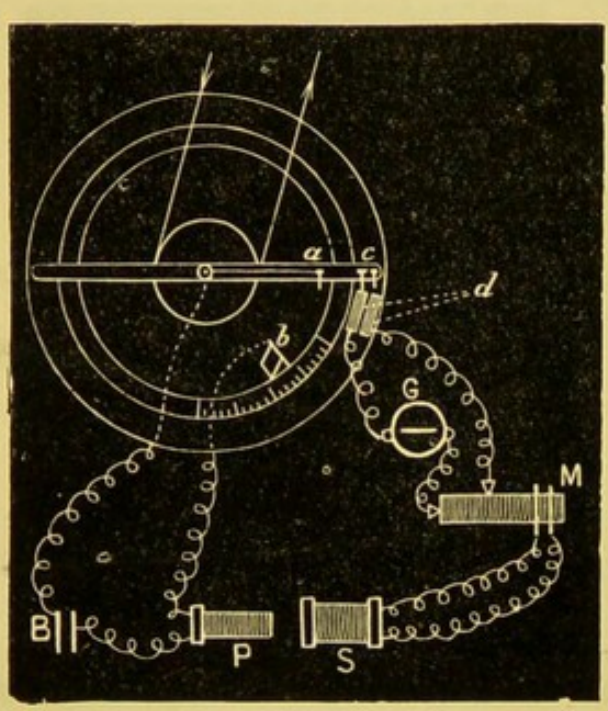


FIG. 205.—DIAGRAM OF DIFFERENTIAL RHEOTOME.

Before Burdon Sanderson introduced the capillary electrometer for the study of the electrical phenomena of living tissues, and Burch perfected a method for the measurement of the curves, the *differential rheotome*, originally constructed by Bernstein, was the most valuable instrument we possessed for experiments on the time-relations of these phenomena. By its aid, for instance, it was shown that the rate of propagation of the electrical change in muscle is the same as that of the mechanical change, and in nerve the same as that of the nervous impulse. Quite recent observations on muscle made by the more accurate method of the capillary electrometer have confirmed those earlier results, the velocity of propagation of the diphasic variation along a fresh sartorius at 14° C. being in one experiment 2·8 metres, in another at 18° C., 3·5 metres (Sanderson). (See p. 575.)

The differential rheotome consists essentially of a stationary metal ring, the whole or part of which is graduated, and of a portion which can be made to revolve at a known rate. The latter carries two contacts: *a*, an obliquely-placed platinum wire which touches at

every revolution a horizontal wire *b* on the fixed ring, thus making and breaking the primary circuit P of an induction machine, and so causing stimulation of a muscle or nerve M connected with the secondary S; and, *c*, a double contact, either in the form of two platinum wires, which dip into two mercury troughs, or of two wire brushes rubbing on copper blocks *d*, at a certain part of the revolution. The troughs or blocks are connected with a circuit containing a galvanometer G, and a portion of the muscle or nerve arranged so as to give a strong action current. This circuit is completed by the wires or brushes, which are in metallic contact with each other; and the relative position of the fixed contact in the primary circuit and of the troughs or copper blocks can be altered so as to alter at will the interval between stimulation and closure of the galvanometer circuit. The proportion of the whole revolution during which this circuit is closed can be varied by changing the relative position of the two copper blocks. Suppose the tissue is stimulated at one end while the leading-off electrodes are at the other. When the contact *a*, *b*, is made at the same time as *c*, *d*, no deflection will be shown by the galvanometer if the rheotome is revolving rapidly (the demarcation current being accurately compensated), because the circuit will be opened before the negative change has time to travel to the leading-off electrodes. But as the distance between *b* and *d* is increased, a small deflection will appear, which, with further increase of the distance, will become larger, reach a maximum, and then begin to fall off again. The first small deflection corresponds to the position in which the negative change has just had time to reach the leading-off electrodes before the galvanometer circuit is opened. The maximum deflection corresponds to a period a little later than this, because the electrical variation does not at once reach its maximum at any point.

There is ample evidence that the negative variation is a normal physiological phenomenon. In human skeletal muscles the current of action has been demonstrated by connecting a galvanometer with ring electrodes passing round the forearm, and throwing the muscles into contraction. A diphasic variation is thus obtained; and the electrical change travels with a velocity of as much as twelve metres per second, which is greater than the velocity in frogs' muscles. Electromotive changes are likewise associated with the beat of the heart. Action currents have also been detected in the phrenic nerves of living animals accompanying the respiratory discharge (Reid and Macdonald), in the vagi accompanying the movements of the lungs, in the œsophagus during swallowing, in the cutaneous sensory nerves in response to the 'adequate' stimulus of pressure (Steinach), in the retina in response to the adequate stimulus of light,

in glands during secretion, in the central nervous system during the passage of impulses along its conducting paths. Some of these will be further considered a little later on.

As to the interpretation of the facts we have been describing, and which are summed up in the three propositions on p. 629, two chief doctrines have divided the physiological world: (1) the theory of du Bois-Reymond, the pioneer of electro-physiology, and (2) the theory of Hermann. It was believed by du Bois-Reymond that the current of rest seen in injured tissues is of deep physiological import, and that the electrical difference which gives rise to it is not developed by the lesion as such, but only unmasked when the electrical balance is upset by injury. He looked upon the muscle or nerve as built up of electromotive particles, with definite positive and negative surfaces arranged in a regular manner in a sort of ground-substance which is electrically indifferent. The 'negative variation' he supposed to depend on an actual diminution of previously-existing electromotive forces; and from this conception arose its historic name. This theory has been highly elaborated and extended to include new facts as they have arisen. But although it explains certain phenomena, such as the currents of a prism of muscle, better than the simpler theory associated with the name of Hermann, most physiologists have now abandoned it in favour of the latter. Hermann and his school assume that the uninjured muscle or nerve is 'streamless,' not because equal and opposite electromotive forces exactly balance each other in the substance of the tissue, but because electromotive forces are absent until they are called into existence at the boundary, or plane of demarcation, between sound and injured tissue. For this reason in the terminology of Hermann du Bois-Reymond's current of rest is called the 'demarcation' current.

Relation between the Negative Variation and Functional Activity.—Although the negative variation is so general an accompaniment of excitation, and is even within tolerably wide limits, in muscle and nerve at least, pretty nearly proportional to the strength of the stimulus, it is at present impossible to say definitely what the chemical or physical changes are which underlie it, nor how closely

they are related to the functional activity of the tissues. It is, of course, clear that energy must be transformed to produce an electromotive force capable of doing work. It may be assumed that this energy is ultimately derived from the stock of chemical energy in the tissue-substance. But whether in the final transformation the electrical phenomena are the expression of chemical changes or of physical changes, or of both, we do not know. Bernstein has supposed that in the chemical process, whose visible outcome is a muscular contraction, there are three stages: (1) The liberation of (intra-molecular) oxygen from the molecules of the living substance, and its appearance as active or atomic oxygen (p. 362); (2) Oxidation of the contractile substance by this oxygen; (3) The assimilation of oxygen by the contractile substance—*i.e.*, its passage into the *inogen* molecules (p. 247). According to him, it is the first of these stages which is associated with the abrupt development of the difference of potential between the excited and unexcited portions of the muscle which we call the negative variation. This first stage he assumes to be completed before the visible contraction begins; and he originally asserted that the same was true of the negative variation. It is now known that the latter, although it begins before the contraction, and very rapidly reaches its maximum, declines more gradually, so that it overlaps the mechanical change of form. This is particularly well seen in veratrinized muscles (p. 569), in which the electrical variation, like the contraction, is greatly prolonged (Garten). Nevertheless, Bernstein's theory, even with this limitation, agrees with what is known as to the influence exerted on the negative variation by the mechanical conditions of the contraction. For the electrical change is little, if at all, affected by the tension of the muscle or the load it has to lift; and this is what we should expect if it depends on a process which is mainly completed before the contraction begins. There are, however, certain facts which warn us against too confidently associating the negative variation with any absolutely essential step in the excitatory process. In regenerating nerves, apparently normal nerve impulses can be set up and propagated without any perceptible electrical variation. And Gotch and Burch sometimes found that in nerves kept (in normal saline solution made with tap-water) for twenty-four to forty-eight hours before observation, two electrical variations could be obtained in response to two successive stimuli from one part of the nerve, and only one from another—an anomaly which, since the physiological condition of the nerves was known to be very uniform, they could only explain by supposing that in the part of the nerve which showed only one variation the second excitatory process, although normally propagated, was not accompanied by a separate electrical change.

Physical explanations of the action current of muscle have been based on the hypothesis that in contraction variations in surface-tension, with accompanying electrical changes, occur at certain surfaces (surface of separation between light and dim discs, or between fluid contents and wall of sarcous capillary tubes). A great

objection to these theories is that in nerve, so far as we know, no sensible mechanical change whatever takes place during excitation, and that differences of potential exist or may be developed in tissues of the most diverse structure.

Although the electromotive changes caused by excitation are much more transient than those caused by injury, everything suggests that there must be some deep analogy between the two conditions. Some have supposed that what may be called a subdued and more or less permanent excitation exists in the neighbourhood of the injured tissue, and that this explains the similarity of electrical condition in activity and injury.

Polarization of Muscle and Nerve.*—We have already spoken of electrical excitation and of the changes of excitability caused by the passage of a constant current (p. 595). We are now to see that these physiological effects are accompanied by, and indeed very closely related to, more physical changes which the galvanometer or electrometer reveals to us. When a current is passed by means of unpolarizable electrodes (Fig. 156, p. 542), through a muscle or nerve for several seconds, and the tissue thrown on to the galvanometer immediately after this *polarizing* current is opened, a deflection is seen indicating a current (negative polarization current) in the opposite direction.

This negative polarization, like the polarization of the electrodes seen after passage of a current through any ordinary electrolytic conductor, dilute sulphuric acid, *e.g.*, depends on the liberation of ions (p. 362) at the kathode and anode. It is seen not only in muscle, nerve, and other animal tissues, but also in vegetable structures, and indeed, to a certain extent, in unorganized porous bodies soaked with electrolytes. In muscle and nerve, however, it is particularly well marked ; and although it is not bound up with the life of the tissue, and may be obtained when this has become quite inexcitable, it is nevertheless dependent on the preservation of the normal structure, for a boiled muscle shows but little negative polarization.

When the polarizing current is strong, and its time of closure short, we obtain, on connecting the tissue with the galvanometer after opening the current, not a negative, but a *positive* deflection, indicating a so-called *positive polarization current* in the same direction as that of the polarizing stream. This is really an action stream, due to the opening excitation set up at the anode (p. 553). It is only obtained when the tissue is living, and is far more strongly marked in the anodic than in the kathodic region.

* The portions in small type on pp. 638 to 643 may be omitted, except by students interested in the subject or reading for a special purpose.

Suppose that the nerve in Fig. 206 is stimulated by the opening of the battery B, and that, immediately after, the nerve is connected with the galvanometer G by the electrodes E, E_1. Suppose, further, that the shaded region near the anode remains more excited for a short time than the rest of the nerve, and we have seen (p. 596) that after the opening of a strong current there is a defect of conductivity, especially in the neighbourhood of the anode, which would tend to localize excitation. The portion of nerve at E being negative relatively to that at E_1, an action current will pass through the galvanometer from E_1 to E, and through the nerve in the same direction as the original stimulating stream; that is, it will have the direction of the positive polarization current.

Under certain conditions a state of continuous excitation in the anodic region of a nerve is shown by a tetanus of its muscle (*Ritter's tetanus*, p. 656, and Fig. 207).

Grützner and Tigerstedt have put forward a different theory of the break contraction. They say it is really a closing contraction due to the closure of the negative polarization current through the tissue itself, as soon as the polarizing current is opened. In fact, they admit only one kind of electrical stimulus, the kathodic, or make.

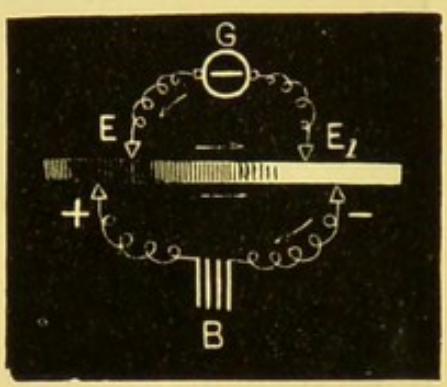


FIG. 206.—DIAGRAM TO SHOW DISTRIBUTION OF 'POSITIVE POLARIZATION' AFTER OPENING POLARIZING CURRENT.

B, battery; G, galvanometer. The dark shading signifies that the excitation to which the positive polarization current is due is greatest in the immediate neighbourhood of the anode, and fades away in the intrapolar region.

Electrotonic Currents.—If a current be passed from the battery through a medullated nerve (Fig. 208) in the direction indicated by the arrows, while a galvanometer is connected with either of the extra-polar areas, as shown in the figure, a current will pass through the galvanometer, in the same direction in the nerve as the polarizing current, so long as the latter continues to flow.

These currents are called *electrotonic* (in the kathodic region *kat-electrotonic;* in the anodic, *anelectrotonic*). The exact mode of their production is obscure. Similar currents can be detected in artificial models consisting of a good conducting core, and a badly conducting envelope; for example, a platinum wire in a glass tube filled with saturated zinc sulphate solution, or a zinc wire covered with cotton-wool soaked in salt solution. In such models it appears to be essential that there should be polarization (separation of ions) at the boundary between the core and the sheath, *i.e.*, between the wire and the liquid, where the current passes from the one to the other.

A current led into the sheath tries, so to speak, to pass mostly by the good conducting wire. If this is not polarizable—if it is, *e.g.*, a zinc wire surrounded by saturated zinc sulphate solution—there is little or no spreading of the current outside the electrodes: it passes at once into the core, and so on to the other electrode. If, however, there is polarization when the current passes from the liquid into the wire, as is the case in the platinum-zinc sulphate, or the zinc-sodium chloride combinations, the stream spreads longitudinally in the sheath since the polarization introduces a virtual resistance at the surface of the wire, in comparison with which the difference in resistance of an oblique and a direct transverse path through the liquid becomes small. It has been supposed that in medullated nerve a similar polarization takes place at the boundary between some part of the nerve-fibre which may be called a core, and another part which may be called a sheath, for instance, between the axis-cylinder and the medullary sheath, or between the latter and the neurilemma. It is known that the electrical resistance of nerve

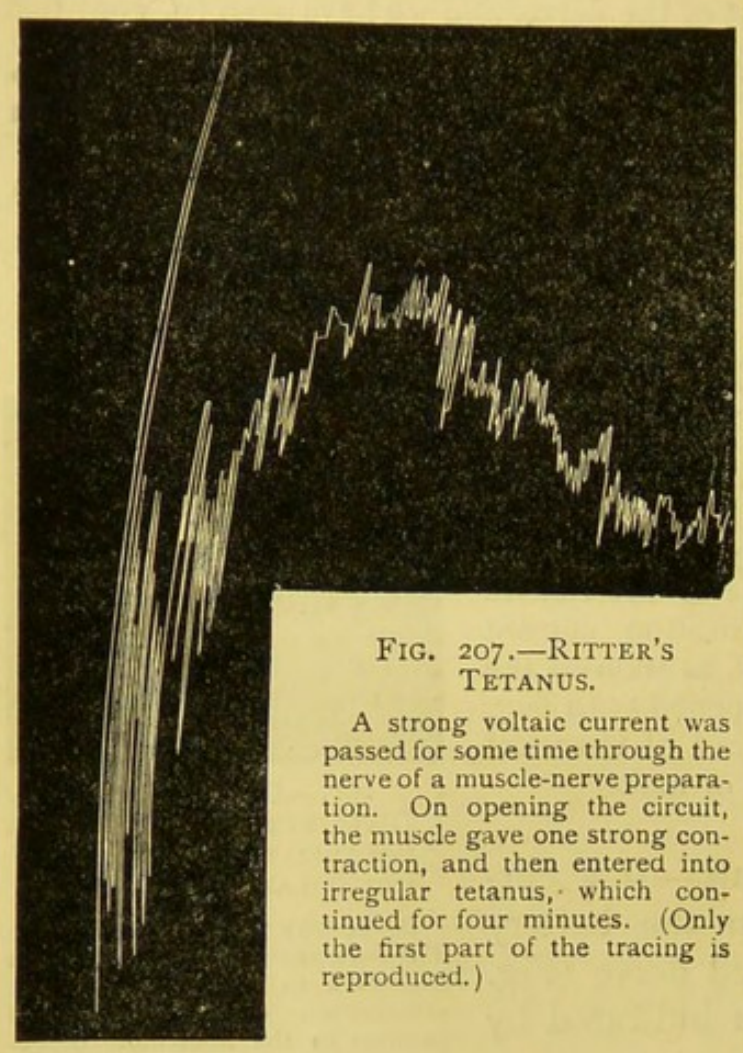


FIG. 207.—RITTER'S TETANUS.

A strong voltaic current was passed for some time through the nerve of a muscle-nerve preparation. On opening the circuit, the muscle gave one strong contraction, and then entered into irregular tetanus, which continued for four minutes. (Only the first part of the tracing is reproduced.)

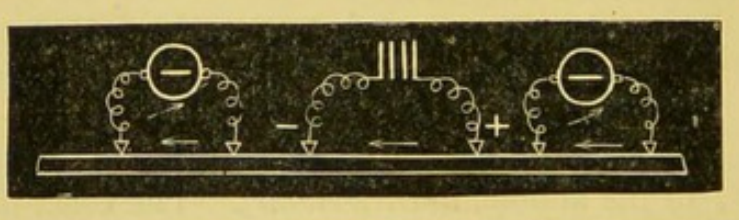


FIG. 208.—DIAGRAM SHOWING DIRECTION OF THE EXTRAPOLAR ELECTROTONIC CURRENTS.

in the transverse direction is much greater (five to seven times)* than

* Since a part of the current is conducted by the connective tissue and other structures lying between the nerve-fibres, and the longitudinal and transverse resistance of these tissues may be supposed equal, the disproportion between the longitudinal and transverse resistance of the nerve-fibres themselves is probably much greater than this.

the longitudinal resistance. Since a rapidly-established polarization would, by the ordinary methods of measurement, appear as a resistance, this has been adduced as evidence of the great capacity of nerve for polarization by a current passing across the fibres. It is, however, equally possible, from what we know of the enormous electrical resistance of the physiological envelopes of such cells as the red blood corpuscles (p. 35), that the great transverse resistance of nerve, and indeed the electrotonic currents, may be due in part if not wholly to the true resistance of one or more of its envelopes (perhaps the medullary sheath). Examples of such differences of resistance even in the fluid constituents of one and the same animal structure are not wanting. For instance, the resistance of the yolk of a hen's egg may be three times greater than that of the white.

The electrotonic currents cannot spread beyond a ligature; they are stopped by anything which destroys the structure of the tissue; they are affected by various reagents. But this does not prove that they are other than physical in origin, for what destroys the structure of the tissue or modifies its molecular condition may destroy or diminish its capacity for polarization, or alter its electrical resistance.

There are, however, certain facts which indicate that physiological factors, as well as physical, are concerned. While the currents obtained from core-models show a general resemblance to the electrotonic currents of medullated nerve, there is one significant difference: in the former the katelectrotonic and anelectrotonic currents are of equal intensity; in the latter the anelectrotonic preponderates. The most probable explanation is that the anelectrotonic current of medullated nerve is made up of two distinct electrical effects, one physiological in nature, the other dependent merely on the structure and physical properties of the fibres, while the katelectrotonic current is wholly physical. It is in favour of this hypothesis that under the influence of ether, which abolishes the physiological functions of nerve, the anelectrotonic current diminishes till it becomes equal to the katelectrotonic. Non-medullated nerves, in which the conditions for physical electrotonus, if present at all, are only feebly developed, and which exhibit no katelectrotonic current, or only a very weak one, show an anelectrotonic current, which is abolished by ether, and seems to represent the physiological portion of the anelectrotonic current of medullated nerve.

Physical electrotonus must be distinguished from the changes of excitability produced by the constant current, to which the name of electrotonus is also sometimes given. For although the decline in the intensity of the electrotonic currents, as we pass away from the electrodes, has its analogue in the distribution of the electrotonic changes of excitability, and there are other facts which suggest a relation between the two, we are ignorant of the real nature of this relation.

Effects of Stimulating a Polarized Nerve.—Stimulation of the nerve while the polarizing current is flowing causes in general in the extrapolar regions a *negative variation of the electrotonic current*, but in the intrapolar region a positive variation. The latter is undoubtedly

an action stream. Hermann has explained its direction on the assumption that the excitation diminishes in intensity as it approaches the kathode or recedes from the anode, and increases in intensity as it passes towards the anode or away from the kathode (law of polarization increment). But the fact that during the flow of a current the conductivity of the nerve is far more depressed around the kathode than near the anode affords a sufficient explanation.

The nerve-impulse, starting from the stimulating electrodes S (Fig. 209), will pass over E, the anode, in greater intensity than over E_1, the kathode; and therefore, upon the whole, during tetanus E will be negative to E_1, and a current of action will be developed in the same direction as the polarizing current, and reinforcing it. When the kathodic block is complete, and the excitation has to pass over the kathode before reaching the intrapolar region, no effect is produced by stimulation.

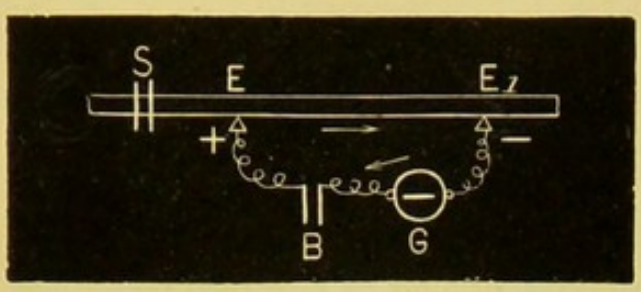


FIG. 209.—DIAGRAM SHOWING DIRECTION OF THE STIMULATION EFFECT IN THE INTRAPOLAR REGION DURING THE FLOW OF THE POLARIZING CURRENT.

The stimulation effects in the extrapolar regions are probably due partly to action currents, as is shown by the fact that when the polarizing current is strong enough to markedly depress the conductivity in the neighbourhood of the anode, the variation becomes positive instead of negative when one of the galvanometer electrodes lies near the anode. For here the excitation coming from S passes E_2 in far less intensity than E_3 (Fig. 210). E_3 is therefore, on the whole, during tetanus negative to E_2, and the direction of the action current in the nerve is from E_3 to E_2.

The negative variation in the extrapolar kathodic region could also be explained as an action current due to diminished conductivity in the neighbourhood of the kathode. But the negative anodic variation cannot be an action current, unless we suppose that with the weaker polarizing currents the conductivity is increased around the anode; and for this there is not sufficient proof. It is probable, therefore, that there is another factor mixed up with the currents of action, and in part opposing them. Some have supposed that the capacity for polarization between core and sheath is diminished during excitation, and that, accordingly, less of the current spreads beyond the electrodes,

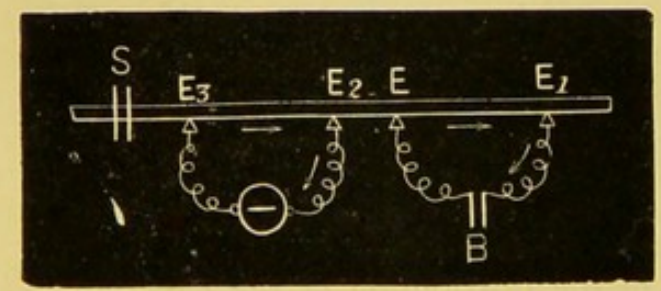


FIG. 210.—DIAGRAM TO SHOW DIRECTION OF THE POSITIVE STIMULATION EFFECT IN THE ANODIC EXTRAPOLAR REGION DURING THE FLOW OF A STRONG POLARIZING CURRENT.

and an apparent negative variation is caused in the extrapolar regions by stimulation. Or it may be that the excitation renders the envelope which interposes the chief resistance to the passage of ions into and out of the core more permeable. But there is no direct evidence for either view.

After the opening of the polarizing current, electromotive changes can, as we have seen, be recognised for a short time in the intrapolar area. This is also true of both extrapolar regions. The main after-current in the anodic region is in the opposite direction to the polarizing stream; but this is, under certain circumstances, preceded by a very short kick of the galvanometer magnet in the same direction. The kathodic after-current is in the same direction as the polarizing stream, and is, except with strong currents and a comparatively long time of closure, much weaker than the main anodic. The latter is to be looked upon as having the same origin as the positive polarization current of the intrapolar region, a state of opening excitation around the anode; in other words, it is an action current. The kathodic and the preliminary anodic after-currents are probably due to negative polarization.

Stimulation of the nerve after opening the polarizing current causes well-marked effects; in the intrapolar region the stimulation effect is in the opposite direction to the polarizing current; in the extrapolar anodic area, in the same direction as the polarizing stream. In the extrapolar kathodic region, it is in the opposite direction, and, except with strong polarizing currents, and a more than momentary time of closure, less in amount than the stimulation effect in the anodic region.

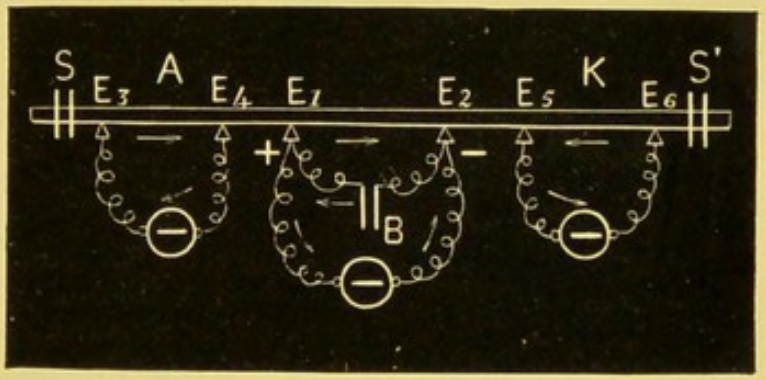


FIG. 211.—DIAGRAM SHOWING THE DIRECTION OF THE STIMULATION EFFECTS AFTER OPENING THE POLARIZING CURRENTS IN THE ANODIC AND KATHODIC EXTRAPOLAR REGIONS (A AND K), AND IN THE INTRAPOLAR REGION E_1, E_2.

All these cases are readily explained by the fact that immediately after opening the polarizing current the conductivity of the nerve is more depressed in the anodic than in the kathodic region, although with strong currents it is depressed in both. An excitation reaching the extrapolar anodic area from S will pass over E_3 in greater intensity than over E_4 (Fig. 211). E_4 will therefore be positive to E_3, and the action current will go through the nerve in the direction of the arrow. An excitation reaching the kathodic extrapolar area from S′ will arrive at E_6 in greater intensity then at E_5. The resultant action stream will therefore have the direction in the nerve from E_6 to E_5. And the effects in the intrapolar region can be similarly explained.

A nerve may be stimulated by an electrotonic current produced in nerve-fibres lying in contact with it. A well-known illustration of this is the experiment known as the *paradoxical contraction* (Practical Exercises, p. 654).

The current of action of a nerve can also stimulate another nerve when the excitability of both is greater than normal, as is the case in the nerves of frogs kept in the cold. This comes under the head of **secondary contraction.** But the best-known form of secondary contraction is where a nerve, placed on a muscle so as to touch it in two points (Fig. 212), is stimulated by the action-current of the muscle, and causes its own muscle to contract. A **secondary tetanus** can be obtained in this way by dropping a nerve on an artificially tetanized muscle. The beat of the heart causes usually only a single secondary contraction when the sciatic nerve of a frog is allowed to fall on it (p. 179). But when the diphasic variation is well marked, as it is in an uninjured heart, there may be a secondary contraction for each phase, *i.e.*, two for each heart-beat. Excitation of one muscle may in the same way cause secondary contraction of another with which it is in close contact.

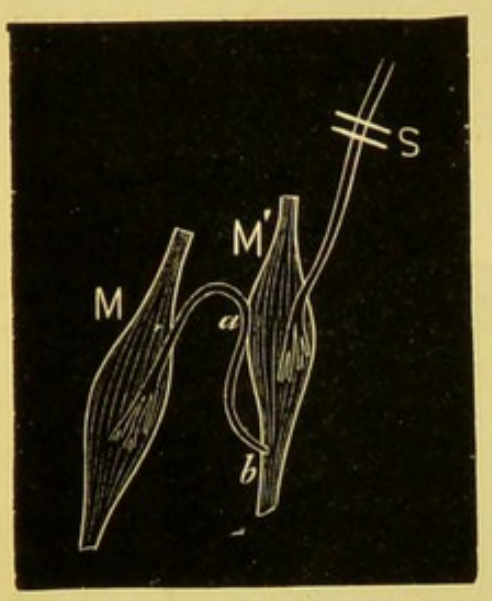


FIG. 212. — SECONDARY CONTRACTION.

The nerve of muscle M touches muscle M′ at *a* and *b*. Stimulation of the nerve of M′ at S causes contraction of M.

The electromotive phenomena of the heart and of the central nervous system are naturally included under those of muscle and nerve.

Heart.—In the frog's heart with each systole the diphasic variation consists of a first phase, during which the base is negative to the apex, and a second phase, during which the apex is negative to the base. The meaning of this is that the negative electrical change, like the contraction, starts at the base, and passes on to the apex. Sometimes a third phase is seen (triphasic variation), in which the base again becomes negative to the apex. It has been supposed that this is due to the contraction of the arterial bulb, which follows

that of the rest of the heart. If the tissue is injured at either leading-off electrode, the corresponding phase of course disappears.

In the uninjured mammalian heart, beating as far as possible under normal conditions, the sequence is the same, the diphasic variation showing first base negative to apex, then apex negative to base. Statements to the contrary seem to have been founded on observation of injured hearts, or hearts placed under abnormal conditions. For example, when the base of the heart is cooled, the variation first becomes triphasic, the sequence of the relative negativity being base—apex—base; and finally diphasic with a sequence the reverse of the normal, the apex being first negative, then the base.

The Human Electro-cardiogram.—An electrical change accompanies every beat of the human heart. Waller has shown how this may be demonstrated by means of the capillary electrometer. His experiments and later work by Bayliss and Starling indicate a triphasic variation—first base negative to apex, then apex negative to base, and then again base negative to apex.

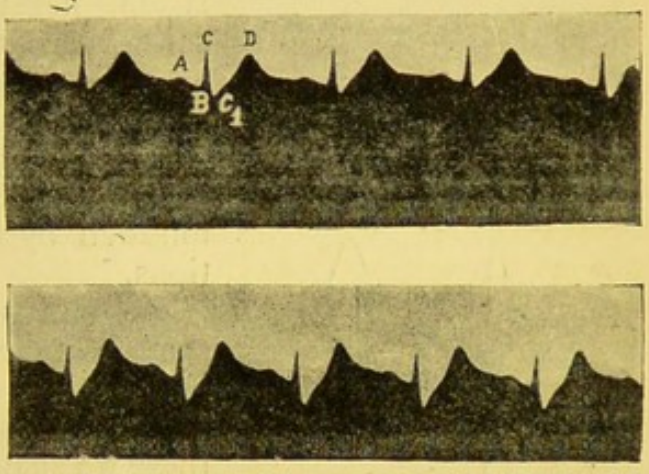


FIG. 213. — ELECTRO-CARDIOGRAMS FROM MAN (EINTHOVEN and LINT).

The image of the capillary magnified eight hundred times was projected on a moving photographic plate. The figure is a reproduction of the record (reduced to two-thirds of its original size) obtained from the same individual at rest (upper curve), and immediately after vigorous muscular exercise (lower curve). The movements of a tuning-fork, making fifty complete vibrations a second, are shown below the cardiograms. The sulphuric acid pole of the electrometer was connected with the thoracic wall in the neighbourhood of the apex of the heart and the mercury with the right arm. The elevations A, C, and D indicate negativity of base to apex; the notches B and C, negativity of apex to base.

Einthoven and Lint have recently investigated the phenomenon on a large number of persons. From the photographic records of the movements of the meniscus (Fig. 213) they have constructed the true electro-cardiographic curves* (Fig. 214), which express the actual changes in the potential difference between the two points led off. They distinguish in every one of these constructed electro-cardiograms five points or cusps, three of which indicate negativity of the base of the heart to the apex, and two negativity of the apex to the base. The electro-cardiograms are distinctly affected by exercise and by the position of the body, and may be useful in the investigation of disease. These observers confirm Waller's statement that it is best to connect one electrode with the thoracic wall over the apex of the heart, and the

* In all accurate work with the capillary electrometer such curves must be obtained by construction from the direct photographic records, which do not themselves give an absolutely true picture of the variations.

other with the right arm or the region of the right scapula. The two feet are the most unfavourable combination.

Central Nervous System.—It was discovered by du Bois-Reymond that the spinal cord, like a nerve, shows a current of rest between longitudinal surface and cross-section, and that a current of action is caused by excitation. Setschenow stated that when the medulla oblongata of the frog was connected with a galvanometer, spontaneous variations occurred which he supposed due to periodic functional changes in its grey matter. Gotch and Horsley have made elaborate experiments on the spinal cord of cats and monkeys. Leading off from an isolated portion of the dorsal cord to the capillary electrometer, and stimulating the motor part of the cortex cerebri, they obtained a persistent negative variation followed by a series of intermittent variations. This agrees remarkably with the muscular contractions in an epileptiform convulsion started by a similar excitation of the cortex, which consist of a tonic spasm followed by clonic (interrupted) contractions.

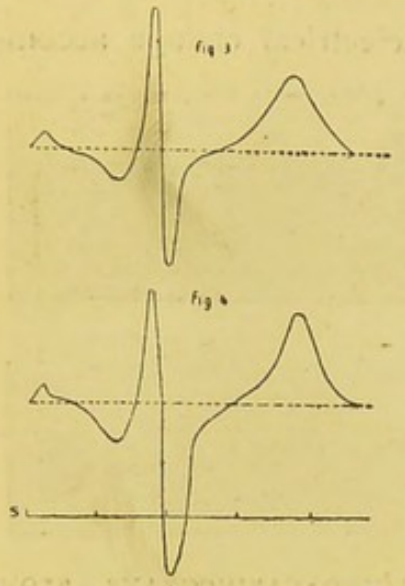


FIG. 214.—CONSTRUCTED ELECTRO - CARDIOGRAMS FROM MAN (EINTHOVEN AND LINT).

The curves are constructed from the photographic records shown in Fig. 213. These and not the photographs are the true expression of the actual changes of potential during the cardiac cycle. Time is laid off along the horizontal, and electromotive force along the vertical axis, the same space being allotted to ten millivolts (*i.e.*, $\frac{1}{100}$ volt) as to one second.

By means of the galvanometer the same observers have made investigations on the paths by which impulses set up at different points travel along the cord. To these we shall have to refer again (p. 702).

Electromotive changes are said to occur in the **cerebral cortex**, when various sensory nerves are stimulated—for example, when the retina is excited by light. But only a few experiments have hitherto been made (by Caton, Beck, and Fleischl), and it is not certain that the observed differences of potential have their seat in the grey matter. They may be due merely to the excitation of the white fibres.

Glandular Currents.—These have been studied with any care only in the sub-maxillary gland and in the skin, although the liver, kidney, spleen, and other organs, also show currents when injured. In the sub-maxillary gland the hilus is positive to any point on the external surface of the gland; a current passes from hilus to surface through the galvanometer, and from surface to hilus through the gland (Fig. 215). When the chorda tympani is stimulated with rapidly-succeeding shocks of moderate strength, there is a positive variation; *i.e.*, the surface becomes still more negative to the hilus. This variation can be abolished by a small dose of atropia, and then stimulation causes a slight negative variation. A further dose of atropia abolishes this, too. With slowly-interrupted shocks (not more than five per second) a large negative

variation is caused, and no positive variation, and the same is true of rapid stimuli too weak to excite secretion.

Single induction shocks cause a diphasic variation, the surface of the gland becoming first more negative and then more positive to the hilus, so that a positive deflection of the galvanometer is followed by a negative.

In nearly all circumstances stimulation of the sympathetic causes a negative variation. Bradford, to whom, and to Bayliss, we are indebted for our knowledge of this subject, explains the different behaviour of the chorda tympani to different kinds of stimulation as due to the existence in it of anabolic fibres, which increase the building up of the proper substance of the gland, in addition to the katabolic fibres, which increase destructive metabolism and cause secretion (p. 339).

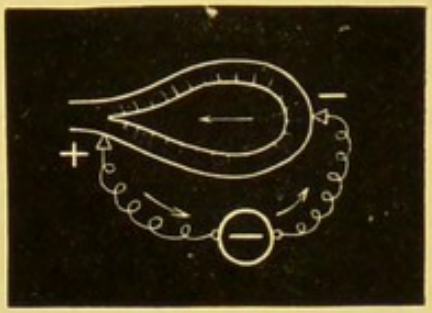


FIG. 215.—CURRENT OF SUB-MAXILLARY GLAND.

Skin Currents.—So far as has been investigated, the integument of all animals shows a permanent current passing in the skin from the external surface inwards. This is feebler in skin which possesses no glands. In skin containing glands the current is chiefly, but not altogether, secretory. As such, it is affected by influences which affect secretion, a positive variation being caused by excitation of secretory nerves, *e.g.*, in the pad of the cat's foot by stimulation of the sciatic. The deflection obtained when a finger of each hand is led off to the galvanometer, which was at one time looked upon as a proof of the existence of currents of rest in intact muscles, is due to a secretion current, and the variation seen during voluntary contraction of the muscles of one arm is also in part a secretion stream.

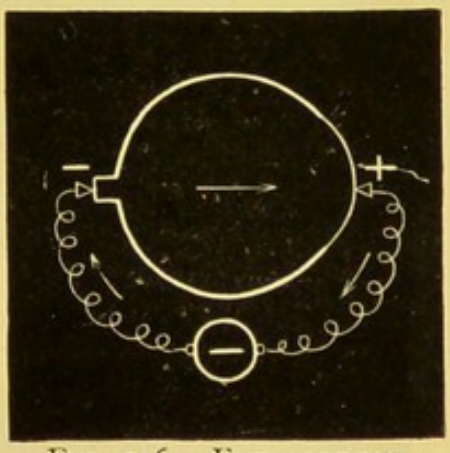


FIG. 216.—EYE-CURRENT.

Of more doubtful origin is the current of **ciliated mucous** membrane, which has the same direction as that of the skin of the frog and the mucous membrane of the stomach of the frog and rabbit—viz., from ciliated to under surface through the tissue, or from ciliated surface to cross-section, if that is the way in which it is led off. The current is strengthened by induction shocks, by heating, and in general by influences which increase the activity of the cilia. Some circumstances point to the goblet-cells in the membrane as the source of the current; but, on the whole, the balance of evidence is in favour of the cilia being the chief factor (Engelmann), although the mucin-secreting cells may be concerned, too.

Eye-currents.—If two unpolarizable electrodes connected with a galvanometer are placed on the excised eye of a frog or rabbit, one

on the cornea and the other on the cut optic nerve, it is found that a current due to the injured nerve passes in the eye from optic nerve to cornea. The current has the same direction if the anterior electrode is placed on the retina itself, the front of the eyeball being cut away, or if one electrode is in contact with the anterior and the other with the posterior surface of the isolated retina. There is nothing of special interest in this ; but the important point is that if light be now allowed to fall upon the eye, or better, the isolated retina, an electrical change is caused, generally first a positive and then a negative variation, succeeded by another positive movement when the light is cut off.

The variations depend upon the retina alone, and do not occur when it is removed. Bleaching of the visual purple does not much affect them, so that they are not connected with chemical changes in

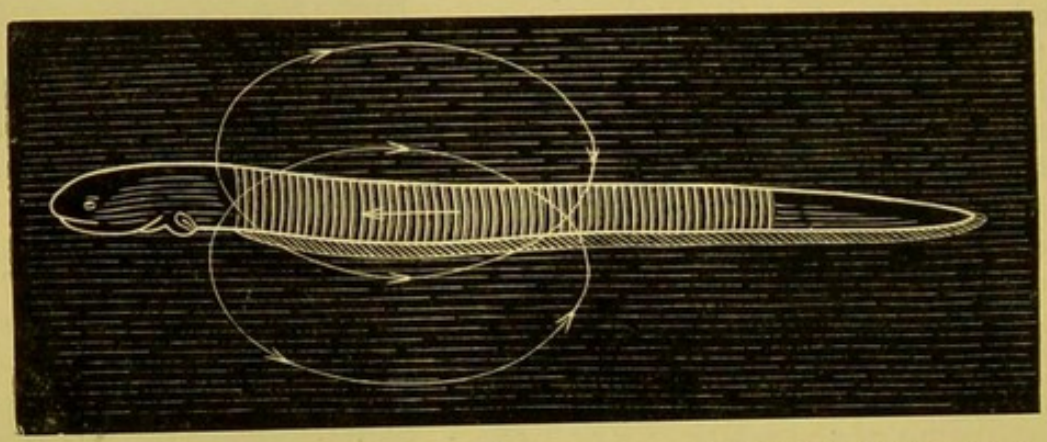


FIG. 217.—DIAGRAM SHOWING DIRECTION OF SHOCK IN GYMNOTUS.

this substance. Of the spectral colours, yellow light causes the largest variation ; blue, the least ; but white light is more powerful than either. (Dewar and McKendrick.) (For 'visual purple' see Chapter XIII.)

Electric Fishes.—Except lightning, the shocks of these fishes were probably the first manifestations of electricity observed by man. The *Torpedo*, or electrical ray, of the coasts of Europe was known to the Greeks and Romans. It is mentioned in the writings of Aristotle and Pliny, and had the honour of being described in verse 1,500 years before Faraday made the first really exact investigation of the shock of the *Gymnotus*, or electric eel, of South America. Another of the electric fishes, *Malapterurus electricus*, although found in

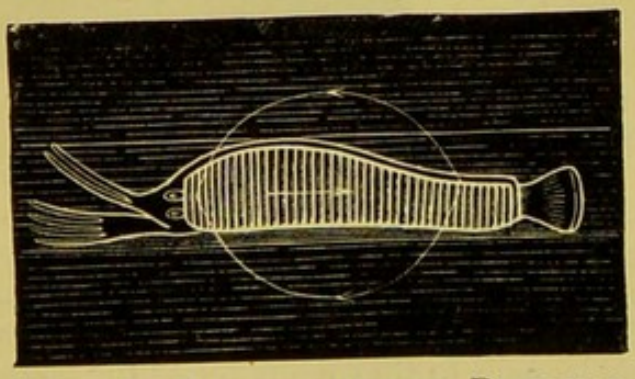


FIG. 218.—DIAGRAM SHOWING DIRECTION OF SHOCK IN MALAPTERURUS.

many of the African rivers, the Nile in particular, and known for ages, was scarcely investigated till forty years ago.

In all these fishes there is a special bilateral organ immediately under the skin, called the electrical organ. It is in this that the shock is developed. It consists of a series of plates arranged parallel to each other. To one side of each plate a branch of the electrical nerve supplying each lateral half of the organ is distributed. This side of the plate during the shock becomes negative to the other (Pacini's rule), so that each half of the organ represents a battery of many cells arranged in series. The direction of the shock through the organ depends on the side of the plate to which the nerve-supply goes, and the arrangement of the plates with reference to the natural position of the animal.

Thus, in Gymnotus the plates are vertical, and at right angles to the long axis of the fish, and the nerves are distributed to their posterior surface; the shock accordingly passes in the animal from tail to head. In Malapterurus, although the arrangement of the plates is the same, the nerve-supply is to the anterior surface; for Max Schultze has shown that although the nerve appears to sink into the posterior surface, it really passes through a hole in the plate, and spreads out on its anterior face. The shock passes from head to tail.

In Torpedo, the plates or septa dividing the vertical hexagonal prisms of which each lateral half of the organ consists are horizontal; the nerve-supply is to the lower or ventral surface; and the shock passes from belly to back through the organ. In all electric fishes the discharge is discontinuous; an active fish may give as many as 200 shocks per second.

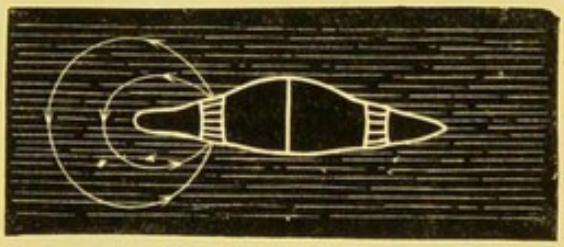


FIG. 219.—DIAGRAM SHOWING DIRECTION OF SHOCK IN TORPEDO.

The electrical nerve of Malapterurus is very peculiar. It consists of a single gigantic nerve-fibre on each side, arising from a giant nerve-cell. The fibre has an enormously thick sheath, the axis cylinder forming a relatively small part of the whole; and the branches which supply the plates of the organ are divisions of this single axis cylinder.

The electromotive force of the shock of the Gymnotus may be very considerable; and even Torpedo and Malapterurus are quite able to kill other fish, their enemies or their prey. Indeed, Gotch has estimated the electromotive force of 1 cm. of the organ of Torpedo at 5 volts, and Schönlein finds that the electromotive force of the whole organ may be equal to that of 31 Daniell cells, or 0·08 volt for each plate, and it is one of the most interesting questions in the whole of electro-physiology, how they are protected from their own currents. There is no doubt that the current density inside the fish must be at least as great as in any part of the water surrounding it, and probably much greater. The central nervous system and the great nerves must be struck by strong shocks, yet the fish itself is not injured; nay more, the young in the uterus of the viviparous Torpedo are unharmed. The only explanation seems to be that the tissues of

electric fishes are far less excitable to electrical stimuli than the tissues of other animals; and this is found to be the case when their muscles or nerves are tested with galvanic or induction currents. It requires extremely strong currents to stimulate them; and the electrical nerves are more easily excited mechanically, as by ligaturing or pinching, than electrically. In general, too, the shock is more readily called forth by reflex mechanical stimulation of the skin than by electrical stimulation. But that the organ itself is excitable by electricity has been shown by Gotch. He proved that in Torpedo a current passed in the normal direction of the shock is strengthened, and a current passed in the opposite direction weakened, by the development of an action current in the direction of the shock. And indeed a single excitation of the electrical nerve is followed by a *series* of electrical oscillations in the organ, which gradually die away. The latent period of a single shock is about $\frac{1}{200}$ second. The skate must now be added to the list of electric fishes. Although its organ is relatively small, and its electromotive force relatively feeble, yet it is in all respects a complete electrical organ. It is situated on either side of the vertebral column in the tail. The plates or discs are placed transversely and in vertical planes. The nerves enter their anterior surfaces; the shock passes in the organ from anterior to posterior end. Gotch and Sanderson have estimated the maximum electromotive force of a length of 1 cm. of the electrical organ of the skate at about half a volt.

Whether the electrical organ is the homologue of muscle or of nerve-ending, or whether it is related to either, has been much discussed. Our surest guide in a question of this sort is the study of development; and researches along this line have shown that there are two kinds of electrical organ, one being modified muscle (as in Gymnotus and Torpedo, and the skate), the other transformed skin glands (as in Malapterurus). Curara does not affect the electrical organ in Torpedo, although, as we have seen, it paralyzes motor nerve-endings.

Galvanotropism is the name given to a group of curious reactions shown by many small animals, and particularly certain unicellular organisms, when the liquid in which they swim is traversed by a constant current. Some kinds of infusoria, *e.g.*, *Paramœcium*, travel in the direction of the current towards the kathode and collect there, others towards the anode. Animals higher in the scale, as small crabs, also exhibit the phenomenon, and move towards the anode. Tadpoles and young fish arrange themselves with their long axis in the direction of the current, and their heads turned to the anode. As to the cause of the effects in those more highly organized animals, it has been suggested that they take up the position in which they are least stimulated, in order to escape disagreeable sensations excited by the current. But the extensive studies of Loeb lend no support to this idea; in vertebrates as well as in crabs he believes that the galvanotropic phenomena are due to alterations produced by the current in the action of associated groups of muscles, whereby movement of the body or turning of the head towards one pole is rendered easier than towards the other.

PRACTICAL EXERCISES ON CHAPTER XI.

1. **Galvani's Experiment.**—Pith a frog (brain and cord). Cut through the backbone above the urostyle, and clear away the anterior portion of the body and the viscera. Pass a copper hook beneath the two sciatic plexuses, and hang the legs by the hook on an iron tripod. If the tripod has been painted, the paint must be scraped away where the hook is in contact with it. Now tilt the tripod so that the legs come in contact with one of the iron feet. Whenever this happens, the current set up by the contact of the copper and iron is completed, the nerves are stimulated, and the muscles contract (p. 628).

2. Make a muscle-nerve preparation from the same frog. Crush the muscle near the tendo Achillis, so as to cause a strong demarcation current. Cut off the end of the sciatic nerve. Then lift the nerve with a small brush or thin glass rod, and let its cross-section fall on or near the injured part of the muscle. Every time the nerve touches the muscle a part of the demarcation current passes through it, stimulates the nerve, and causes contraction of the muscle (p. 628).

3. Make a muscle-nerve preparation. Lay it on a glass plate A, supported on a block of wood. Snip off the end of the nerve N, and arrange the cut surface on a pad of kaolin B, moistened with normal saline. Another pad B′ is placed under the nerve a little way from its cut end. Both pads project down over the edge of the glass plate. A watch-glass C filled with normal saline solution is lifted up below the projecting ends till they are immersed. Whenever this happens, a circuit is completed for the demarcation current of the nerve itself, by which it is stimulated, and the muscle M contracts (Fig. 220).

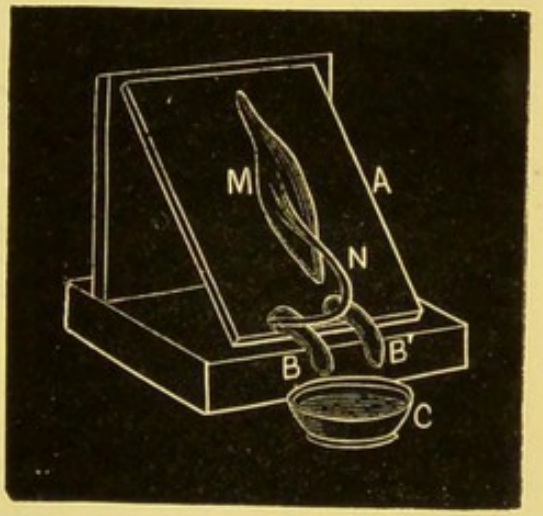


FIG. 220.—STIMULATION OF A NERVE BY ITS OWN DEMARCATION CURRENT.

4. **Secondary Contraction.**—Make two muscle-nerve preparations. Lay the cross-section of one of the sciatic nerves on the muscle of the other preparation (Fig. 212, p. 644). Place under the nerve near its cut end a small piece of glazed paper or of glass rod, and let the longitudinal surface of the nerve come in contact with the muscle beyond this. Lay the nerve of the other preparation on electrodes connected with an induction machine arranged for single shocks, with a Daniell cell and a spring key in the primary circuit (Fig. 189). On closing or opening the key *both* muscles contract. Arrange the induction machine for an interrupted current. When it is thrown into one nerve, both muscles are tetanized; the nerve lying on the muscle whose nerve is directly stimulated is excited by the action current of the muscle.

5. **Demarcation Current and Current of Action with Capillary Electrometer.**—(*a*) Study the construction of the capillary electrometer (Fig. 153, p. 538). Raise the glass reservoir by the rack and pinion screw, so as to bring the meniscus of the mercury into the field. Place two moistened fingers on the binding-screws of the electrometer, open the small key connecting them, and notice that the mercury moves, a difference of potential between the two binding-screws being caused by the moistened fingers.

(*b*) *Demarcation Current.*—Set up a pair of unpolarizable electrodes (Fig. 156, p. 542). Fill the glass tubes about one-third full of kaolin mixed with normal saline solution till it can be easily moulded. To do this, make a piece of the clay into a little roll, which will slip down the tube. Then with a match push it down until it forms a

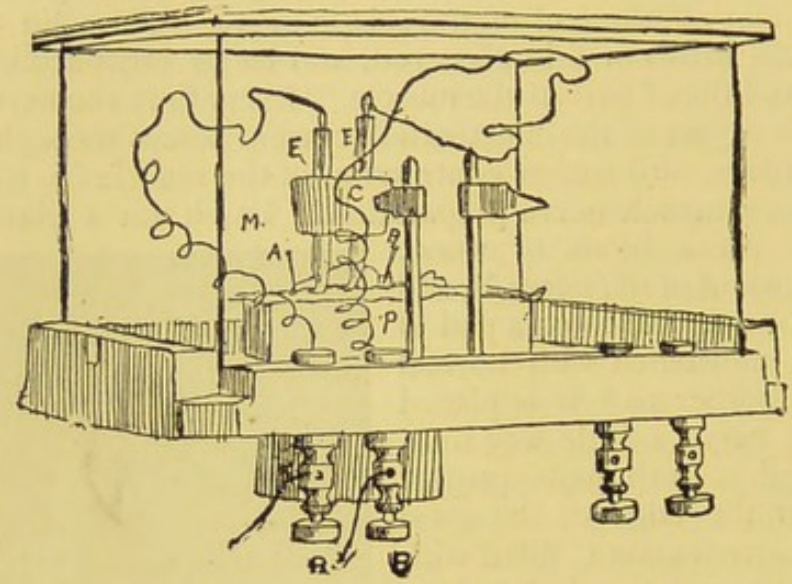


FIG. 221.—MOIST CHAMBER.

E, unpolarizable electrodes supported in the cork C; M, muscle stretched over the electrodes and kept in position by the pins A, B stuck in the cork plate P; B, binding-screws connected with galvanometer or capillary electrometer. The other pair of binding-screws serves to connect a pair of stimulating electrodes inside the chamber with the secondary coil of an induction machine.

firm plug. Next put some saturated zinc sulphate solution in the tubes, above the clay, with a fine-pointed pipette. Fasten the tubes in the holder fixed in the moist chamber (Fig. 221). Now amalgamate the small pieces of zinc wire (p. 173), which are to be connected with the binding-screws of the chamber.

The zincs are now placed in the tubes, dipping into the zinc sulphate. A piece of clay or blotting-paper moistened with normal saline is laid across the electrodes to complete the circuit between their points, and they are connected with the electrometer to test whether they have been properly set up. There ought to be little, if any, movement of the mercury on opening the side-key of the electrometer. If the movement is large, the electrodes are 'polarized,' and must be set up again. The second pair of binding-screws in the chamber are connected with a pair of platinum-pointed electrodes on

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the one side, and on the other, through a short-circuiting key, with the secondary coil of an induction machine arranged for tetanus.

Next pith a frog (cord and brain), and make a muscle-nerve preparation. Injure the muscle near the tendo Achillis. Lay the injured part over one unpolarizable electrode, and an uninjured part over the other. Put a wet sponge in the chamber to keep the air moist, and place the glass lid on it. Focus the meniscus of the mercury, and open the key of the electrometer; the mercury will move, perhaps right out of the field. Note the direction of movement, and remembering that the real direction is the opposite of the apparent direction, and that when the mercury in the capillary tube is positive to the sulphuric acid, the movement is from capillary to acid, determine which is the positive and which the negative portion of the muscle (p. 629).

(*c*) *Action Current.*—Now fasten the muscle to the cork or paraffin plate in the moist chamber, without disturbing its position on the electrodes, by pins thrust through the lower end of the femur and the tendo Achillis. Lay the nerve on the platinum electrodes. Open the key of the electrometer, and let the meniscus come to rest. This happens very quickly, as the capillary electrometer has but little inertia. If the meniscus has shot out of the field, it must be brought back by raising or lowering the reservoir. Stimulate the nerve by opening the key in the secondary circuit; the meniscus moves in the direction opposite to its former movement.

(*d*) Repeat (*b*) and (*c*) with the nerve alone, laying an injured part (crushed, cut, or over-heated) on one electrode, and an uninjured part on the other. Of course the nerve does not need to be pinned.

Clean the unpolarizable electrodes, and be sure to lower the reservoir of the electrometer; otherwise the mercury may reach the point of the capillary tube and run out.

In 5 a galvanometer (p. 535) may be used with advantage by students, if one is available, instead of the electrometer, the unpolarizable electrodes being connected to it through a short-circuiting key. The spot of light is brought to the middle of the scale by moving the control-magnet; or if a telescope-reading (Fig 149, p. 535) is being used, the zero of the scale is brought by the same means to coincide with the vertical hair-line of the telescope. The short circuiting-key is then opened.

6. **Action-current of Heart.**—Pith a frog (brain and cord). Excise the heart, and lay the base on one unpolarizable electrode, and the apex on the other, having a sufficiently large pad of clay on the tips of the electrodes to ensure contact during the movements of the heart, or having little cups hollowed in the clay and filled with normal saline, into which the organ dips. Connect the electrodes with the capillary electrometer and open its key. At each beat of the heart the mercury will move (p. 644).

7. **Electrotonus.**—Set up two pairs of unpolarizable electrodes in the moist chamber. Connect two of them with a capillary electrometer (or galvanometer), and two with a battery of three or four small Daniell cells, as in Fig. 208. Lay a frog's nerve on the electrodes. When the key in the battery circuit is closed, the mercury (or the

needle of the galvanometer) moves in such a direction as to indicate that in the extrapolar regions parts of the nerve nearer to the anode are positive to parts more remote, and parts nearer to the kathode are negative to parts more remote. The direction of movement of the mercury (or galvanometer needle) must be made out first for one direction of the polarizing current. Then the latter must be reversed, and the movement of the mercury (or needle) on closing it again noted (p. 639).

8. **Paradoxical Contraction.**—Pith a frog (brain and cord). Dissect out the sciatic nerve down to the point where it splits into two divisions, one for the gastrocnemius *b*, and the other for the peroneal muscles *a*. Divide the peroneal branch as low down as possible, and make a muscle-nerve preparation in the usual way. Lay the central end of the peroneal nerve on electrodes connected through a simple key with a battery of two Daniell cells. When the peroneal nerve is stimulated the gastrocnemius muscle contracts. This result is not due to the current of action, for it is not obtained with mechanical stimulation of the nerve ; but it is not the result of an escape of current, for if the peroneal nerve be ligatured between the point of stimulation and the bifurcation, no contraction is obtained. The contraction is really due to a part of the electrotonic current set up in the peroneal nerve passing through the fibres for the gastrocnemius, where they lie side by side in the trunk of the sciatic.

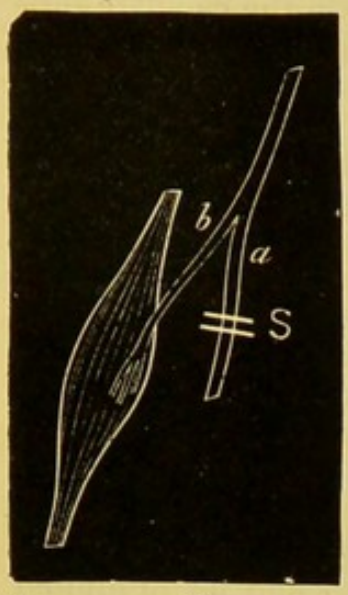


FIG. 222.—PARADOXICAL CONTRACTION.

9. **Alterations in Excitability and Conductivity produced in Nerve by the Passage of a Voltaic Current through it.**—(*a*) Set up two pairs of unpolarizable electrodes in the moist chamber.

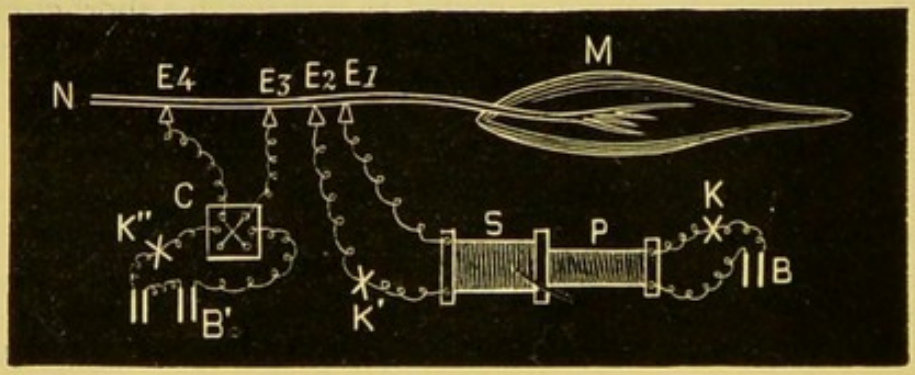


FIG. 223.—ARRANGEMENT FOR SHOWING CHANGES OF EXCITABILITY PRODUCED BY THE VOLTAIC CURRENT.

M, muscle ; N, nerve ; E_1, E_2, electrodes connected with secondary coil S ; E_3, E_4, unpolarizable electrodes connected with Pohl's commutator (with cross-wires) C ; B′, 'polarizing' battery ; B, 'stimulating' battery in primary circuit P ; K, K″, simple keys ; K′, short-circuiting key.

Connect a battery of two or three Daniell cells, arranged in series through a simple key with the side-cups of a Pohl's commutator with

cross-wires in. Connect the commutator to one pair of the unpolarizable electrodes ('the polarizing electrodes'), as in Fig. 223. The other pair of unpolarizable electrodes ('the stimulating electrodes') are to be connected through a short-circuiting key with the secondary of an induction machine arranged for tetanus. A single Daniell is put in the primary coil. Pith a frog (brain and cord), make a muscle-nerve preparation, pin the lower end of the femur to the cork plate in the moist chamber, attach the thread on the tendo Achillis to the lever connected with the chamber through the hole in the glass provided for this purpose, and arrange the nerve on the electrodes so that the stimulating pair is between the muscle and the polarizing pair. By moving the secondary, seek out such a strength of stimulus as just suffices to cause a weak tetanus when the polarizing current is not closed. Set the drum off (slow speed), and take a tracing of the contraction. Then close the polarizing current with the Pohl's commutator so arranged that the anode is next the stimulating electrodes, *i.e.*, the current ascending in the nerve. Again open the short-circuiting key in the secondary; the contraction will now be weaker than before, or no contraction at all may be obtained. Allow the preparation two minutes to recover, then stimulate again, as a control, without closing the polarizing current. If the contraction is of the same height as at first, close the polarizing current with the bridge of the commutator reversed, so that the kathode is now next the stimulating electrodes. On stimulating, the contraction will now be increased in height. (See Figs. 184, 185, p. 597.)

(*b*) Arrange everything as in (*a*), except that one of the polarizing electrodes is placed at each end, and the two stimulating electrodes close together in the middle of the nerve. A large carbon resistance (say 500,000 ohms) is introduced into the circuit of the secondary coil, to prevent more than a very small fraction of the polarizing current from passing through the coil. Seek out the strength of stimulation which just causes contraction when the polarizing current is not closed. Now close the polarizing current in such a direction that the anode is between the stimulating electrodes and the muscle. If no contraction occurs on stimulation, push up the secondary towards the primary till the muscle contracts. Then stop stimulation, open the polarizing current, and allow an interval of two minutes. Now pass the polarizing current through the nerve in the opposite direction, so that the kathode is between the stimulating electrodes and the muscle. No contraction will be obtained on exciting with the same strength of stimulus as caused contraction when the anode was next the muscle. The kathode has diminished the conductivity of the nerve; and if four or five small Daniell cells are put on in the polarizing circuit, no contraction may be obtained, even with the coils close together, while the excitation will still pass the anode and cause contraction.

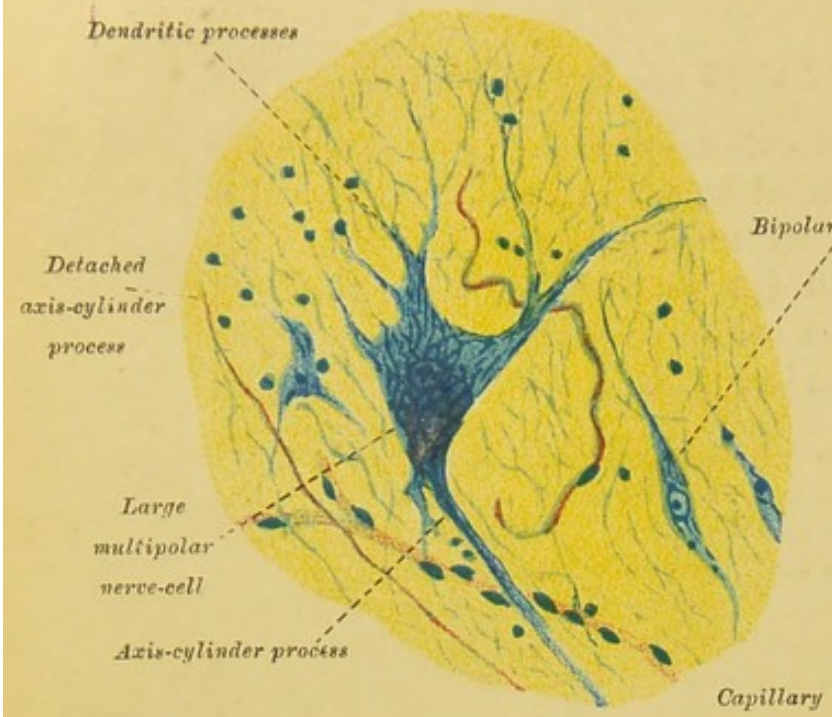
10. **Pflüger's Formula of Contraction** (p. 597).—To demonstrate this, connect two unpolarizable electrodes, through a spring key and a commutator, with a simple rheocord (Fig. 191), so as to lead off a twig of a current from a Daniell cell. The unpolarizable elec-

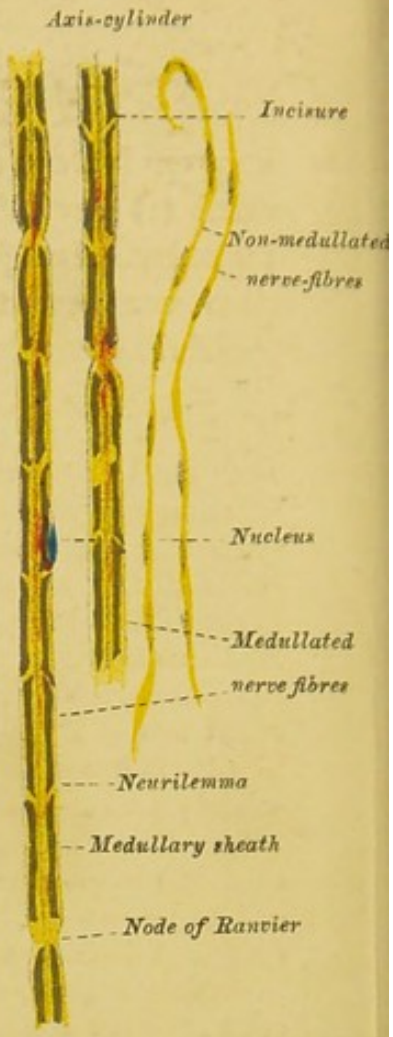
trodes are placed in a moist chamber. A muscle-nerve preparation is arranged with the nerve on the electrodes and the muscle attached to a lever. The effects of make and break of a weak current, ascending and descending, can be worked out with the simple rheocord. The effects of a medium current will probably be obtained with a single Daniell connected directly with the electrodes through a key. The effects of a strong current will be got when three or four Daniells are connected with the electrodes. Care must be taken to keep the preparation in a moist atmosphere, and more than one preparation may be needed to verify the whole formula.

11. **Ritter's Tetanus.**—Lay the nerve of a muscle-nerve preparation on a pair of unpolarizable electrodes connected through a simple key with a battery of three or four small Daniells. Connect the muscle with a lever. Pass an ascending current (anode next the muscle) for a few minutes through the nerve, and let the writing-point trace on a slowly-moving drum. When the current is closed there may be a single momentary twitch, or the muscle may remain somewhat contracted (galvanotonus) as long as the current is allowed to pass, or it may continue to contract spasmodically ('closing tetanus'). When the current is opened the muscle will contract once, and then immediately relax, or there may be a more or less continued tetanus (Ritter's or 'opening tetanus'). If opening tetanus is obtained, divide the nerve between the electrodes: the tetanus continues. Divide it between the anode and the muscle: the tetanus at once disappears. This shows that the seat of the excitation which causes the tetanus is in the neighbourhood of the anode (p. 640).

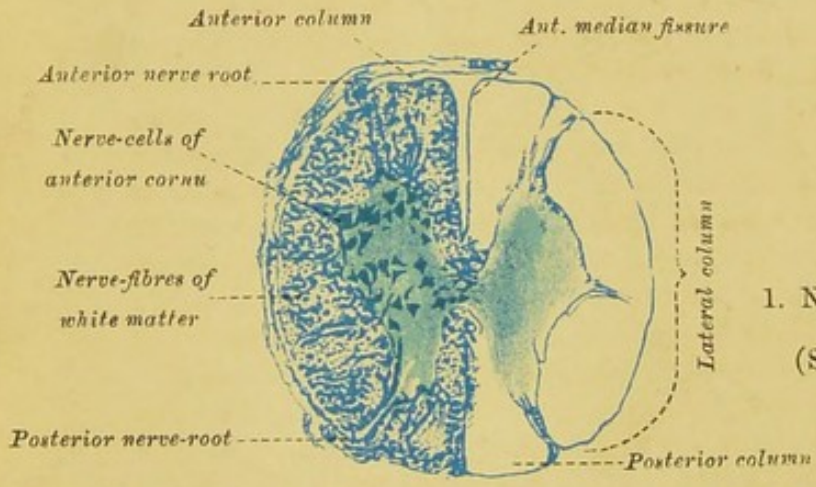
12. **Galvanotropism.**—Place at each end of a rectangular trough filled with tap-water a metallic plate, or a plate of carbon, connected through a commutator and key with the poles of a Grove or bichromate battery of several cells, or, if the laboratory is provided with a current from the street, with the switch through one or more incandescent lamps. Put into the water a number of tadpoles, which should not be too young. When the current is closed, the tadpoles will arrange themselves in a definite way with their long axes in the direction of the lines of flow, the head being turned towards the anode. Reverse the current, and they turn their heads in the opposite direction. If the current is taken from the laboratory supply, the anode may be known as the electrode at which least gas comes off, or at which a mixture of potassium iodide and starch becomes blue (p. 650).

2. Cover-glass preparation of spinal cord of ox, × 250. (Stained with methyl blue.)

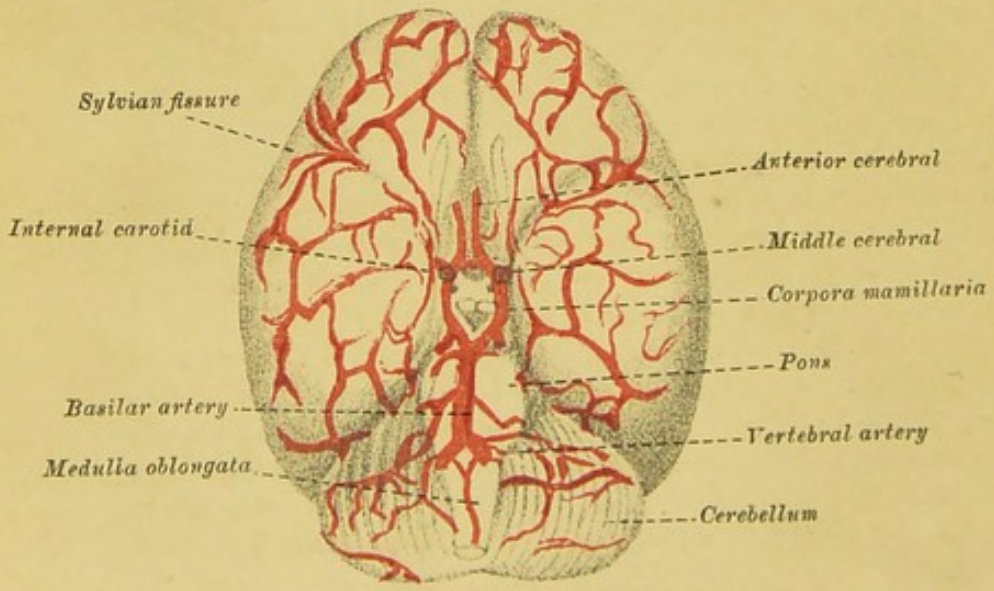




1. Nerve-fibres of frog, teased in osmid acid, × 300. (Stained with hæmatoxylin.)



3. Transverse section of spinal cord. (Stained with aniline blue-black.)



4. Base of brain, with arteries injected.

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CHAPTER XII.

THE CENTRAL NERVOUS SYSTEM.

In other divisions of our subject we have been able to follow to a greater or less extent the processes which take place in the organs described. The chemistry and the physics of these processes have bulked more largely in our pages than the anatomy and histology of the tissues themselves. In dealing with the central nervous system we must adopt a method the very reverse of this. Its anatomical arrangement is excessively intricate. The events which take place in that tangle of fibre, cell, and fibril are, on the other hand, almost unknown. So that in the description of the physiology of the central nervous system we can as yet do little more than trace the paths by which impulses *may* pass between one portion of the system and another, and from the anatomical connections deduce, with more or less probability, the nature of the physiological nexus which its parts form with each other and the rest of the body. And here it may be well to remark that, although for convenience of treatment we have considered the general properties of nerves in a separate chapter, there is not only no fundamental distinction between the central nervous system and the outrunners which connect it with the periphery, but obviously a central nervous system would be meaningless and useless without afferent nerves to carry information to it from the outside, and efferent nerves along which its commands may be conducted to the peripheral organs.

I. Structure of the Central Nervous System.

In unravelling the complex structure of the central nervous system, we avail ourselves of information derived (1) from its gross anatomy; (2) from its microscopical anatomy; (3) from its development; (4) from what we may call, although the term is open to the criticism of cross-division, its physiological and pathological anatomy.

Certain tracts of white or grey matter are differentiated from each other by the size of their fibres or cells. For example, the postero-median column of the spinal cord has small fibres, the direct cerebellar tract large fibres; the pyramidal cells in what we shall afterwards have to distinguish as the 'leg area' (p. 743) of the cerebral cortex are large; those of the 'face area' are comparatively small.

The study of development enables us not only to determine the homology, the morphological rank, of the various parts of the brain and cord, but also, by comparison of animals of different grades of organization, sometimes to decide the probable function and physiological importance of a strand of nerve-fibres or a column of nerve-cells. It is of special value in helping us to differentiate and to trace the various tracts or paths into which the white matter of the central nervous system may be divided. For the medullary sheath is not developed at the same time in all the tracts, and a strand of nerve-fibres in which it is wanting—*e.g.*, the pyramidal tract (p. 687) at birth in man and such animals as are unable to stand and run when they are born—is readily distinguished under the microscope.

Then, again—and this is what we propose to include under the fourth head—experimental physiology and clinical and pathological observation throw light not only on the functions, but also on the structure, of the central nervous system. For instance, complete or partial section, or destruction by disease, of the white fibres of the cord or brain, or of the nerve roots, or removal of portions of the grey matter, is followed by degeneration in definite tracts. And since, as we have already seen, degeneration of a nerve-fibre is caused when it is cut off from the cell of which it is a process, the amount and distribution of such degeneration teaches us the extent and position of the central connections of the given tract. And, particularly in young animals, removal of a peripheral organ—an eye or a limb—or section of its nerves, may be followed by atrophy of portions of the central nervous system immediately related to it.

'Softening' of a definite portion of the white or grey matter may also in certain cases be caused by depriving it of its blood-supply by the injection of artificial emboli, and the resulting degenerations may then be studied. For instance, fine particles like lycopodium spores are injected into the abdominal aorta between the origins of the renal and inferior mesenteric arteries. They are prevented by clamps from entering these vessels, and, passing through the lumbar

arteries, stick in the branches of the anterior spinal artery, and cause softening mainly of the grey matter of the lumbar portion of the cord. When the abdominal aorta of a rabbit is temporarily compressed (for about an hour) below the origin of the renal arteries, the grey matter of the corresponding portion of the cord is so seriously injured that it and the fibres that arise from it degenerate, while the fibres whose cells of origin are not situated in this part of the grey matter are not affected, or at least completely recover.

Certain tracts may also be marked out by means of the electrical variation, which gives token of the passage of nervous impulses along them when portions of the central nervous system or peripheral nerves are stimulated (Horsley and Gotch.)

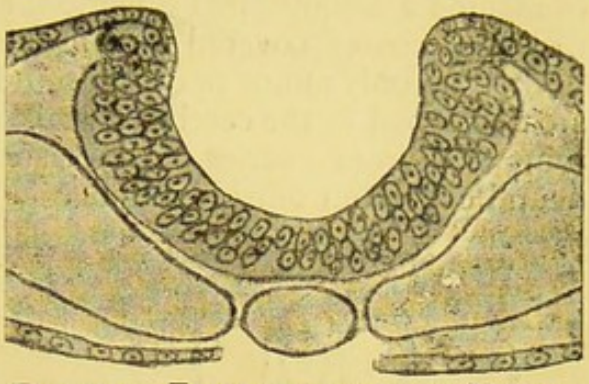

FIG. 224.—FORMATION OF THE NEURAL CANAL AT AN EARLY STAGE (AFTER BEARD).

Development of the Central Nervous System.—Very early in development (Fig. 224) the keel of the vertebrate embryo is laid down as a groove or gutter in the epiblast of the blastodermic area (Chap. XIV.). The walls of this 'medullary groove' grow inwards, and at length there is formed, by their coalescence, the 'neural canal' (Fig. 225), which expands at its anterior end to form four cerebral vesicles (Fig. 226). Thus there is a continuous tunnel from end to end of the primary cerebro-spinal axis; and this persists as the central canal of the spinal cord and the ventricles of the brain, whose ciliated epithelium represents the epiblastic lining of the primitive neural canal. In the adult portions of the canal may become obliterated from an evergrowth of the lining cells, and the cilia are, if present at all, less distinct than in the child, and far less distinct than in the lower animals. From the wall of this canal is formed the cerebro-spinal axis, in which developing nerve-cells or neuroblasts soon become differentiated from the supporting cells or spongioblasts, and wander outwards from the neighbourhood of the central canal (Fig. 233) till their further progress is checked by the barrier of the marginal veil, a closely-woven network or thicket, into

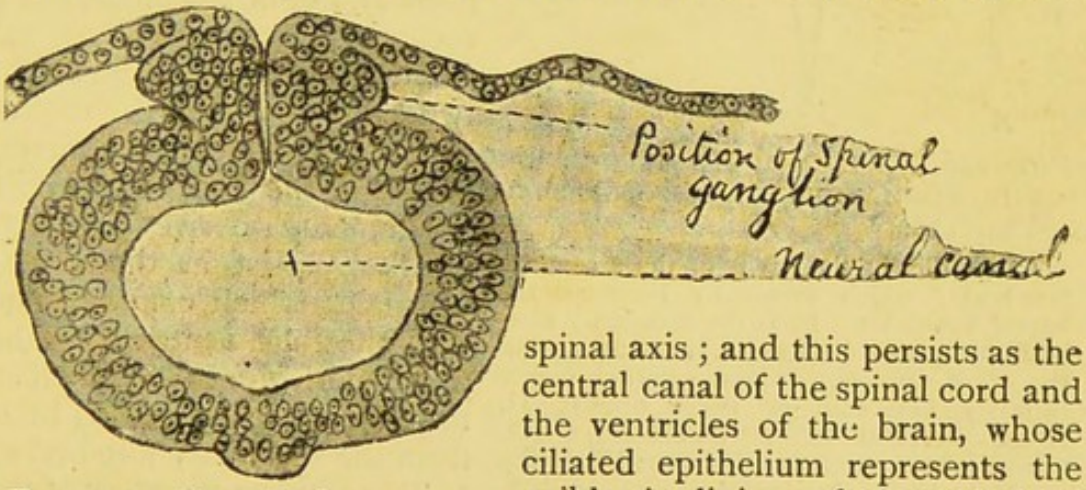

FIG. 225.—NEURAL CANAL AT A LATER STAGE (AFTER BEARD).

which the processes of the spongioblasts break up at the outside of the primitive cerebro-spinal axis. Although the neuroblasts themselves are unable to penetrate the marginal veil, the axis-cylinder processes of some of them do so, and form the motor roots of the spinal nerves. The neuroblasts from which the fibres of the white columns of the cord are developed are apparently unable to send their axons through the marginal veil. They are accordingly forced to assume a longitudinal direction, and in this way the central grey matter becomes covered with a sheath of longitudinal white fibres. For a time only motor nerve-cells and the fibres connected with them are developed in the cerebro-spinal axis. The ganglia on the posterior roots arise from a series of epiblastic thickenings arranged along the neural canal, but outside its wall. From both poles of each ganglion cell a process grows out, one towards the periphery, which forms a peripheral nerve-fibre, the other centrally to connect the cell with the cord. From the after-brain is developed the medulla oblongata, from the hind-brain the cerebellum and pons, from the mid-brain the corpora quadrigemina and crura cerebri. The fore-brain, or primary fore-brain, gives rise of itself only to the third ventricle and optic thalamus, but a secondary fore-brain buds off from it and soon divides into two chambers, from the roof of which the cerebral hemispheres, and from the floor the corpora striata, are derived. Their cavities persist as the lateral ventricles, which communicate with the third ventricle by the foramen of Monro. The olfactory tracts are formed as buds from the secondary fore-brain.

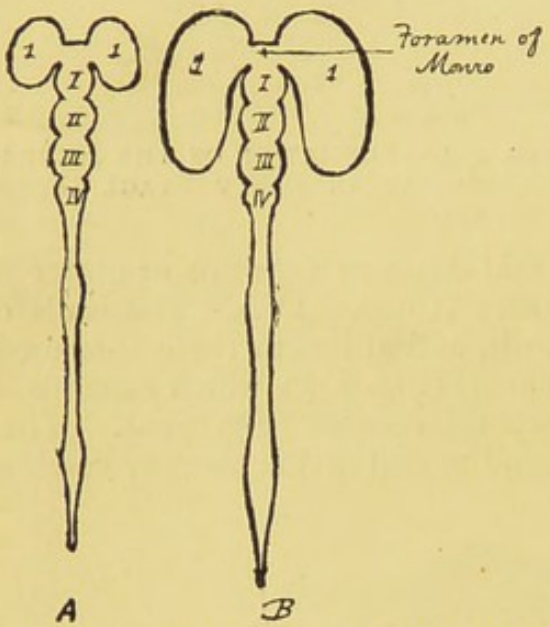

FIG. 226. — DIAGRAM TO ILLUSTRATE THE FORMATION OF THE CEREBRAL VESICLES.

A. 1 indicates the cavity of the secondary fore-brain, which eventually becomes the lateral ventricles. In B the secondary fore-brain has grown backwards so as to overlap the other vesicles. I, first cerebral vesicle (primary fore-brain or 'tween brain); II, second cerebral vesicle (mid-brain); III, third cerebral vesicle (hind-brain); IV, fourth cerebral vesicle (after-brain).

To complete the story of the development of the brain, it may be added that the retina is really an expansion of its nervous substance. A hollow process, the optic vesicle, buds out on each side from the primary fore-brain. A button of epiblast, which afterwards becomes the lens, grows against the vesicle and indents it, so that it becomes cup-shaped, the inner concave surface of the cup representing the retina proper, the outer convex surface the choroidal epithelium. The stalk becomes the optic nerve.

Histological Elements of the Central Nervous System.—The central nervous system is built up (1) of true nervous elements, (2) of supporting tissue. The nervous elements have usually been described

as consisting of nerve-fibres and nerve-cells, but the antithesis of a time-honoured distinction must not lead us to forget that the essential part of a nerve-fibre, the axis-cylinder, is a process of a nerve-cell, and the medullary sheath probably a product of the axis-cylinder.* In strictness, the term 'nerve-cell' ought to include not only the cell-body, but all its processes, out to their last ramifications. But the habit of speaking of the position of the cell-body† as that of the nerve-cell is so ingrained that it seems better to continue the use of the latter term in its old signification, and to speak of the cell and branches together as a neuron.

The Neurons.—A typical nerve-cell (Plate V., 2 ; Figs. 227-229) is a knot of granular protoplasm, containing a large nucleus, inside of which lies a highly refractive nucleolus. A centrosome and attraction sphere (p. 18) have also been found in some nerve-

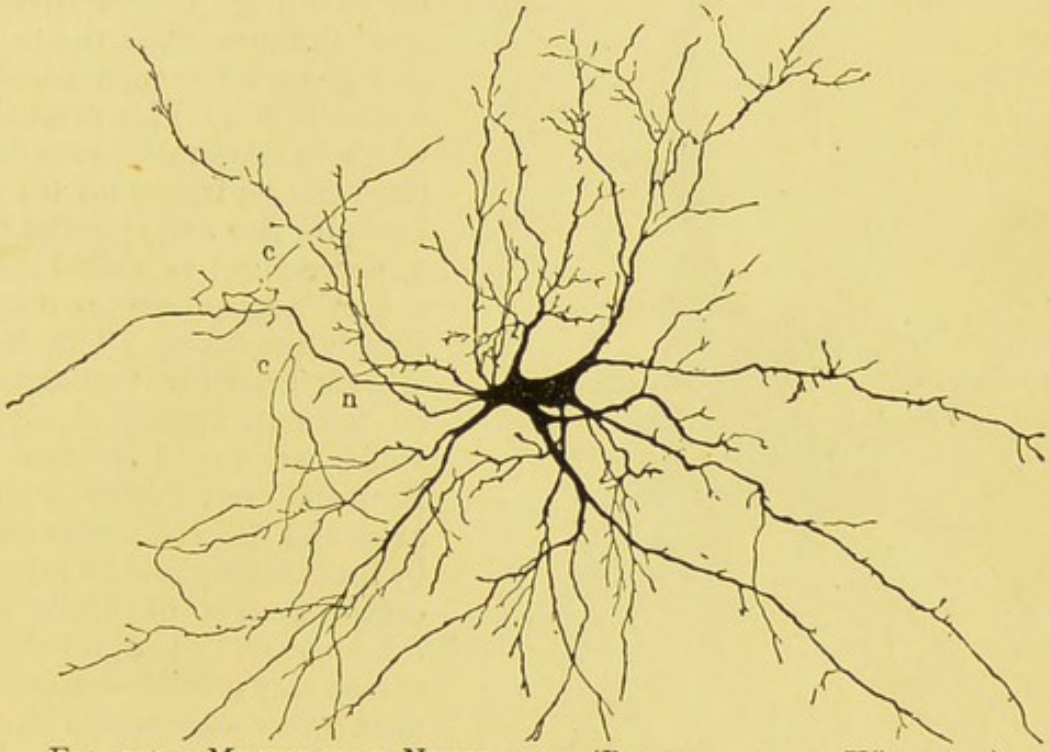

FIG. 227.—MULTIPOLAR NERVE-CELL (BARKER, AFTER KÖLLIKER). (Golgi preparation.) *n*, axon ; *c*, collaterals.

cells, though not as yet demonstrated in all. Pigment may also be present, especially in old age. By certain methods of staining it may be shown that fibrils run through the cell, while in

* Although each internode of the medullary sheath of a peripheral nerve-fibre has been supposed to be formed from a cell that, in the course of development, comes in contact with the axis-cylinder and ultimately encircles it, a similar origin can hardly be admitted for the medulla of the fibres of the spinal cord and brain, where, indeed, a segmental genesis seems excluded by the absence of regularly placed internodal nuclei and nodes of Ranvier. In any case the nuclei of the peripheral fibres belong to the neurilemma and not to the medullary sheath, and while the medullary sheath, like the axis-cylinder, is as regards its nutrition under the control of the nerve-cell, and must therefore be looked upon as an integral portion of the neuron, the neurilemma in respect both of its nutrition and its development appears to be an independent structure.

† Foster and Sherrington call the cell-body the *perikaryon*.

the ground substance between the fibrils lie round, angular, or spindle-shaped bodies (Nissl's bodies) which stain with basic dyes (Fig. 235).* These bodies vary in appearance in different kinds of nerve-cells, and in the same nerve-cell under different conditions. In a multipolar cell, like those in the anterior horn of the spinal cord, several processes—it may be five or six, or even more—pass off from the cell-body. The most complete pictures of them are given by preparations impregnated according to the method of Golgi † (Figs. 227, 229). One of the processes is distinguished from the rest by the fact that it maintains its original diameter for a comparatively great distance from the cell, and gives off comparatively few branches. This process, which in favourable preparations can be traced on till it becomes the axis-cylinder of a nerve-fibre, is called the axis-cylinder process, or more shortly the *axon*. The few slender branches that come off from it, usually at right angles, are called *collaterals*. Both the main thread of the axon and the collaterals end by breaking up into an arborescent system of fibrils or *telodendrion*. The telodendrions vary greatly in appearance from simple end-brushes to far-branching thickets, or such special end-organs as motor-plates (Fig. 231) or muscular spindles (Fig. 329). The rest of the processes of the cell, which are termed *dendrites* or protoplasmic processes, very rapidly diminish in diameter, as they pass away from the cell, by breaking up into fibrils like the branches of a tree. The Nissl bodies extend for some distance into the dendrites, but not into the axon. The dendrites of some cells, especially the pyramidal

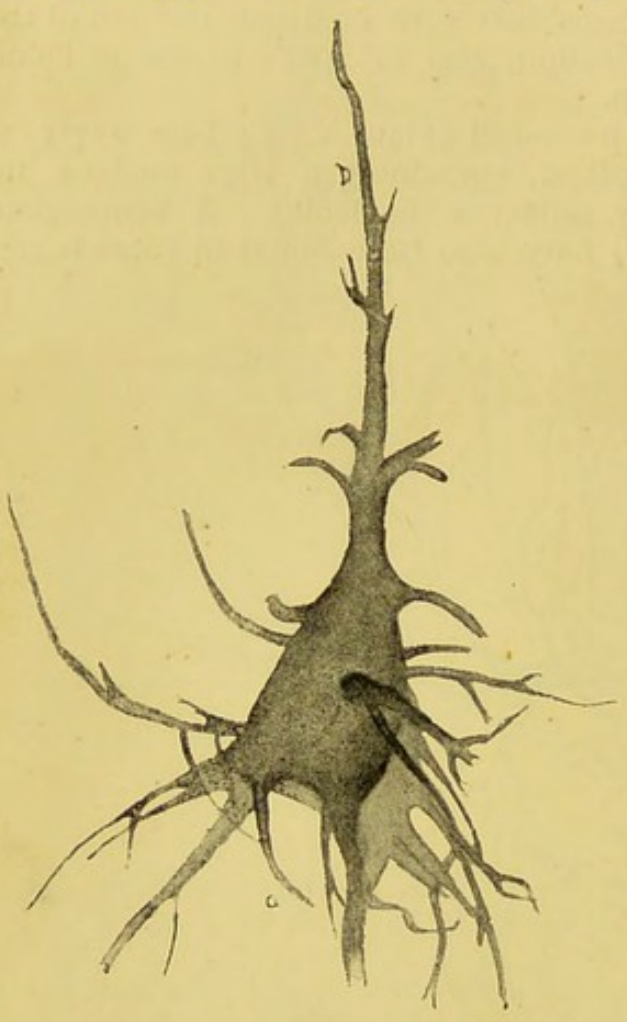

FIG. 228.—LARGE PYRAMIDAL CELL OF CEREBRAL CORTEX (BARKER, AFTER BECHTEREW).

a, axon; *b*, dendrite.

* In Nissl's method the sections are stained in a solution of methylene blue, and decolourized in anilin-alcohol.

† The method depends upon the deposition of mercury, or silver, in or around the cell-bodies and their processes in tissues which have been hardened in bichromate of potassium and then soaked in a solution of mercuric chloride or silver nitrate. In Pal's improvement of Golgi's method a solution of sodic sulphide follows the mercuric chloride.

cells of the cerebral, and the Purkinje's cells of the cerebellar cortex, have small swellings, the so-called *lateral buds* or *gemmules*, on their course. Their significance is unknown. The dendrites terminate at a little distance from the cell, where they come into relation with the end brushes of the axons of other neurons. In this way two or more neurons are linked together to form a nervous path. The relation is not one of actual anatomical continuity, but the processes come so close together that nerve impulses are able to pass across from the terminal brush of the axon of one nervous element to the dendrites or cell-body of another. Foster and Sherrington call the connection a *synapsis*.

It has been suggested that the contact may be rendered more or

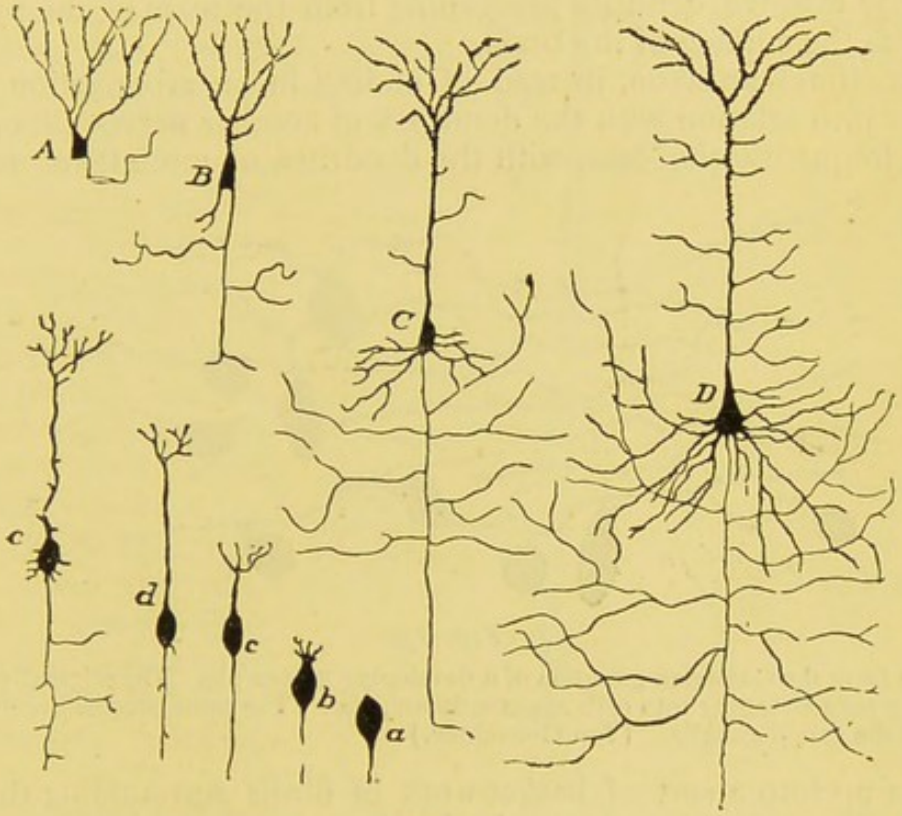

FIG. 229.

a—*e* shows the development of the pyramidal nerve-cells of the cerebral cortex in a typical mammal; *a*, neuroblast with commencing axon; *b*, dendrites appearing; *d*, commencing collaterals. A—D shows the different degree of complexity in the fully-developed pyramidal cells in different vertebrates: A, frog; B, lizard; C, rat; D, man. (Donaldson, after Ramón y Cajal.)

less close through amœboid movements of the dendrites, and that in this way the nervous impulse may be switched like a railway train from one path to another. But there is at present scarcely any experimental basis for this fascinating hypothesis. Whatever the nature of the relation between two superposed neurones may be, it does not permit the conduction of nerve-impulses indiscriminately in both directions. For instance, stimulation of the central end of the posterior root of a spinal nerve causes a negative variation (p. 630) in the anterior root of the same segment, while no electrical change is produced in the posterior root by stimulation of the anterior. We shall see later on (p. 682) that some of the fibres of the

posterior root and their collaterals end by arborising around the dendrites of the cells of the anterior horn. The excitation is, therefore, able to pass from the telodendrions of the posterior root fibres through the dendrites of the anterior horn cells towards their cell bodies, but not in the opposite direction, and in general the direction of conduction is from the dendrites towards the cell-body.

Varieties of Neurons.—Nearly all the nerve-cells of the cerebro-spinal axis agree with the cells of the anterior horn in the possession of an axon and one or more dendrites, although sometimes the dendrites are scanty in number and insignificant in size. In the cerebral cortex the typical cells are of pyramidal shape. From the base comes off the axon, and from the angles dendritic processes, a particularly massive dendrite proceeding from the apex of the pyramid towards the surface of the brain.

Sometimes an axon, instead of ending in an arborization which comes into relation with the dendrites of another nerve-cell, or, as is more frequently the case, with the dendrites of more than one cell,

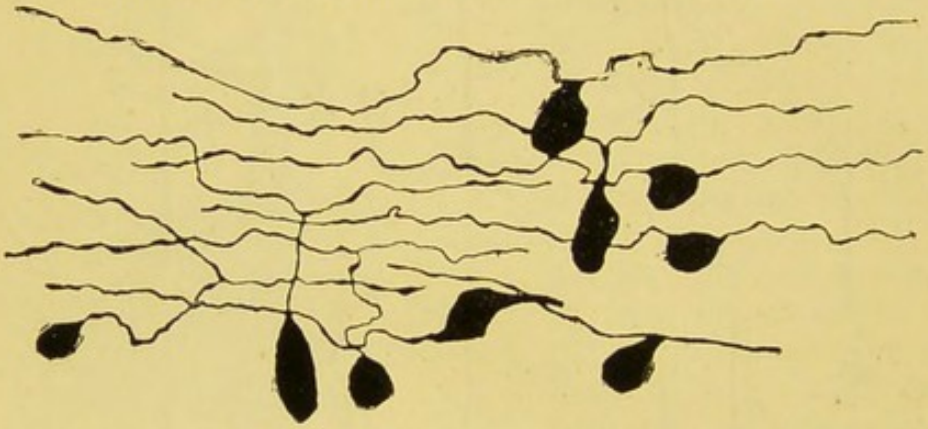

FIG. 230.

Cells from the Gasserian ganglion of a developing guinea-pig. The originally bipolar cells are seen changing into cells apparently unipolar. The same process occurs in the cells of the spinal ganglia. (Van Gehuchten.)

breaks up into a sort of basket-work of fibrils surrounding the cell-body. The cells of Purkinje, for instance, in the cerebellum, are surrounded by such pericellular baskets (Fig. 232). The cells of the spinal ganglia have two axons, which in the embryo arise one from each end of the bipolar cell, but in the adult are connected to the cell by a single process (Fig. 230). The great majority of them have no dendrites, unless, as some have supposed, the peripheral process really represents a dendrite. Another kind of cell which seems undoubtedly to be of nervous nature is the '**granule-cell**.' Granule-cells are much smaller than the nerve-cells we have been describing. Their processes are much less easily followed, but all appear to give off an axon and several dendrites. They contain a relatively large nucleus (5 to 8 μ in diameter), with only a mere fringe of cell-substance. The nucleus, unlike that of a large nerve-cell, stains deeply with hæmatoxylin. Some parts of the grey matter are crowded with these granule-cells, *e.g.*, the nuclear layer of the cerebellum and the substantia gelatinosa, or substance of Rolando, which caps the posterior horn in the cord. In other parts they are more thinly

scattered, but probably they are as widely diffused as the large nerve-cells proper, and no extensive area of the grey matter is wholly without them.

Although there are several varieties of granules (Hill), they all agree in this, that their axons run a comparatively short course, and never, or rarely, pass beyond the grey matter. Another kind of neuron which is also confined to the grey matter, and is typically seen in the cortex of the cerebrum and cerebellum, presents the peculiarity of an axon which branches into an intricate network immediately after coming off from the cell (cell of Golgi's second type). Unlike the long axon of the typical large nerve-cell, the axis-cylinder process of this Golgi cell remains unmedullated.

The sympathetic ganglion cells, which are developed from immature neuroblasts that migrate, in the course of development, from the spinal ganglia, and gathering in clumps form the ganglia of the sympathetic chain (His), agree in general with the cells of the cerebro-spinal axis in possessing an axon and one or more dendrites, although a few of them are devoid of dendrites.

The epithelium lining

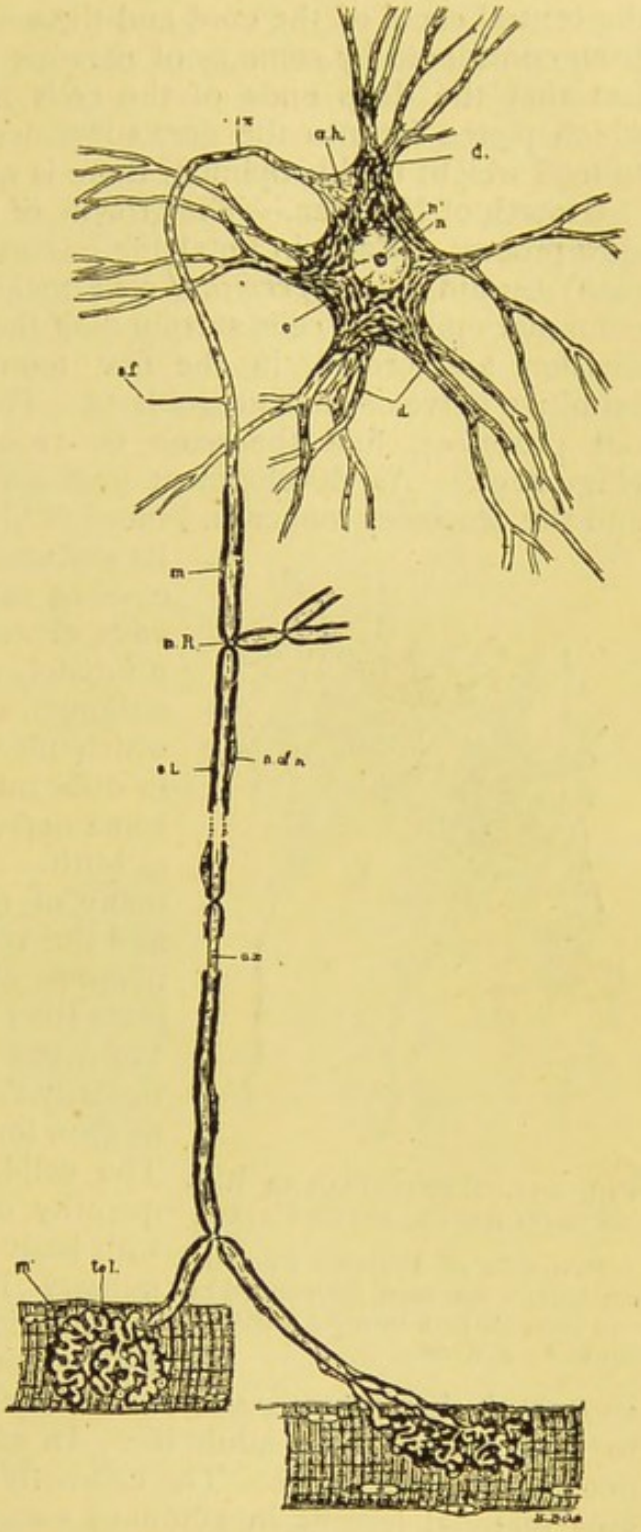

FIG. 231.—SCHEME OF LOWER MOTOR NEURON (BARKER).

a. h, axon-hillock (the portion of the cell from which the axon comes off), containing no Nissl bodies, and showing fibrillation; *ax*, axis-cylinder or axon; *m*, medullary sheath, outside of which is the neurilemma; *c*, cell-substance (cytoplasm), showing Nissl bodies in a lighter ground substance; *d*, protoplasmic processes or dendrites containing Nissl bodies; *n*, nucleus; *n'*, nucleolus; *n. R*, node of Ranvier; *s. f*, side fibril; *n* of *n*, nucleus of the neurilemma; *tel.*, motor end plate; *m'*, striped muscle fibre; *s. L*, incisure.

the central canal of the cord and the ventricles of the brain has also been considered by some as of nervous nature; but in spite of the fact that the deep ends of the cells are continued into processes which pierce far into the grey substance, which has been supposed to lend weight to this opinion, there is no good ground for it.

Growth of Neurons.—The growth of a neuron is a comparatively slow process. Early in fœtal life (about the third or fourth week in man) certain round *germinal* cells make their appearance amid the columnar epiblastic cells surrounding the neural canal. From their division are formed, in the first months of embryonic life, the primitive nerve-cells or neuroblasts. These soon elongate and push out processes, first the axon or axons, and then the dendrites (Fig. 229). As development goes on the cell-body grows larger, and the processes longer and more richly branched. The axon and its collaterals, when it has any, in the case of the great majority of the nervous elements of the brain and cord, ultimately acquire a medullary sheath, although, as we have said, the time at which medullation is completed varies in different groups of elements, and in some nervous tracts it is even wanting at birth. At birth, too, the branches of many of the cells are less numerous, and the connections between different nervous elements therefore less intimate than they will afterwards become. For many years the processes, and particularly the axons, continue not only to grow longer, but also to grow thicker. The cell-body also enlarges, and the quantity of material in it that stains with basic dyes increases. Even after puberty is reached the anatomical organization of the nervous system may still continue to advance, although at an ever slackening rate, and the finishing touches may only be given to its architecture in adult life. In old age the nervous elements decay as the body does. The cell-body diminishes in size; the stainable material lessens in amount; vacuoles form in the protoplasm and pigment accumulates; the nucleus shrinks; the nucleolus is obscured or may disappear altogether. At the same time the processes of the cell, and especially the dendrites, tend to atrophy (Fig. 234).

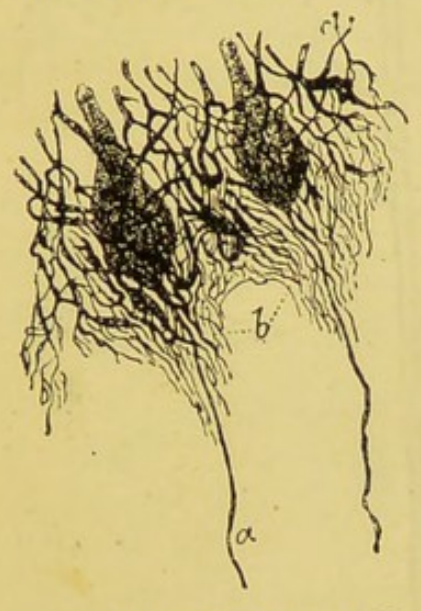

FIG. 232.—PERICELLULAR BASKETS (SCHÄFER, AFTER CAJAL).

Two cells of Purkinje from the cerebellum are seen surrounded by end ramifications forming a basket-work, *b*; *a*, axon.

Nutrition of the Neuron.—We have already seen that when an axon is cut off from its cell-body, it and its medullary sheath, when it possesses one, undergo a rapid degeneration. It was stated by Waller, and was long supposed to be true, that no change took place in the nerve-cell. The researches of recent years have shown that not only does loss of function of the cell-body affect the nutrition of the axon, but

loss of function of the axon reacts on the cell-body. When a nerve-fibre is divided from its cell characteristic changes are produced in the latter and in its dendritic processes, and they are scarcely less rapid, although usually not so far-reaching, as the degeneration in the peripheral portion of the nerve-fibre. Many of the Nissl bodies (Fig. 235) are reduced to a finely granular condition (chromatolysis). Many of them disappear altogether. The nucleus may be displaced to one side of the cell. In rabbits after division of the facial nerve the alterations in its nucleus of origin have been found to reach a maximum in about three weeks, after which there is a tendency to recovery on the part of the majority of the cells, even when regenera-

FIG. 233. — SECTION THROUGH HALF OF NEURAL TUBE (BARKER, AFTER HIS).

The pear-shaped neuroblasts are seen migrating outwards. The axons of some of them are seen pushing their way out through the marginal veil as the anterior root of a spinal nerve.

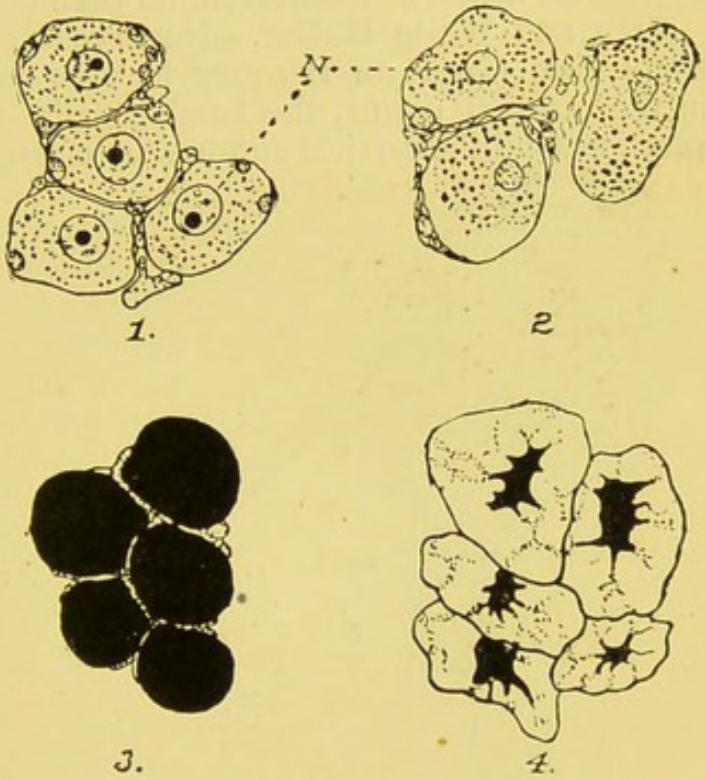

FIG. 234.

1, spinal ganglion cells of a still-born male child ; 2, of a man ninety-two years old (× 250)—N, nuclei ; 3, nerve-cells from the antennary ganglion of a honey-bee just emerged in the perfect form ; 4, of an old honey-bee. The nucleus is black in the figure. In 3 it is very large, in 4 it is shrunken, and the cell-substance contains vacuoles. (Hodge.)

tion of the nerve has been prevented by cutting out a portion of it. Some of the cells may completely atrophy and disappear. Similar changes have been found by Warrington in the motor cells of the anterior horn after section of the posterior (dorsal) spinal roots. Since in this case no anatomical injury has been inflicted on the motor neurons, it has been surmised that the cause of the alterations is the loss of impulses which normally reach them along their dendrites. In short, we may say with Marinesco, that the functional and anatomical integrity of the neuron depends on the integrity of all its constituent parts, and of the neurons which carry to it functional excitations, *i.e.*, excitations connected with its proper physiological

work. The neuron, in fact, lives by its function, or, in common language, by doing its work.

Chromatolysis may also be produced in nerve-cells in extensive superficial burns, in tetanus caused by the injection of bacterial cultures, in acute alcoholic poisoning, and in other ways. In several kinds of intoxication—for example, chronic alcoholism—Berkley observed, in preparations impregnated with silver nitrate according to the method of Golgi, that the earliest changes were the disappearance of the gemmules of the dendrites. It is probable that neither the chromatolysis nor the loss of the gemmules should be looked upon as the token of any specific lesion; they are simply signs that the normal action of the neuron has been deranged.

Grey and White Matter.—Nerve-cells are the most distinctive histological feature of the **grey nervous substance**. Sown thickly in the cerebral cortex, the basal ganglia, the floor of the fourth ventricle, and the cervical and lumbar enlargements of the cord, they

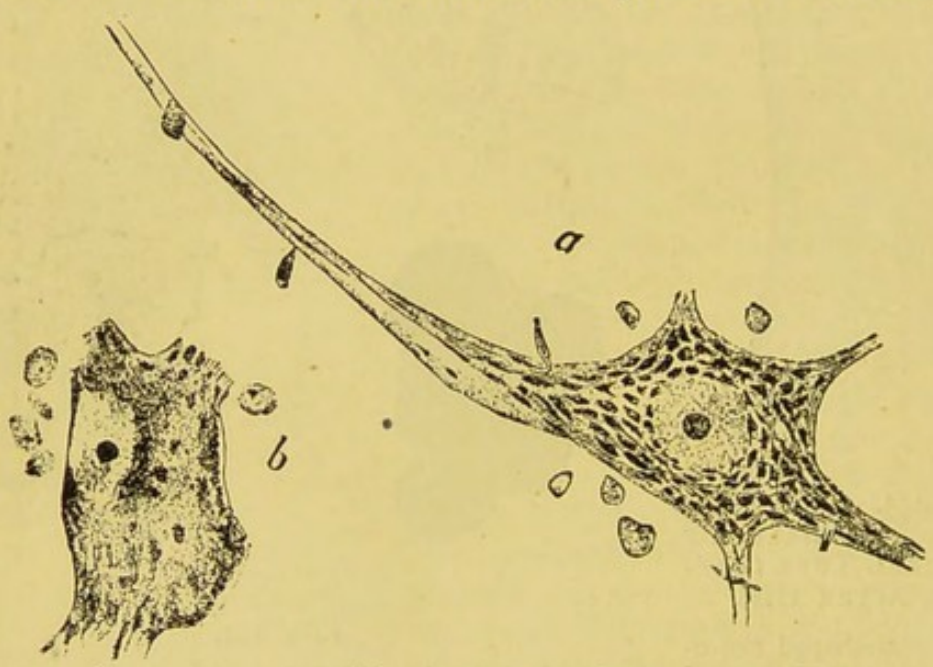

FIG. 235.—CELLS FROM THE NUCLEI OF THE OCULOMOTOR NERVES OF THE CAT THIRTEEN DAYS AFTER DIVISION OF THE ROOT FIBRES ON ONE SIDE (BARKER, AFTER FLATAU). (NISSL'S STAIN.)

a, normal cell from side on which the roots were not cut; *b*, cell from side operated upon. Only a few Nissl bodies are present in *b*, and the nucleus is displaced to one side of the cell.

are scattered more sparingly wherever the grey matter extends. They also occur in the spinal ganglia and their cerebral homologues (such as the Gasserian ganglion), in the ganglia of the sympathetic system and the sporadic ganglia in general. But wide as is their distribution and great as is the size of the individual cells, some of which have a diameter of 140 μ, or even more, they yet make up but a small portion of the whole of the central nervous substance, the total weight of the 9,000 millions of nerve-cell bodies in the human brain being less than 27 grammes (Donaldson). And although it is not to be wondered at that objects so notable when viewed under the microscope should have struck the imagination of physiologists, it is

probable that the very high powers which it is so common to attribute exclusively to them are, in part at least, shared with their processes.

The grey matter, in addition to non-medullated fibres and filaments representing the dendrites and such axons and collaterals as terminate within itself, contains also, as may be seen in preparations stained by Weigert's method,* great numbers of exceedingly fine medullated fibres, many of which are the collaterals of fibres that are passing out to the white matter.

Only medullated nerve-fibres are met with in the **white matter** of the cerebro-spinal axis. They are devoid of a neurilemma. In diameter they vary from 2 μ to 20 μ. In *Malapterurus electricus* the fibre in the cord which supplies the electrical organ is of immense size; and in the anterior column of many fishes may also be seen a single gigantic fibre on each side with a diameter of nearly 100 μ. It cannot be said that any relation between the functions of neurons and the calibre of their axons has been definitely established. Many afferent fibres, it is true, are small—this is notably the case with the fibres of the posterior column, and many motor fibres are large. But the distinction can by no means be generalized, for the fibres of the direct cerebellar tract (p. 676), which certainly are afferent, are among the largest in the spinal cord; and the vaso-motor fibres, which pass from the cord by the anterior (ventral) roots (Fig. 236) into the sympathetic, are smaller than the fibres of the posterior column. Even the motor nerve-fibres of striated muscles vary considerably in diameter, those of the tongue, *e.g.*, being smaller than those of the muscles of the limbs. Further, the medullated fibres of the brain are, without reference to function, in general finer than the fibres of the cord. As a rule the fibres whose course is the longest are the thickest, but the rule is often broken. The cause of these differences in the size of nerve-fibres is quite unknown. It is more likely to be morphological than physiological.

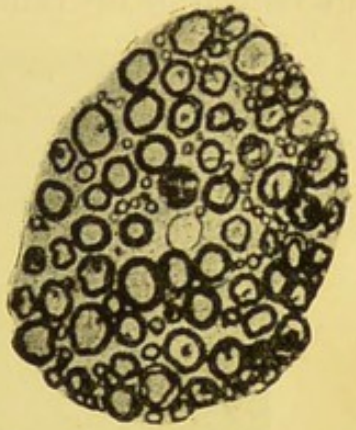

FIG. 236. — TRANSVERSE SECTION OF A BUNDLE OF NERVE-FIBRES FROM THE ANTERIOR (VENTRAL) ROOT OF THE FIRST COCCYGEAL NERVE OF THE CAT (DALE).

The great difference in the diameter of the fibres is well shown. The small fibres are vaso-motor.

Supporting Tissue.—The **protective membranes** of the central nervous system consist of ordinary connective tissue derived from the mesoblast, the **supporting framework** which interpenetrates the nervous substance of a peculiar form of tissue derived from the epiblast, and called *neuroglia*. The whole cerebro-spinal axis is wrapped in four concentric sheaths. Next the walls of the bony hollow in which it lies is the dura mater. Next the nervous substance itself, following the convolutions of the brain and the fissures

* Weigert's is a special method of staining the medullary sheath with hæmatoxylin.

of the cord, and giving off bloodvessels to both, is the pia mater. Between the dura and the pia, separated from the latter by a jacket of cerebro-spinal fluid, is the double layer of the arachnoid. The comparatively coarse septa that run into the nervous substance as if coming off from the pia mater are the main beams in the scaffolding of non-nervous material with which that substance is interwoven, and by which it is supported. The interstices are filled in by a thick-set feltwork of interlacing but unbranched neuroglia fibres, which lie close against the small glia cells, but in the adult at least are perfectly distinct from them. In preparations impregnated by the Golgi method the fibres appear to be processes running out from the attenuated cell-body like the arms of a microscopic crab or spider. But this is a deceptive appearance, as Weigert has shown by means of a special method, in which the neuroglia fibres are alone stained. It is possible, however, that in the embryo the fibres are formed by the cells, and afterwards become detached from them.

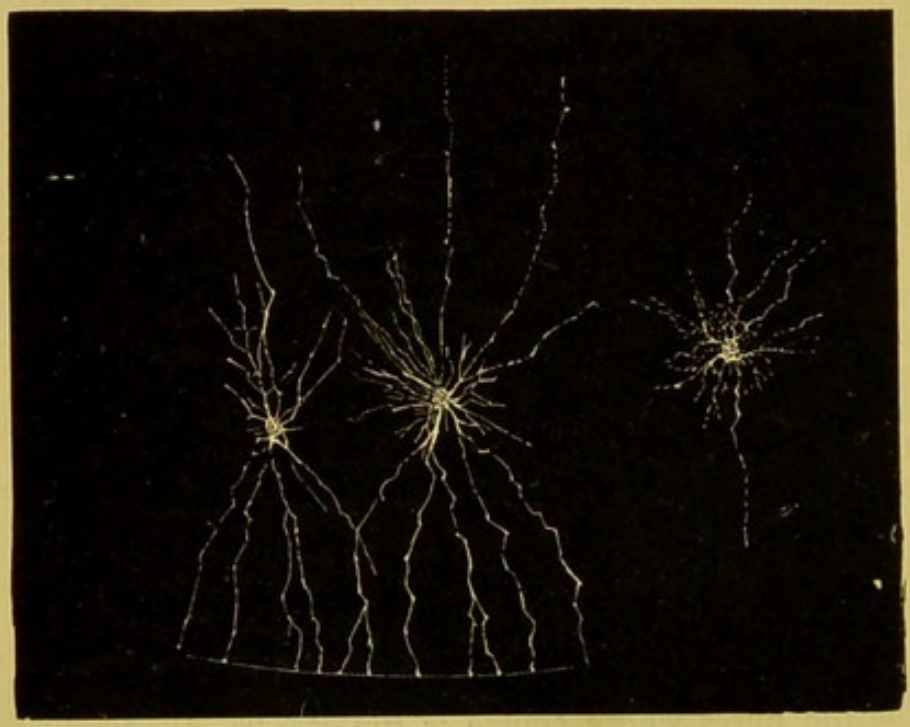

FIG. 237.—NEUROGLIA FIBRES AND CELLS (from a human embryo 30 cm. in length). The small cell on the right is from the grey, the other two from the white substance; Golgi's method (Kölliker).

The glia fibres are perfectly distinct from the nervous substance proper, but they are not ordinary connective tissue. Indeed, it would appear that no connective tissue of mesoblastic origin exists within the nervous substance; even the coarse septa, and particularly the one which constitutes the so-called posterior fissure, seem to consist of neuroglia, and not to be processes of pia mater. In the white matter nearly every medullated nerve-fibre is divided from its neighbours by glia fibres, which form a wide-meshed network. The network is denser in most parts of the grey substance, though not in all. The neuroglia is present in greatest abundance in the grey matter immediately surrounding the central canal of the cord and

the ventricles of the brain (the ependyma, as it is called). Contrary to the common opinion, the substance of Rolando is poor in neuroglia (Weigert).

General Arrangement of the White and Grey Matter in the Central Nervous System.—(1) Around the central canal, as we have seen, a tube of grey matter sheathed with white fibres is developed. This tube, from optic thalamus to conus medullaris, may be conveniently referred to as the *central grey axis or stem*, which, in the lowest vertebrates, *e.g.*, fishes, is much the most important part of the central nervous system.

(2) On the outer surface of the anterior portion of the neural axis, but not in the part corresponding to the spinal cord, is laid down a second sheet or mantle of *cortical* grey matter. Between this and the primitive grey stem are interposed (*a*) the sheath of white fibres that clothes the latter, and connects its various parts, and (*b*) a new development of white matter (corona radiata, cerebellar peduncles), which serves to bring the cortex into relation with the primitive axis, and through it with the rest of the body.

Although there are histological and developmental differences between the cerebral and the cerebellar cortex, we may, for some purposes, classify them together as *cortical formations*. And we may also include under this head the corpora striata, which, although generally grouped with the optic thalami and the other clumps of grey matter at the base of the brain, as the basal ganglia, are to be regarded as cortical in character. As we mount in the vertebrate scale the cortex formation of the secondary fore-brain and hind-brain acquires prominence.

In other words, the grey matter developed in the roof of the cerebral vesicles I and III. (Fig. 226) (the grey matter of the cerebral and cerebellar cortex) comes to overshadow the superficial grey matter hitherto present only in the roof of vesicle II. (in the corpora bigemina). And this cortex formation becomes larger in amount, and, in the case of the cerebral grey matter, more richly convoluted, the higher we ascend, until it reaches its culmination in man. As the anterior cerebral vesicles develop, they spread continually backward until at length the cerebral hemispheres cover over, and almost completely surround, the primary fore-brain, and the mid- and hind-

brains, so that the anterior portion of the primitive stem comes, as it were, to be invaginated into the second wider tube of cortical grey matter. This development of the cortical grey substance is accompanied with a corresponding development of nerve-fibres, for an isolated nerve-cell is no more conceivable than a railway-station the track from which leads nowhere in particular, or a harbour on the top of a hill.

But it is to be particularly observed that the new formation does not supplant the old, but works through and directs it. The neuroblasts of the cortex do not throw out their axons to make direct junction with muscles and sensory surfaces. Such junction the cortex finds already established between the primitive cerebro-spinal axis and the periphery. It joins itself on by nerve-fibres to the cells of the central stem; and we have reason to believe that no single axon in an ordinary spinal or cranial nerve* runs all the way from the periphery to the cortex, and no axon of a cortical nerve-cell all the way from the cortex to the periphery, but that the connection is made by a chain of at least two neurons, the cell-body of one of which is situate in this primitive grey tube.

The fibres from the cortex of each cerebral hemisphere (corona radiata), radiating out like a fan below the grey matter, are gathered together into a compact leash as they sweep down through the isthmus of the brain in the internal capsule, to join the crura cerebri. The cortex of each cerebellar hemisphere, and the ribbed pouch of grey matter, known as the corpus dentatum, which is buried in its white core, are also connected by strands of fibres with the central stem and the cerebral mantle. The restiform body or inferior peduncle brings the cerebellum into communication with the spinal cord. The superior peduncle by one path, and the middle peduncle by another, connect it with the cerebral cortex. A great transverse commissure, the corpus callosum, unites the cerebral hemispheres across the middle line, while transverse fibres that break through the middle lobe or worm, form a similar though far less massive junction between the two hemispheres of the cerebellum.

The fibres of the nervous system may be divided into (1) fibres connecting the peripheral organs with nerve-cells in the central grey axis; (2) fibres connecting nerve-cells in this central axis with cells in the external or cortical grey tube; and (3) fibres linking cortex with cortex, or central ganglia with each other. In the third group are included (*a*) fibres which connect portions of the cortex on the same side (association fibres) and (*b*) fibres which connect por-

* The olfactory and possibly to some extent the optic nerves are exceptions to this statement. Their relation to the cortex, as is easily understood from the manner of their development (p. 660), is different from that of the other nerves.

tions on opposite sides of the middle line (commissural fibres). Our first task is, therefore, to trace the peripheral nerves to their cells of origin or centres of reception* in the nervous stem. And although there is reason to believe that the whole of the peripheral nerves, cerebral and spinal (with the exception of the olfactory and optic, which are

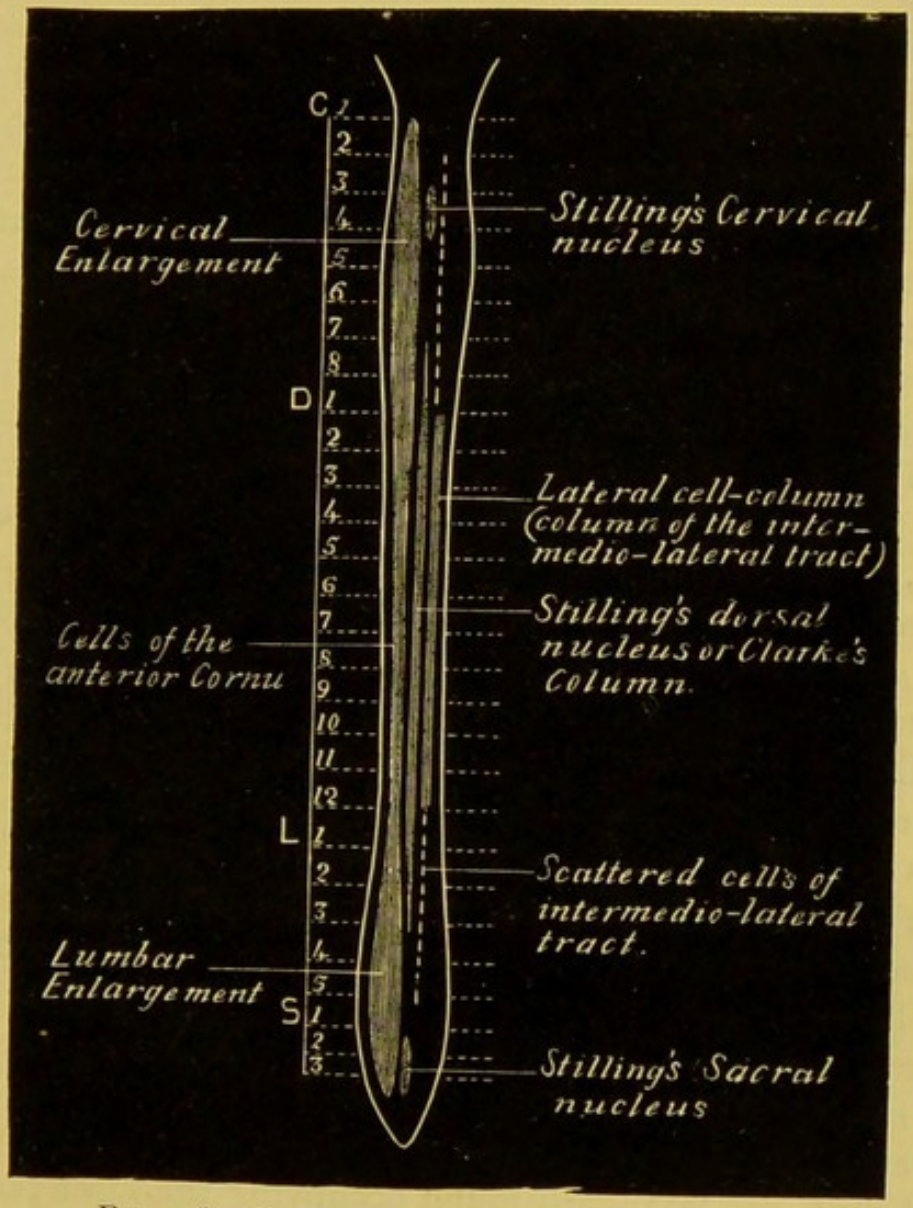

FIG. 238.—DIAGRAM OF GREY TRACTS OF CORD.

rather portions of the brain than true peripheral nerves), form a morphological series, it will be well to begin with the spinal nerves, since their motor and sensory fibres are gathered into different and definite roots, whose course within the cord is, in general, more easily traced than the course of the cerebral root-bundles within the brain.

* The centre or nucleus of reception of a nerve contains the nerve-cells around which its axons terminate; the nucleus of origin of a nerve contains the cells from which its axons arise.

Arrangement of the Grey and White Matter in the Spinal Cord.—The **grey matter** of the spinal cord is arranged on each side in a great unbroken column of roughly crescentic section (Plate V., 3), joined with its fellow across the middle line by a grey bar or bridge, which springs from the convexity of the crescent, and is pierced from end to end by the central canal. The anterior horn of the crescent, although it varies in shape at different levels of the cord, is, in general, broad and massive in comparison with the slender and tapering posterior horn. In the lower cervical and upper dorsal region a moulding or projection, forming a lateral horn, springs from the fluted outer side of the grey substance. Within the grey matter nerve-cells are found, sometimes so regularly arranged that they form veritable cellular or vesicular strands. Of these the best marked are: (1) The tract or tracts made up by the *cells of the anterior horn* (Fig. 238), which practically run from end to end of the cord, swell out in the cervical and lumbar enlargements, where the cells are very numerous and of great size (70 μ to 140 μ in diameter), and contract to a thin thread in the thoracic region, where they are relatively few, scattered, and small. (2) *Clarke's column*, whose cells are situated at the inner side of the root of the posterior horn just where it joins on to the grey cross-bar. It gradually increases in size from above downwards, usually appearing first at the level of the seventh or eighth cervical nerve, attaining its maximum development at the eleventh or twelfth dorsal and disappearing altogether, as a continuous strand, at the level of the second or third lumbar nerves. Scattered nerve-cells, however, constituting the so-called cervical and sacral nuclei of Stilling, are frequently found occupying the same position towards the upper and lower ends of the cord, and may be looked upon as isolated portions of Clarke's column. (3) A tract called the *intermedio-lateral tract*, situated at the outer edge of the grey matter, about midway between the anterior and posterior horns. It is best marked in the thoracic region, but extends also down into the lumbar swelling and up until it blends with certain cells of the anterior horn of the cervical cord. (4) The *cells of the posterior horn* are less numerous

and smaller than those of the anterior horn. Throughout the whole cord, however, two small groups of cells may be distinguished, one on the lateral side of the horn, about its middle, and the other on the mesial side, a little in front of (*i.e.*, ventral to) the edges of the substance of Rolando. Both of these groups are broken up by the passage through them of bundles of fibres which form a network, and they are therefore called respectively the group of the lateral and the group of the posterior *reticular formation*.

The **white matter** of the cord is anatomically divided by

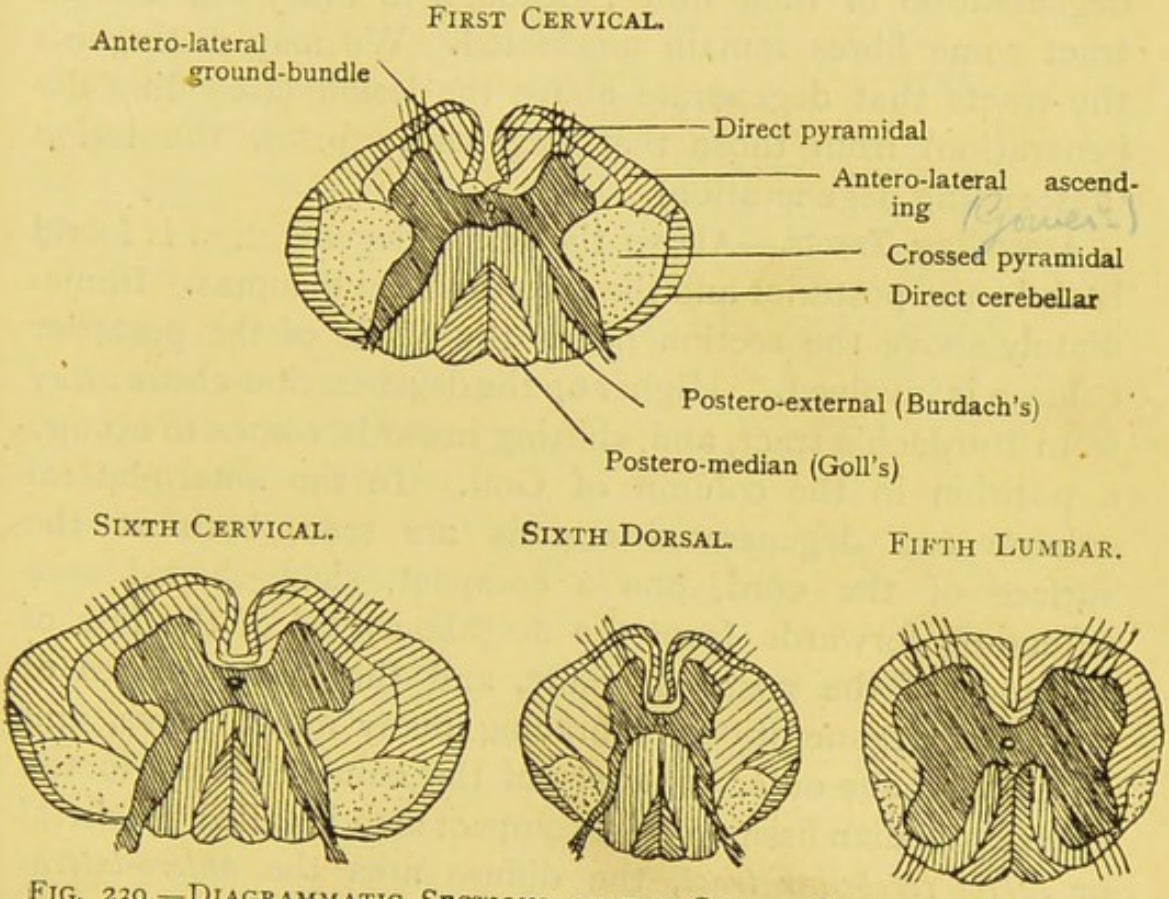

Fig. 239.—Diagrammatic Sections of the Spinal Cord to show the Tracts of White Matter at Different Levels.

the position of the nerve-roots and the anterior and posterior fissures into three columns on each side: the anterior, lateral, and posterior columns (Plate V., 3). The first two are often grouped together as the antero-lateral column. In the cervical region it may be seen with the microscope that the posterior white column is almost bisected by a septum running in from the pia mater towards the grey commissure. The inner half is called the postero-median column, or

column of Goll; the outer half the postero-external column, or column of Burdach (Fig. 239). No localization of any of the other conducting paths in the cord is possible by anatomical examination; but by means of the developmental method and the method of degeneration the columns of Goll and Burdach can be followed throughout the cord, and several similar areas can be mapped out. We shall only mention those that are physiologically the most important.

When the spinal cord is divided, and the animal allowed to survive for a time, certain tracts are picked out by the degeneration of their fibres, although in every degenerated tract some fibres remain unaffected. We may distinguish the tracts that degenerate above the lesion (ascending degeneration) from those that degenerate below the lesion (descending degeneration).

Ascending Tracts.—Above the lesion degeneration is found both in the posterior and the antero-lateral columns. Immediately above the section nearly the whole of the posterior column is involved. Higher up the degeneration clears away from Burdach's tract, and, shifting inwards, comes to occupy a position in the column of Goll. In the antero-lateral column two degenerated regions are seen, both at the surface of the cord, one a compact, sickle-shaped area extending forwards from the neighbourhood of the line of entrance of the posterior roots, and the other an area of scattered degeneration, embracing many intact fibres, and completing the outer boundary of the column almost to the anterior median fissure. The compact area is called the *dorsal* or *direct cerebellar tract*, the diffuse area the *antero-lateral ascending tract*, or *tract of Gowers*, or *ventral cerebellar tract*.

Descending Tracts.—When the cord is divided, say in the upper dorsal or cervical region, the following tracts degenerate below the lesion:

(1) A small group of fibres close to the antero-median fissure, which has received the name of the *direct pyramidal tract—pyramidal*, because higher up in the medulla oblongata it forms part of the pyramid; *direct*, because it does not cross over at the decussation of the pyramids, but continues down on the same side.

(2) A tract of degenerated fibres in the posterior part of the lateral column. This is the *lateral or crossed pyramidal tract*, and is much larger than the direct. In the medulla it also lies within the pyramid, but, unlike the direct pyramidal tract, it crosses to the opposite side of the cord at the decussation.

(3) A tract of scattered degeneration lying internal to and partly overlapping the tract of Gowers. It is called the *antero-lateral descending tract.*

(4) A small comma-shaped island of degeneration (comma tract) can be followed downwards for a short distance in the middle of Burdach's column. It is only seen in the cervical and upper thoracic regions.

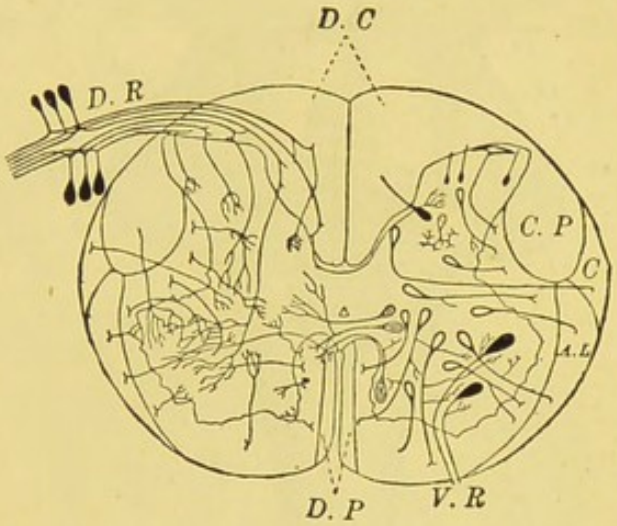

FIG. 240.—SCHEME OF CROSS-SECTION OF SPINAL CORD (DONALDSON, AFTER LENHOSSEK).

On the left side only the afferent fibres are shown; the efferent fibres and the spinal cells on the right side. *D. R*, posterior (dorsal) root; *V. R*, anterior (ventral) root; *C. P*, crossed pyramidal fibres; *C*, direct cerebellar tract; *A. L*, antero-lateral tract; *D. C*, posterior columns.

When we have deducted the long ascending and descending tracts which have been described, there still remains, both in the anterior and in the lateral column, a balance of white matter unaccounted for. This white substance, which does not degenerate for any great distance either above or below a lesion, is called the *antero-lateral ground-bundle*, and lies chiefly in the form of an incomplete ring around the anterior cornu. It is believed to consist of fibres which run only a comparatively short course in the cord, and serve to connect nerve-cells at different levels.

The next question which arises is: How are the long tracts connected below, *i.e.*, with the periphery, and above, *i.e.*, with the higher parts of the central nervous system? The answer to this question, partly derived from clinical records and partly from experimental results, is in the case

of some of the tracts unexpectedly full and minute, though meagre in regard to others. But to render it intelligible it is necessary, first of all, to describe briefly—

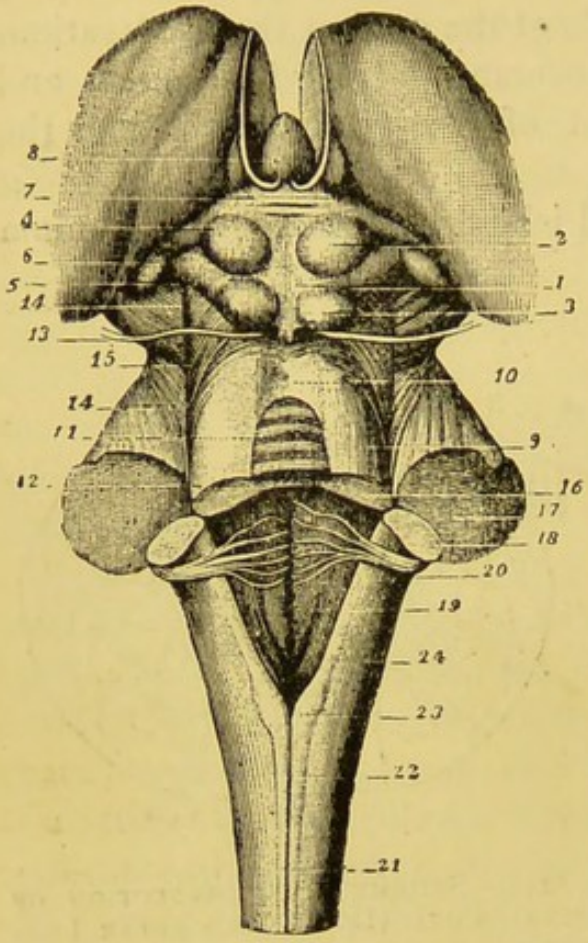

FIG. 241. — MEDULLA OBLONGATA, PONS AND CORPORA QUADRIGEMINA (DORSAL OR POSTERIOR VIEW) (SAPPEY).

1, corpora quadrigemina; 2, nates; 3, testes; 4, anterior brachium uniting the nates to the lateral geniculate body; 5, posterior brachium uniting the testes to the internal geniculate body 6; 7, posterior commissure; 8, pineal gland pulled forward to show nates; 9, superior peduncle of the cerebellum; 10, 11, 12, valve of Vieussens; 13, trochlear nerve; 14, lateral sulcus; 15, fillet; 16, superior, 17, middle, and 18, inferior peduncle of the cerebellum; 19, floor of fourth ventricle; 20, auditory nerve; 21, spinal cord; 22, postero-median column, continued in the medulla as the funiculus gracilis; 23, the clava, the continuation of the funiculus gracilis.

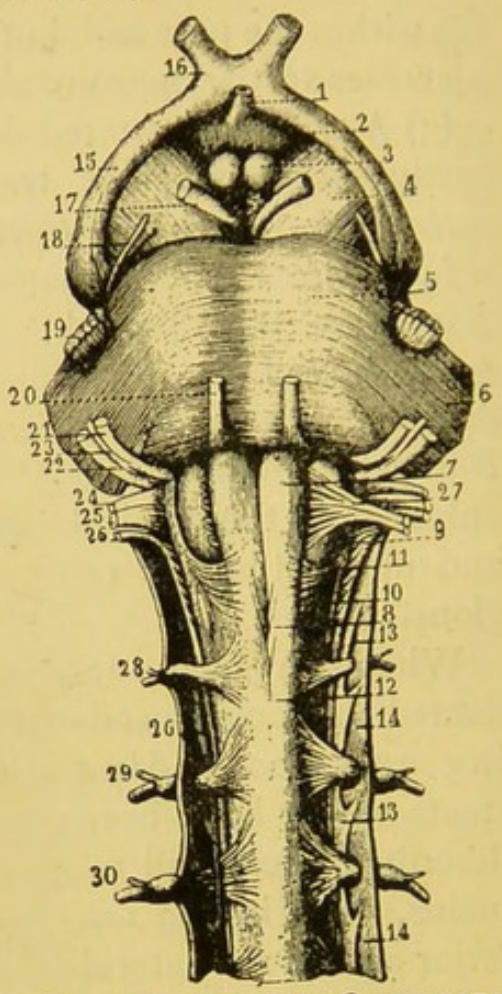

FIG. 242.—MEDULLA OBLONGATA, PONS AND CRURA CEREBRI (VENTRAL OR ANTERIOR VIEW).

1, infundibulum; 2, tuber cinereum; 3, corpus mammillare; 4, cerebral peduncle or crus cerebri; 5, pons; 6, middle peduncle of cerebellum; 7, pyramid; 8, decussation of the pyramids; 9, olive; 10, tubercle of Rolando; 11, external arcuate fibres; 12, upper end of spinal cord; 13, ligamentum denticulatum; 14, dura mater of spinal cord; 15, optic tract; 16, chiasma; 17, third or oculo-motor nerve; 18, fourth or trochlear nerve; 19, fifth or trigeminal nerve; 20, sixth nerve or abducens; 21, seventh or facial nerve; 22, eighth or auditory nerve; 23, nerve of Wrisberg (portio intermedia), which unites with the facial; 24, glosso-pharyngeal nerve; 25, vagus nerve; 26, spinal accessory nerve; 27, hypoglossal nerve; 28, 29, 30, first, second, and third pairs of cervical spinal nerves.

The Arrangement of the Grey and White Matter in the Upper Portion of the Cerebro-spinal Axis.—In the medulla oblongata the

grey and white matter of the spinal cord is rearranged, and, in addition, new strands of fibres and new nuclei of grey substance make their appearance. Of these nuclei the most conspicuous is the dentate nucleus of the inferior olive, which, covered by a crust of white fibres, appears as a projection on the antero-lateral surface of the medulla. In front of the olive, between it and the continuation of the anterior median fissure, is another projection, the pyramid, which looks like a prolongation of the anterior column of the cord, but is made up of very different constituents. Dorsal to the olive is the restiform body or inferior peduncle of the cerebellum, and behind the restiform body lie two thin columns, the *funiculus cuneatus*, which continues the postero-external column of the cord, and the *funiculus gracilis*, which continues the postero-internal column. In these funiculi are contained respectively the *nucleus cuneatus* and the *nucleus gracilis*. The rearrangement of the constituents of the cord is due mainly to two causes: (1) The opening up of the central canal to form the fourth ventricle, and the folding out, on either side, of the grey matter which lies posterior to it in the cord; (2) the breaking up of the grey matter of the anterior horn by strands of fibres as they sweep through it from the lateral pyramidal tract to take up a position in the pyramid of the opposite side (decussation of the pyramids), and a little higher up by fibres passing across the middle line from the gracile and cuneate nuclei (sensory decussation or decussation of the fillet). The mosaic of grey and white matter formed in the medulla by the interlacing of longitudinal and transverse fibres with each other and with the relics of the anterior horn, is called the reticular formation (*formatio reticularis*). It occupies the anterior and lateral portions of the bulb behind the pyramids and olivary bodies, and is continued upwards in the dorsal portion of the pons and crura cerebri.

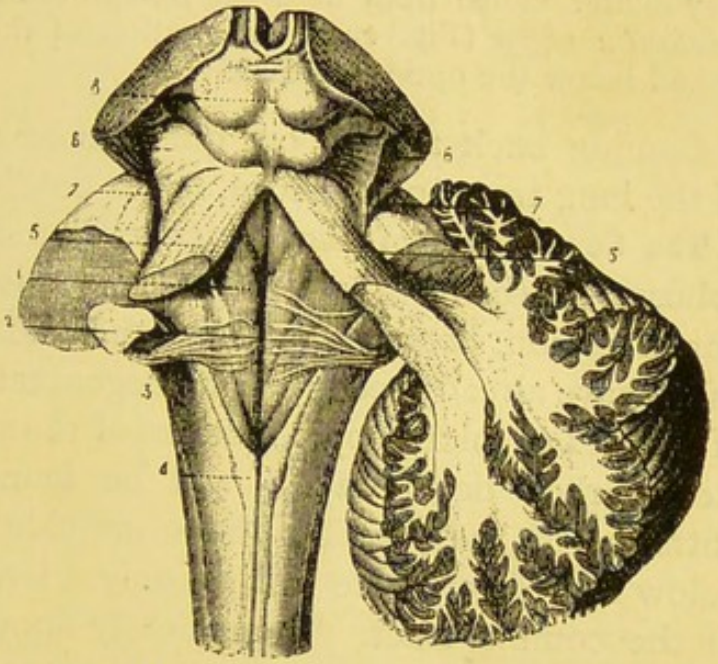

FIG. 243.—MEDULLA OBLONGATA AND CEREBELLUM, WITH FOURTH VENTRICLE (HIRSCHFELD).

1, mesial groove of floor of ventricle running down to the calamus scriptorius; 2, striæ acusticæ; 3, inferior peduncle of the cerebellum; 4, clava; 5, superior peduncle crossing the inferior and passing to its internal side; 7, 7, lateral sulcus; 8, corpora quadrigemina.

The cerebro-spinal axis passes up from the medulla through the pons, encircled and traversed by the transverse pontine fibres derived from the middle cerebellar peduncle or commissure, which enclose

everywhere between them numerous collections of nerve-cells (*nuclei pontis*). Enlarged by the accession of many of these fibres which come from the cortex of the cerebellum on the opposite side, as well as of fibres from the nuclei of the cranial nerves that take origin in this neighbourhood (fifth and eighth), the central nervous stem bifurcates above the pons into the two diverging crura cerebri. From each crus a great sheet of fibres passes up between the optic thalamus and the caudate nucleus of the corpus striatum on the one hand, and the globus pallidus of the lenticular nucleus on the other, as the internal capsule, from which they are dispersed, in the corona radiata, to the cerebral cortex. Both in the upper part of the pons and in the crus a ventral portion, or *crusta*, containing the fibres of the pyramidal tract, and a dorsal portion, or *tegmentum*, can be distinguished, the line of separation being marked in the crus by a collection of grey matter, called from its usual, though not invariable, colour the *substantia nigra* (Fig. 249). A portion of the tegmentum is continued below the optic thalamus.

Coming back now to our question as to the connections of the long tracts of the cord, let us consider, first of all,

The Connections of the Postero-median and Postero-external Columns.—When a single posterior root is divided, say in the dorsal region, between the cord and the ganglion, its fibres, as we have already seen (p. 606), degenerate above the section. If a series of microscopic sections of the spinal cord be made, well-marked degeneration will be found at the level of entrance of the root on the same side of the cord, while below that level there will be only a few degenerated fibres in the comma tract. Immediately above the plane of the divided root the degeneration will be confined to Burdach's column and to its external border. Higher up it will be found in the internal portion of Burdach's and the external rim of Goll's column. Still higher up the degenerated fibres will be confined to the postero-median column; the postero-external will be entirely free from degeneration.

When a number of consecutive posterior roots are cut, the whole of the postero-external column in the sections immediately above the highest of the divided roots will be found occupied by degenerated fibres, while Goll's column may be free from degeneration, or degenerated only at its outer border. Higher up degeneration will be found to have involved the whole of the postero-median column, and to have cleared away altogether from the postero-external. The degeneration in the column of Goll may be traced along the whole length of the cord to the medulla, although the number of degenerated fibres diminishes as we pass upward. The explanation of

these appearances seems to be as follows. It may be seen in preparations of the cord impregnated by Golgi's method that the fibres of the posterior roots soon after their entrance into the cord divide into two processes, one of which runs up and the other down in the posterior column, or in the adjoining portion of the posterior horn. From both of these collaterals are given off at intervals. The descending branches run downwards only for a short distance, and the degeneration in the comma tract seen after section of the cord is due to the division of these branches. Many of the ascending branches pass up for a short distance in the postero-external column, sweeping obliquely through it to gain the tract of

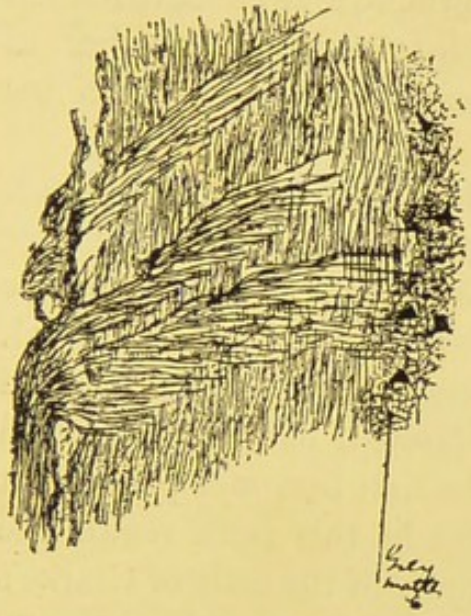

FIG. 244. — POSTERIOR ROOTS ENTERING SPINAL CORD (at the left of the figure). (From a preparation stained with aniline blue-black.)

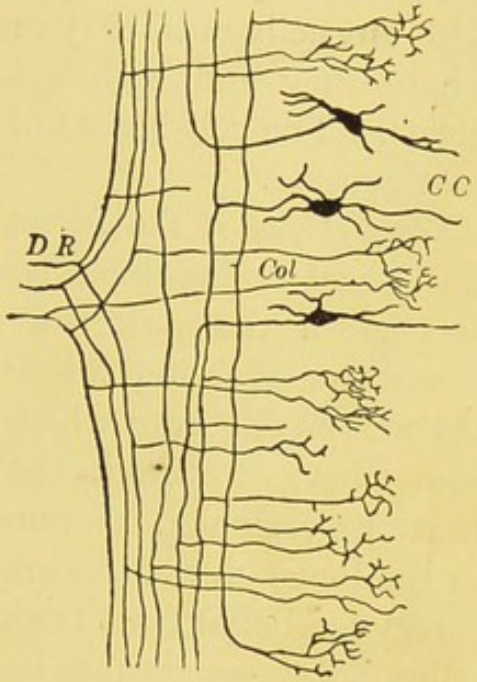

FIG. 245.—BRANCHING OF POSTERIOR ROOT FIBRES IN CORD (DONALDSON, AFTER CAJAL). Collaterals, *Col*, are seen coming off from the two main branches of the root-fibres, D R, and ending in arborisations.

C, C, cells in the grey matter of the cord, whose axons also give off collaterals.

Goll. In this tract some of them run right on to the medulla oblongata, to end in a collection of grey matter, the nucleus gracilis. Others must end at various levels in the cord, their collaterals, and ultimately the main branches themselves, coming into relation with nerve-cells in the grey matter. When the cervical posterior roots are cut, many of the degenerated fibres remain in Burdach's column up to the medulla, where they terminate in the nucleus cuneatus. In the posterior column, then, the fibres of the posterior roots which do not form synapses with nerve-cells in the spinal cord are arranged in layers, the fibres from the lower roots being

nearest the median fissure, and those from the higher roots farthest away from it. Other collaterals from the posterior root-fibres, and many of the root-fibres themselves, run into the anterior horn; some pass into the posterior horn, and doubtless come into relation with its scattered cells and with the cells of Clarke's column. Other collaterals and probably some axons cross the middle line in the anterior and posterior commissures and end in the grey matter of the opposite side.

We may, therefore, conclude without hesitation that some of the fibres of the posterior roots ascend to the medulla in the posterior column of the cord without forming synapses with any cells until they reach the gracile and cuneate nuclei, where they end by breaking up into terminal brushes of fibrils. The cell-bodies of these neurons lie in the posterior root-ganglia.

Connections of the Direct or Dorsal Cerebellar Tract.—Since the dorsal or direct cerebellar tract does not degenerate after section of the posterior nerve-roots, but does degenerate above the level of the lesion after section of the spinal cord, the nerve-cells from which its axons arise must be situated somewhere or other in the cord. Now, it has been observed that the vesicular column of Clarke first becomes prominent in the lower dorsal region, and that in this same region the direct cerebellar tract begins. Atrophy of the cells of Clarke's column has sometimes in disease been shown to accompany degeneration of the direct cerebellar fibres. After an experimental lesion of these fibres in animals, some of the cells of the vesicular column show the changes in the Nissl bodies which we have already described, under the name of chromatolysis, as occurring in nerve-cells whose axons have been cut. After two or three months these cells may be found almost completely atrophied (Schäfer). Finally axis-cylinder processes have been seen sweeping out from Clarke's column into the direct cerebellar tract (Mott). The evidence, then, is very strong that some of the cells of Clarke's column are the cells of origin of this tract. Clarke's cells are surrounded by arborisations, some of which represent the terminations of posterior root-fibres and of their collaterals. The direct cerebellar tract runs right up to the cerebellum through the restiform body, without crossing and without being further interrupted by nerve-cells. The restiform body ends partly

in the dentate nucleus of the cerebellum, partly in the vermis, and among the fibres which end in the vermis are those of direct cerebellar tract.

Connections of the Antero-lateral Ascending Tract.—According to Schäfer, the axons of this tract are also connected with cells situ-

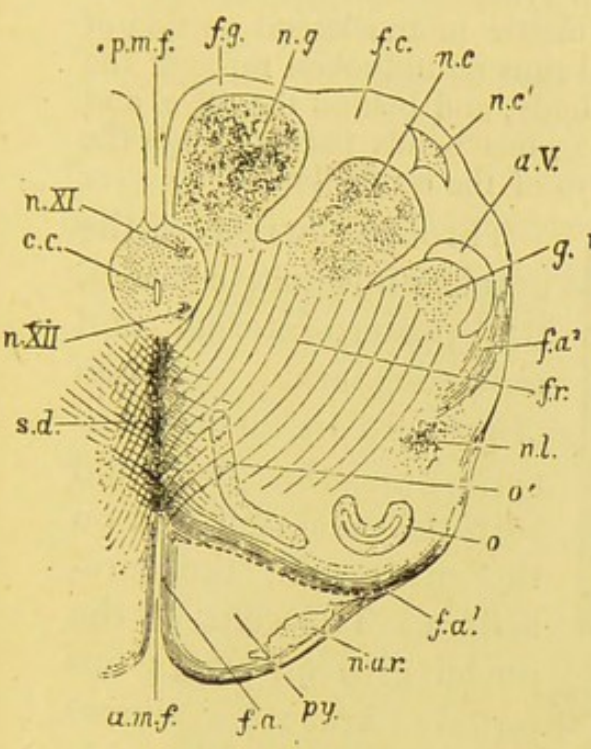

FIG. 246. — TRANSVERSE SECTION OF MEDULLA OBLONGATA AT THE LEVEL OF THE DECUSSATION OF THE FILLET (HALLIBURTON, AFTER SCHWALBE).

a. m. f., anterior, and *p. m. f.*, posterior median fissure; *f. a* and *f. a²*, external arcuate fibres; *f. a'*, internal arcuate fibres becoming external; *n. a. r*, nuclei of arcuate fibres; *py*, pyramid; *o*, *o'*, lower end of nucleus of olive; *f. r*, formatio reticularis; *n. l*, lateral nucleus; *n. g*, nucleus gracilis; *f. g*, funiculus gracilis; *n. c*, nucleus cuneatus; *nc'*, external cuneate nucleus; *f. c*, funiculus cuneatus; *g*, substance of Rolando; *c. c*, central canal surrounded by grey matter; *n. XI*, nucleus of spinal accessory; *n. XII*, of hypoglossal; *a. V*, ascending root of fifth nerve; *s. d.*, the decussation of the fillet, or superior decussation.

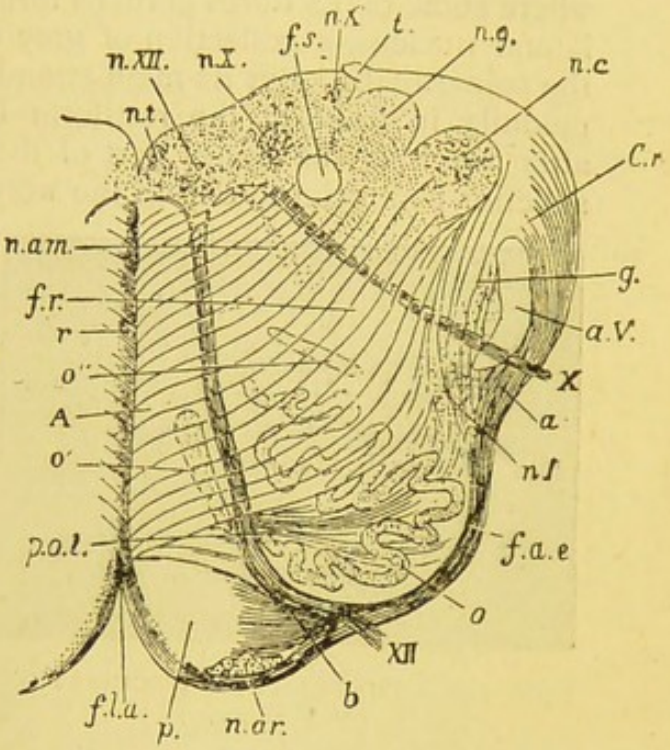

FIG. 247. — TRANSVERSE SECTION OF MEDULLA OBLONGATA AT ABOUT THE MIDDLE OF THE OLIVE (HALLIBURTON, AFTER SCHWALBE).

f. l. a, anterior median fissure; *n. a. r*, arcuate nucleus; *p*, pyramid; *n. XII*, hypoglossal nucleus; *XII*, root bundle of hypoglossal nerve coming off from the surface; at *b* it runs between the pyramid and the dentate nucleus of the olive, *o*; *f. a. e*, external arcuate fibres; *n. l*, lateral nucleus; *a*, arcuate fibres going to restiform body *c. r*, partly through the substantia gelatinosa *g*, partly superficial to the ascending root of the fifth nerve *a. V*; *X*, root-bundle of vagus; *n. X*, *n. X'*, two portions of vagus nucleus; *f. r*, formatio reticularis; *n. g*, nucleus gracilis; *n. c*, nucleus cuneatus; *n. t*, nucleus of the funiculus teres; *n. am*, nucleus ambiguus; *r*, raphe; *o'*, *o''*, accessory olivary nucleus; *p. o. l*, peduncle of the olive.

ated in Clarke's column. For when both the antero-lateral ascending and the direct cerebellar tracts are divided a much larger number of the cells of the vesicular column are involved in the resulting chromatolysis and atrophy than when the lesion is confined to the direct cerebellar tract alone. But some of the fibres of the tract may have a different source (from cells at the base of the anterior horn on the

same and also on the opposite side), and the fact that it begins lower down in the cord than the direct cerebellar tract is in favour of the view that their cells of origin are not confined within exactly the same boundaries. None of the fibres of the tract can come directly from the posterior nerve-roots, since no degeneration is seen in it on section of the roots alone.

The antero-lateral ascending tract passes up through the medulla, where some of its fibres perhaps form synapses with the cells of the lateral nucleus, a collection of grey matter in the lateral portion of the spinal bulb. But its main strand runs on unbroken through the medulla, in front of the restiform body, and behind the olive, and after reaching the upper part of the pons bends back through the superior peduncle, to end in the worm of the cerebellum.

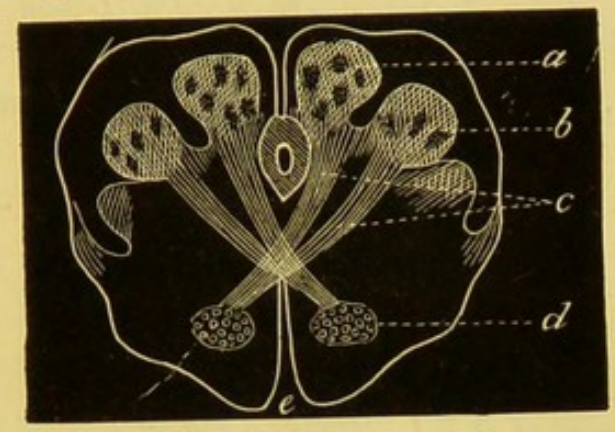

FIG. 248.—DIAGRAM OF DECUSSATION OF FILLET.

a, nucleus gracilis; *b*, nucleus cuneatus; *c*, internal arcuate fibres crossing the middle line from *a* and *b* to the fillet *d*, and forming the decussation of the fillet; *e*, anterior median fissure.

Through the relay of the gracile and cuneate nuclei, the postero-internal and postero-external columns of the cord are further connected on the one hand with the cerebrum, and on the other with the cerebellum. The cells of the nuclei give off fibres (internal arcuate fibres) which, sweeping in wide arches across the mesial raphe to the opposite side, take up a position behind the pyramid in the *fillet*, a bundle of fibres which becomes more compact, and therefore more distinct as it passes brainwards. Receiving fibres from other sources on its way, and also giving off fibres, it runs upwards into the dorsal or tegmental portion of the pons. Here it divides into two portions, the *mesial fillet* and the *lateral fillet*. The lateral fillet contains fibres arising in the cochlear nucleus of the auditory nerve, and ends in the posterior corpus quadrigeminum, and partly below the anterior corpus quadrigeminum. It appears to be a path for the conduction of auditory impulses. The mesial fillet contains the fibres that come off from the gracile and cuneate nuclei. Enlarged by the accession of fibres from the sensory nuclei of the cranial nerves, it pursues its course through the tegmentum of the crus, and terminates for the most part in

the optic thalamus and the region below it (sub-thalamic region) by forming synapses with nerve-cells, whose axons, passing through the posterior limb of the internal capsule and the corona radiata, continue the afferent path to the cerebral cortex. A few of the fibres of the mesial fillet may, however, run straight on to the cortex without being interrupted by nerve-cells.

Some of the internal arcuate fibres, instead of passing into the fillet after crossing the middle line, bend out (as external arcuate fibres) along the edge of the anterior median fissure, and coursing superficially around the pyramid and olive, reach

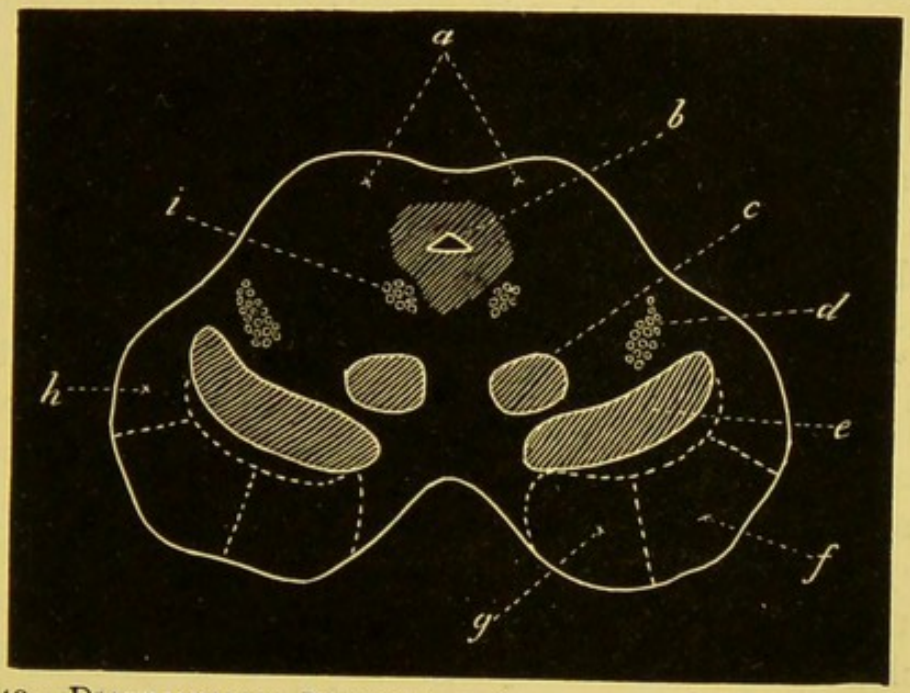

FIG. 249.—DIAGRAMMATIC TRANSVERSE SECTION OF CRURA CEREBRI AND AQUEDUCT OF SYLVIUS.

a, anterior corpora quadrigemina; *b*, aqueduct; *c*, red nucleus; *d*, fillet; *e*, substantia nigra; *f*, pyramidal tract in the crusta of the crura cerebri; *g*, fibres from frontal lobe of cerebrum; *h*, fibres from temporo-occipital lobe; *i*, posterior longitudinal bundle.

the restiform body. A connection is thus established between the two nuclei and the opposite side of the cerebellum. Numerous fibres also go directly from the nuclei, and especially the nucleus cuneatus, to the restiform body of the same side.

Connections of the Pyramidal Tracts.—When the cortex around the fissure of Rolando is destroyed by disease in man, or removed by operation in animals, it is found that in a short time degeneration has taken place in the fibres of the corona radiata which pass off from this area. The degeneration can be followed down through the genu and the anterior

two-thirds of the posterior limb of the internal capsule (Fig. 250), and the crusta of the cerebral peduncle of the corresponding side into the medulla oblongata. Below the decussation of the pyramids it is found that the degeneration has involved the two pyramidal tracts, and only these—the crossed pyramidal tract on the side opposite the cortical lesion, the direct pyramidal tract on the same side—and that the cross-section of the two degenerated tracts goes on continually diminishing as we pass down the cord. (We overlook, for the moment, in the interest of simplicity of statement, the fact that in the monkey and in man, at any rate, some degenerated fibres may be found in the crossed pyramidal tract on the same side as the lesion.) This is proof positive that the cell-bodies of the neurons whose axons run in these tracts are situated in the cerebral cortex. They have indeed been identified with certain of the large pyramidal cells in the Rolandic area. Among these the so-called giant-cells, which are most numerous in the upper portions of this area, and the majority of which are connected with the long pyramidal fibres that run down into the cord, are especially conspicuous. The fact that the degeneration does not spread to the anterior roots shows that at least one relay of nerve-cells intervenes between the pyramidal fibres and the root-fibres. The results both of normal and morbid histology enable us to identify the cells of the anterior horn as the cells of origin of the axons of the anterior root-fibres. For

(1) Axis-cylinder processes have been actually observed passing out from certain of the so-called motor cells of the anterior horn to become the axis-cylinders of fibres of the anterior root.

(2) In the pathological condition known as anterior poliomyelitis, the cells of the anterior horn degenerate, and so do the anterior roots of the affected region, the motor fibres of the spinal nerves, and the muscles supplied by them.

(3) An enumeration* has been made in a small animal (frog) of the cells of the anterior horn and of the anterior root-fibres, and it has been found that the numbers agree in a remarkable manner. From all this it cannot be doubted that most, at any rate, of the cells of the anterior horn are connected with fibres of the anterior root. But since the number of fibres in the pyramidal tracts falls far short of

* Such enumerations can now be made with great accuracy from photographs of sections of the nerves (Hardesty, Dale). (See Fig. 236, p. 669.)

the number of cells in the anterior horn, and of the number of fibres in the anterior roots, it is necessary to assume that one pyramidal fibre may be connected with several cells. While there is no doubt that the anterior root-fibres and the pyramidal fibres of the brain and cord form segments of the same nervous path, it is still a question whether another neuron may not be intercalated between the pyramidal fibres and the cells of the anterior horn. Schäfer supposes that the pyramidal fibres end around some of the cells of Clarke's column, which in turn send off axons that come into relation with the anterior horn cells.

Connections of the Antero-lateral Descending Tract.—These are not well known. Some writers have stated that degeneration is caused in this tract by extirpation of the corresponding half of the cerebellum. This would, of course, indicate that the cells of origin lie in the cerebellum. But recent observations, on the whole, cast doubt upon the statement. Russell, *e.g.*, finds only a few degenerated fibres in the cord after hemi-extirpation of the cerebellum, although the restiform body contains many degenerated fibres going to the olives. He believes that the main origin of the antero-lateral descending fibres is the nucleus of Deiters, a collection of large multipolar nerve-cells in the floor of the fourth ventricle near the inner auditory nucleus. The fibres appear, pass into the anterior horn, where most of them end by arborizing amongst the cells of the horn.

Thus far, then, we have been able to map out two great paths from the cerebral cortex to the periphery, one efferent, the other afferent.

(1) **The great efferent or motor pyramidal path**, which, starting in the cortex around the fissure of Rolando, where its axons give off numerous collaterals soon after emerging from the cells, and sweeping down the broad fan of the corona radiata, passes through the narrow isthmus of the internal capsule into the crusta of the crus cerebri, and thence into the pons. At this level, the fibres destined to make connection with the motor nuclei of the cranial nerves in the grey matter underlying the aqueduct of Sylvius and the fourth ventricle terminate. Most of these fibres decussate to end in nuclei on the opposite side, but some join nuclei on the same side. On their way through the pons they send off collaterals to the nuclei pontis. The rest of the pyramidal fibres run on into the pyramid of the bulb, where the greater part (usually about 90 per cent.) of the fibres decussate, appearing in the cervical cord as the massive crossed pyramidal tract of the opposite side. A few (usually about

10 per cent.) remain on the same side as the slender direct pyramidal tract; but the breadth of this tract constantly diminishes as it proceeds down the cord, and it disappears before the middle of the thoracic region is reached, its fibres continually decussating across the anterior white commissure and plunging into the opposite anterior horn. They either end among its cells, or passing through it, reinforce the crossed pyramidal tract. The fibres of this crossed tract are, in their turn, continually passing off into the grey matter, where they break up into terminal brushes, and thus make connection either directly or through the interposition of other neurons with the cells of the anterior horn, whose axis-cylinder processes enter the anterior roots of the spinal nerves. The losses which it suffers as it passes along the cord may be in some slight degree compensated by the bifurcation of some of its fibres (geminal fibres), but ultimately the whole tract forms synapses with cells in the grey matter, and dwindles away as the lumbar region is reached (Fig. 239). It has been asserted that on their way down the cord the two crossed pyramidal tracts exchange some fibres with each other (recrossed fibres); and it was supposed that this would explain the escape in hemiplegia (paralysis of one side of the body) of those muscles which are accustomed to work with the corresponding muscles on the opposite side, *e.g.*, the respiratory muscles. But although there is no doubt that such muscles are innervated to some extent from both cerebral hemispheres, this is due not to *recrossed*, but to *uncrossed* (*homolateral*), fibres, which in the cord run down in the lateral pyramidal tract, and are represented by the fibres that degenerate in that tract after a lesion in the Rolandic area of the same side (p. 686).

(2) **A great afferent or sensory path** by which some at least of the impulses carried up through the posterior roots of the spinal nerves, after passing through various relays of nerve-cells, reach the cortex of the cerebellum; or the upper portions of the central grey tube, the corpora quadrigemina and optic thalamus; or, finally (both indirectly and by a more direct route which certain fibres of the mesial fillet follow through the tegmentum and the posterior limb of

the internal capsule behind the motor fibres), the cerebral cortex itself.

The efferent pyramidal path from the cortex is broken by but one relay of nerve-cells, the motor cells of the anterior horn and the cranial nuclei; or at any rate if another intervenes (p. 687) its axon is of insignificant length, and it constitutes rather a joint between two segments of the nervous path than an independent segment. The afferent path is interrupted by at least two relays with axons of considerable length. One of the cells is situated in the ganglion on the posterior root, another in the medulla; and on some of the routes another, or even more than one, is intercalated between the medulla and the cortex.

Connections of the Grey Matter of the Cerebellum with the Periphery and other Parts of the Central Nervous System.— Numerous as are the nervous ties of the cerebral cortex, those of the grey matter of the cerebellum are, in proportion to its mass, still more extensive, and perhaps not less important. Speaking broadly, we may say that the restiform body connects chiefly the dentate nucleus and the grey matter of the worm with both sides of the spinal cord and medulla oblongata, and through them with the periphery. The fibres which it receives from the direct cerebellar tract of its own side, and the gracile and cuneate nuclei of its own and of the opposite side, it carries to the worm; the fibres which reach it from the olivary nucleus of the opposite, and also in smaller numbers from that of the same side, run mainly to the dentate nucleus. The middle peduncle is in the main a link between the cerebellar cortex and the cerebral cortex of the opposite side, through the relay of the pontine grey matter. The superior peduncle connects chiefly the dentate nucleus of one side with the cortex of the opposite cerebral hemisphere through the red nucleus of the tegmentum of the crus cerebri on the opposite side. Since the cortex of the cerebellum is linked to the dentate nucleus the superior peduncle affords an indirect connection between it and the cerebral cortex. Through the restiform body afferent impulses pass up to the cerebellum. From the cerebellum they *may* proceed to the cerebrum. So that the path by the restiform body, dentate nucleus, and superior peduncle may form an alternative route for afferent impressions passing from the periphery to the great brain—a path broken by at least four relays of nerve-cells. The cerebellar hemisphere may be connected by an efferent path through the nucleus of Deiters and the descending antero-lateral tract with the motor roots of the same side. An uncrossed connection also exists between the cerebellum and the vestibular branch of the auditory nerve, through one of its nuclei of origin, and possibly between it and other cranial nerves, such as the optic and trigeminal.

The Internal Capsule.—We have already recognised the pyramidal tract and the afferent tegmental path as constituents of the internal capsule. The cranial fibres of the pyramidal tract occupy the genu or knee, the spinal fibres the anterior two-thirds of the posterior limb. The posterior third of the posterior limb contains the sensory path.*

But we have not yet exhausted the constituents of the internal capsule. Two great cones of fibres sweep down into it, one from the frontal, the other from the occipital

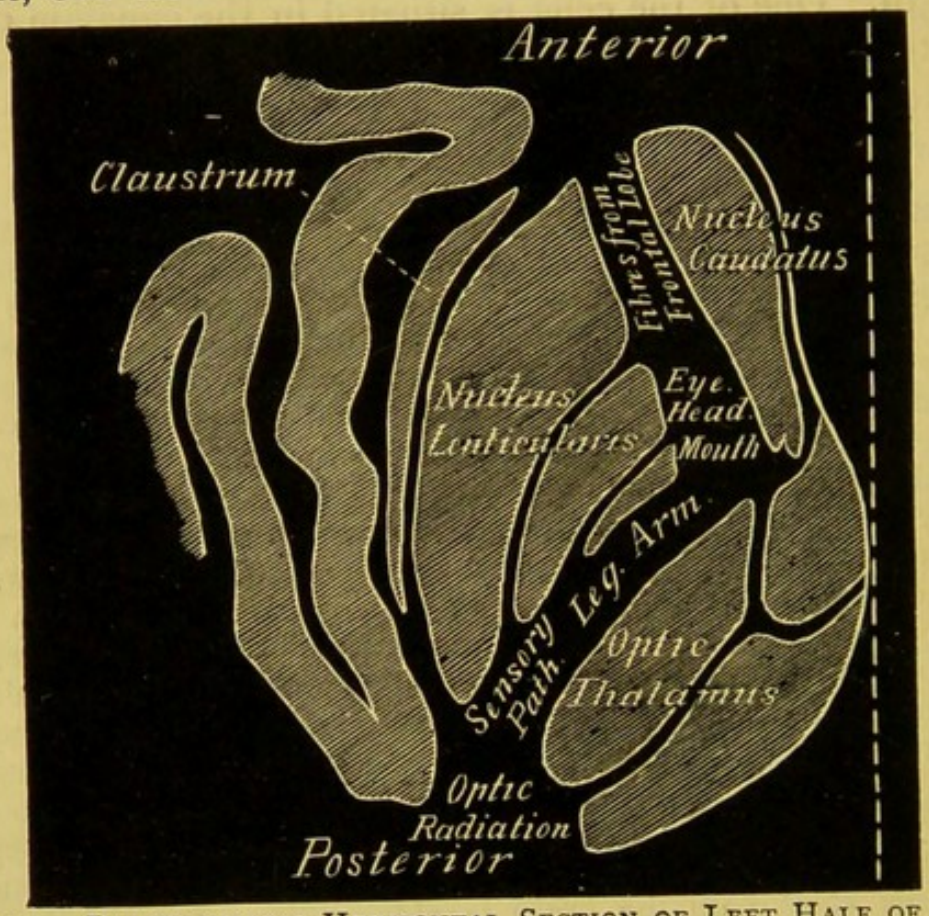

FIG. 250.—DIAGRAMMATIC HORIZONTAL SECTION OF LEFT HALF OF BRAIN TO SHOW INTERNAL CAPSULE.

and temporal portions of the cerebral cortex. The first passes through its anterior limb, the second behind the sensory path in its posterior limb. The cells of origin of

* The common statement that the efferent (motor) path occupies the anterior two-thirds, and the afferent (sensory) path the posterior third of the posterior limb of the internal capsule, while no doubt true in a general sense, is not strictly correct. Some motor fibres seem to be intermingled with the sensory in the posterior third, for lesions of this region produce a certain degree of paralysis as well as anæsthesia on the opposite side of the body. A pure capsular hemianæsthesia, that is, a loss of sensation on the opposite side due to a lesion in the internal capsule and unaccompanied by motor defect, does not appear to exist.

the frontal fibres are known, and those of the occipital and temporal fibres are supposed, to be situated in the cortex. Running on through the crusta of the cerebral peduncle (Fig. 249), the frontal tract internal, the occipito-temporal external, they end in the grey matter of the pons, and probably serve as one segment of an extensive commissural connection between the cerebral and the cerebellar cortex of the opposite side, the other segment being formed by neurons whose cell-bodies are situated in the pons, and whose axons, crossing the middle line, pursue their course through the middle cerebellar peduncle, to terminate as the so-called mossy

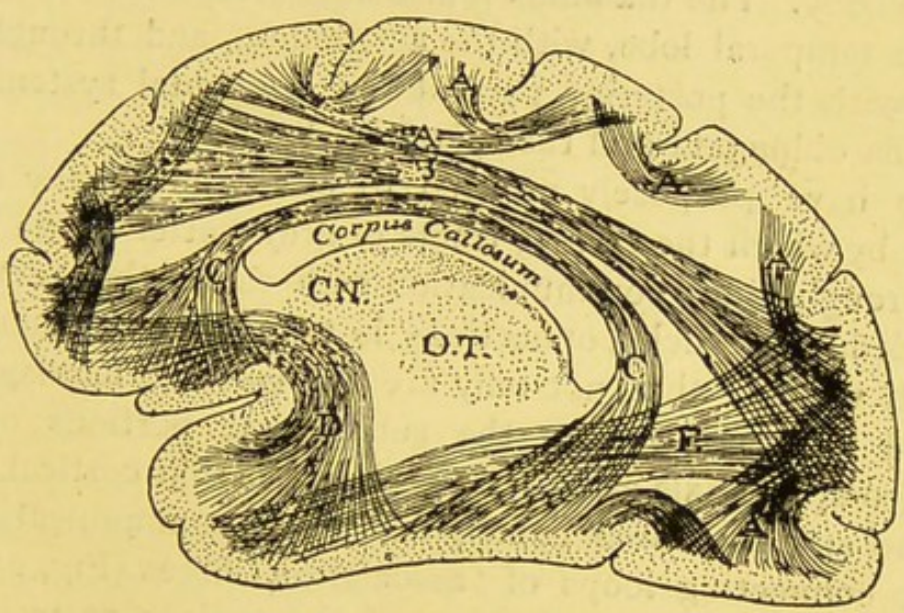

FIG. 251.—ASSOCIATION FIBRES (AFTER STARR).

Cerebral hemisphere seen from the side. A, A, association fibres between adjacent convolutions; B, between frontal and occipital lobes; C, cingulum, connecting frontal and temporo-sphenoidal lobes; D, uncinate fasciculus between frontal and temporal regions; E, inferior longitudinal bundle between occipital and temporo-sphenoidal lobes; O.T., optic thalamus; C.N., caudate nucleus.

fibres in the superficial grey matter of the cerebellum. It is evident that the junction of the cerebral cortex with this pontine grey matter, through and into which so many nerve-tracts pass, multiplies the number of possible routes by which impulses may travel between one part of the brain and another. The corpus callosum forms a mighty link between the two cerebral hemispheres. And intertwined in the corona radiata with the callosal fibres are other systems, of which it is especially necessary to mention the fibres that join nearly every part of the cerebral cortex with the optic

thalamus. Such fibres pass from the thalamus to the frontal and parietal regions through the anterior border of the internal capsule in front of the frontal fibres previously described as running in the anterior limb of the capsule to the pons; and from the thalamus to the occipital region through the extreme posterior border of the internal capsule, behind the occipital fibres that proceed to the pons. The fibres that connect the thalamus with the occipital cortex are spoken of as the optic radiation. Some of the fibres of the optic radiation, however, proceed, not to the thalamus, but to the anterior corpus quadrigeminum and the lateral geniculate body. The thalamus is also connected with the cortex of the temporal lobe, with the cerebellum, and through the fillet with the posterior part of the tegmental system, the medulla oblongata and the spinal cord (p. 685).

We have purposely omitted to enumerate many other paths by which the various tracts of grey matter in the brain are brought into communication with each other, and our knowledge of such connections is constantly augmenting. When we add that not only are the cerebral hemispheres united by many ties to the subordinate portions of the cerebro-spinal axis and to each other, but that cortical areas of one and the same hemisphere are in communication by short connecting loops of 'association' fibres (Fig. 251), it will be seen that the linkage of the various parts of the central nervous system is extremely complex; that an excitation, blocked out from one path, may have the choice of many alternative routes; and that the apparent simplicity and isolation of the pyramidal tracts must not be allowed too far to govern our views of the possibilities open to a nervous impulse once it has been set going in the labyrinth of the nervous network. Nor is it only by the main channel of the axis-cylinder that nervous impulses can be conducted. It cannot be doubted that they can also pass along the collaterals. And the actual route taken by a given impulse is, in all probability, determined not only by anatomical relations, but also by molecular conditions, particularly in the terminal fibrils of the axons, collaterals and dendrites, and in the substance, if such a substance there be, which

intervenes between the end arborizations of a neuron and the dendrites or cell-bodies of the neurons with which they lie in contact. So that a road open at one moment may be closed at another. We may suppose that the greater the number of connections between the cells of the central nervous system, the greater is the complexity of the processes which may be carried on within it. And, indeed, comparison of the brains of different animals shows us that it is not so much by excess in the number of nerve-cells as by the increased complexity of linkage, that a highly developed brain differs from a brain of lower type; the higher the brain, the more richly branched are the dendrites and the terminations of the axons and their collaterals, and, therefore, the greater is the number of possible paths between one nerve-cell and another.

II. Functions of the Central Nervous System.

Much of our knowledge of the functions of the central nervous system and of its divisions has been gained by the removal or destruction of more or less extensive tracts of nervous substance, or the cutting off of connection between one part and another. But it is well to warn the reader at the very outset that in no other part of physiology is such caution required in making deductions as to the working of the intact mechanism from the phenomena which manifest themselves after such lesions.

In the first place, every operation of any magnitude on the brain or cord is immediately followed by a depression of the functional power of the nervous tissue, a depression which may extend far from the actual seat of injury and manifest itself by various phenomena, which are grouped together under the name of 'shock.' Thus, when the spinal cord of a dog is divided, *e.g.*, in the dorsal region, all power, all vitality, one might almost say, seems to be for ever gone from the portion of the body below the level of the section. The legs hang limp and useless. Pinching or tickling them calls forth no reflex movements. The vaso-motor tone is destroyed, and the vessels gorged with blood. The urine accumulates, overfills the paralyzed bladder, and continually dribbles away from it. The sphincter of the anus has lost its tone, and the fæces escape involuntarily. And if we were to continue our observations only for a short time, a few hours or days, we should be apt to appraise at a very low value the functions of that part of the cord which still remains in connection with the paralyzed extremities. But these symptoms are essentially

temporary. They are the results of shock; they are not true 'deficiency' phenomena. And if we wait for a time, we shall find that this torpor of the lower dorsal and lumbar cord is far from giving a true picture of its normal state; that, cut off as it is from the influence of the brain, it is still endowed with marvellous powers. If we wait long enough, we shall see that, although voluntary motion never returns, reflex movements of the hind-limbs, complex and co-ordinated to a high degree, are readily induced. Vaso-motor tone comes back. The functions of defæcation and micturition are normally performed. Erection of the penis and ejaculation of the semen take place in a dog. A man with complete paralysis below the loins and destitute of all sensation in the paralyzed region has been known to become a father (Brachet). Pregnancy carried on to labour at full term has been observed in a bitch whose cord was completely divided above the lumbar enlargement.

We cannot doubt that the spinal cord takes an important share in this recovery of function. But here again it would be erroneous to conclude that everything is due to the cord. For Goltz and Ewald have been able to keep dogs alive for long periods after preliminary section of the cord in the cervical region and subsequent removal of large portions of it. They find that even after destruction of the lumbar and sacral regions of the cord the external sphincter of the anus, striped and even voluntary muscle though it be, regains its tone, although it is temporarily lost after the first cervical section. The bladder ultimately recovers the power of emptying itself spontaneously and at regular intervals. A pregnant bitch in which the lumbar enlargement and the whole cord below it to the cauda equina had been removed, and therefore all the nerve-roots supplying fibres to the uterus cut, whelped in a normal manner, and the corresponding mammary glands behaved exactly as the rest. Digestion went on as usual when practically nothing of the cord except its cervical portion was left. Certain vaso-motor phenomena were also observed which suggest that the sympathetic system, independently of the cerebro-spinal system, is itself possessed of regulative powers.

Secondly, we must not run into the opposite error, and assume, without proof, that all the functions which the brain or cord is capable of manifesting under abnormal circumstances are actually exercised by either when, under ordinary conditions, it is working along with and guiding, or being guided by, the other. For example, in many animals the reflex powers of the cord are, if not increased, at all events more freely exercised when the controlling influence of the higher centres has been cut off than when the central nervous system is intact.

Thirdly, there is another class of phenomena which we must make allowance for, and perhaps more frequently in the case of pathological lesions in man than in experimental lesions in the lower animals. This is the class of 'irritative' phenomena. The irritation set up by a blood clot or a collection of pus, or in any other way, in

a wound of the grey or white matter, may cause a stimulation of nervous tracts by which, for a time, the 'deficiency' effects of the lesion may be masked.

In the fourth place, we must not hastily conclude that when no obvious deficiency seems to follow the removal of a portion of the central nervous system, the function of that portion must necessarily be of such a nature as to give rise to no objective signs. For we have reason to believe that, to a certain extent, the function of one part may, in its absence, be vicariously performed by another.

Bearing in mind the cautions we have just been emphasizing, we may broadly distinguish between the functions of the cord (including the bulb) and those of the brain proper by saying that the cord is essentially the seat of reflex actions, the brain the seat of automatic actions and conscious processes. But neither of these conceptions is entirely correct. Both err by defect and by excess. The brain, it is true, is pre-eminently automatic. The movements which are started in the grey matter of the cerebral cortex are pre-eminently voluntary (p. 739), but we cannot deny to the brain the possession of reflex powers as well. The movements in which the only nerve centres concerned are those of the spinal cord are above all reflex (p. 704). But some of its centres, and especially those lying in the medulla—for example, the respiratory centre—are perhaps, much as they are influenced by afferent impulses, capable of discharging automatic impulses too. And while consciousness is certainly bound up with the integrity of the brain, and in all the higher mammals is probably associated with cerebral activity alone, it has been plausibly maintained that the spinal cord, even of such an animal as the frog, is also endowed with something which might be called a kind of hushed consciousness. If this is so for the frog, with its distinct though relatively ill-developed cerebral hemispheres, it must be still more likely in the case of fishes and animals below them, which are practically devoid of a cerebral cortex altogether.

Functions of Spinal Cord (including Medulla Oblongata).

The functions of the spinal cord may be classified thus:

1. The conduction of impulses set up elsewhere—either in the brain or at the periphery.
2. The modification of impulses set up elsewhere (reflex action).
3. The origination of impulses (?).

1. **Conduction of Nervous Impulses by the Cord.**—The old controversy as to whether the white fibres of the spinal cord are directly excitable may be considered as definitely settled in the affirmative. The inquiry was complicated by the presence of the spinal roots, which since the experiments of Charles Bell have been known to be capable of excitation by artificial stimuli. But at length the difficulty was overcome in this way. The posterior (dorsal) portion of several segments of the cord with the attached posterior roots and the grey matter was excised. Long strands of the white matter of the anterior (ventral) portion of the cord were isolated, and laid on electrodes, and contractions of muscles were seen to follow stimulation, even when the anterior roots nearest the stimulating electrodes had been cut, and every precaution taken to avoid escape of current on to the distant anterior roots of the nerves supplying the muscles. Indeed, apart from direct experimental evidence, the fact that the white fibres of the brain are universally admitted to be excitable by artificial means would be of itself almost sufficient to decide the question, for we know of no essential difference between the cerebral and the spinal fibres. But the conditions must rarely occur under which direct stimulation of white fibres in their course is possible in the intact body; and the only impulses with which we need concern ourselves here are those that reach the conducting paths from grey matter in the cord itself or in the brain, or from the peripheral organs.

What sort of impulses, then, do the various tracts of the spinal cord conduct? For the posterior roots this question was first fully answered by Magendie; for the anterior roots

by Sir Charles Bell. Bell observed that when, in an animal just killed, he mechanically stimulated the anterior roots, muscular contractions were obtained at each touch of the

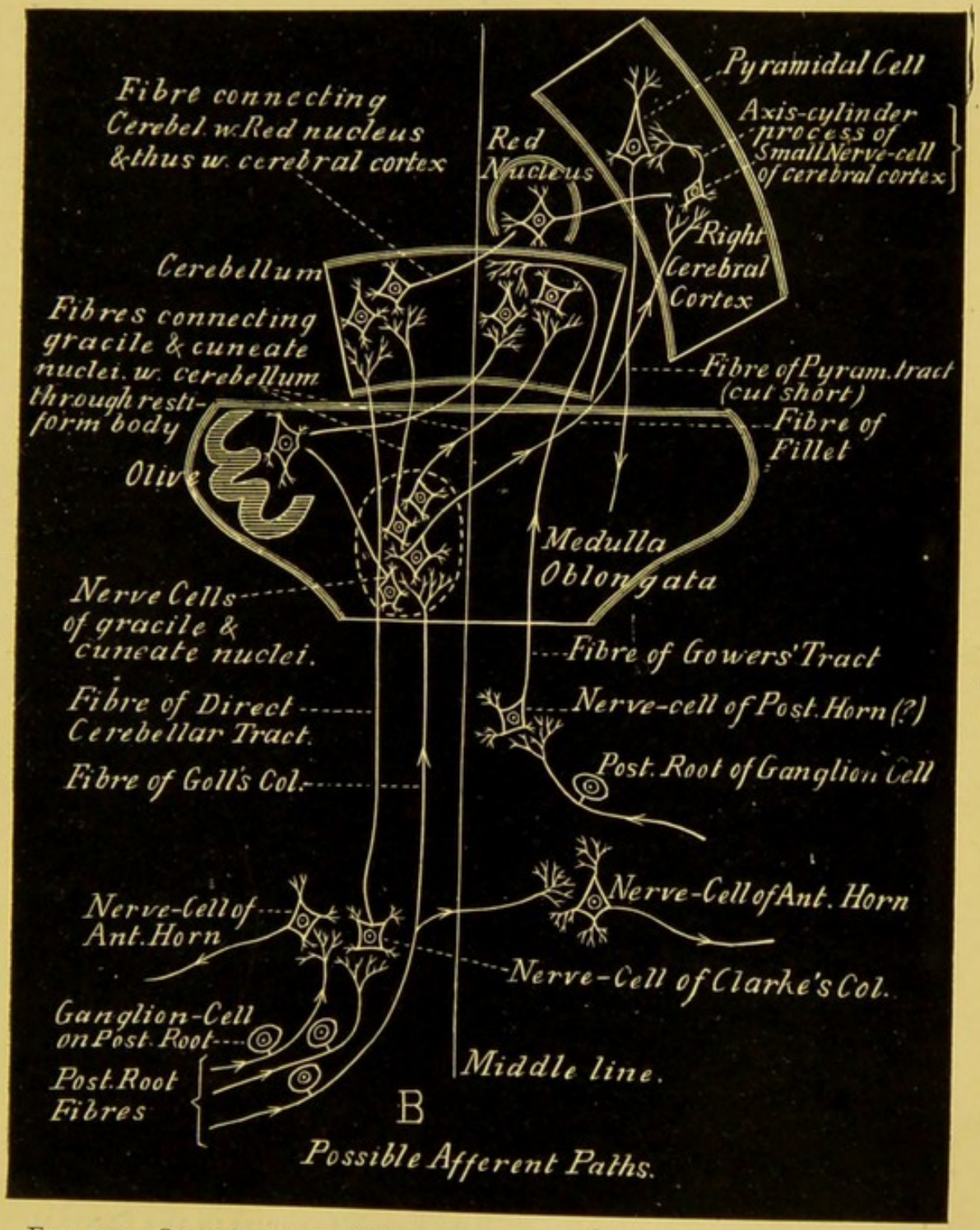

FIG. 252.—SOME POSSIBLE PATHS OF AFFERENT IMPULSES IN THE CENTRAL NERVOUS SYSTEM (SCHEMATIC)

forceps. He concluded from this that the anterior roots are motor; but although he is often credited with the discovery of the functions of the posterior roots as well, he was not

the first to make the decisive experiment necessary to show that they are the conductors of sensory impulses.

When the posterior roots are divided, loss of sensation

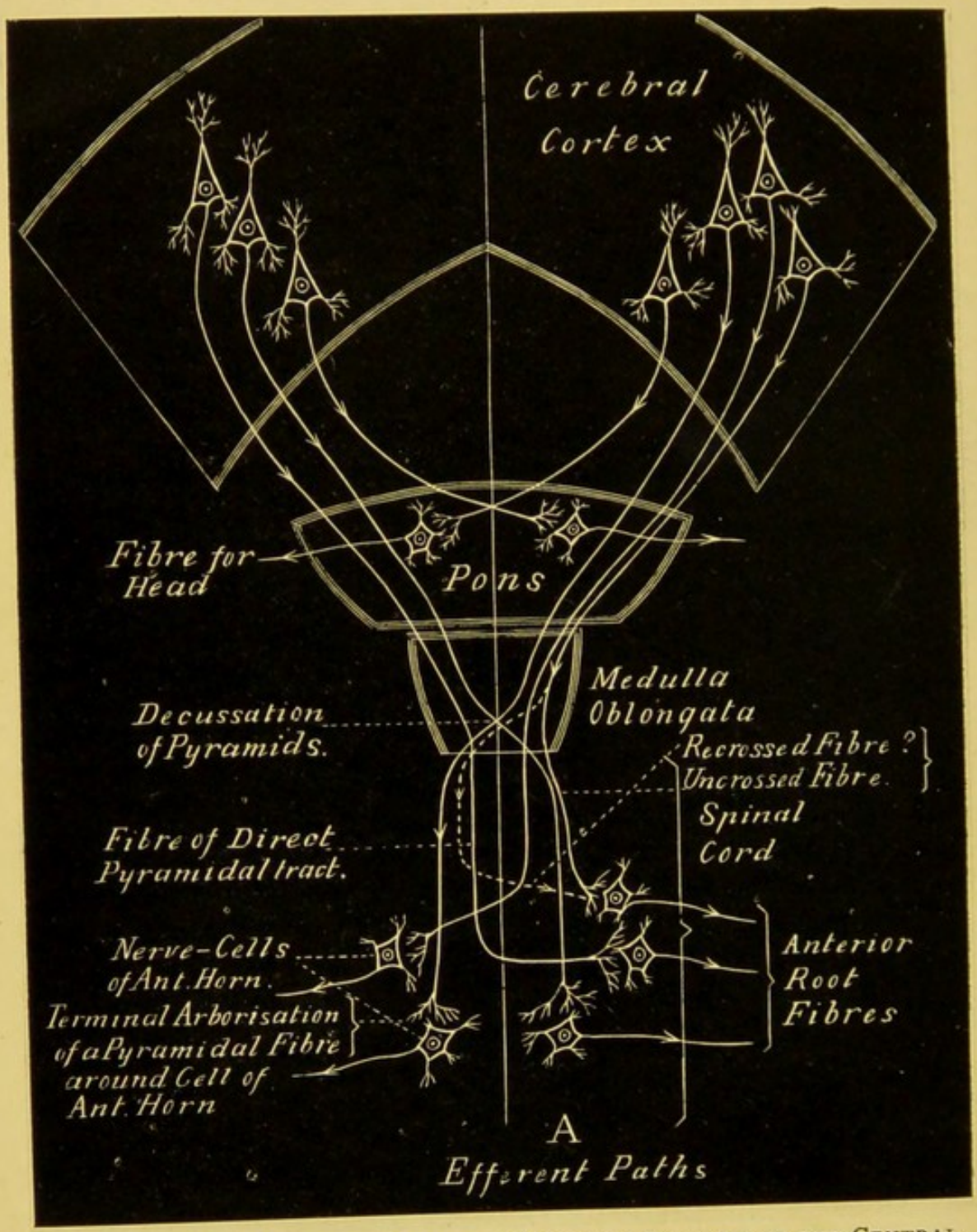

FIG. 253.—SOME POSSIBLE PATHS OF EFFERENT IMPULSES IN THE CENTRAL NERVOUS SYSTEM (SCHEMATIC).

Details are omitted from the scheme. For instance, each pyramidal fibre is represented as arborizing around one anterior cornual cell only, and no collaterals are shown.

occurs in the region to which they are distributed. If only one root is cut, the loss of sensation is never complete in

any part of the skin; and Sherrington has found that the cutaneous areas of distribution of consecutive nerve-roots are not perfectly independent, but to some extent overlap. Stimulation of the peripheral end of the divided posterior root has no effect. Stimulation of the central end gives rise, if the animal be conscious, to evidences of pain, and other signs of the passage of afferent impulses, *e.g.*, a rise in blood-pressure. The latter may also be observed when the animal is anæsthetized.

The posterior roots contain sensory fibres not only for the skin, but also for the deeper structures and the viscera. Recent clinical observations have thrown much light upon the distribution of the visceral fibres and their relation to the cutaneous sensory nerves. It has long been known that in disease of an internal organ the pain is often referred to some superficial part. It has now been demonstrated that each organ is related to a definite region of the skin. In disease of the organ the excitability for impressions of touch or temperature is increased in this area, and the reflexes elicited by stimulation are exaggerated (Head, Dana).

The bond of connection appears to be the origin from the same spinal segment of the sympathetic sensory fibres of any viscus and the sensory supply of the corresponding cutaneous area. The common anatomical origin seems to carry with it a physiological correlation, the nature of which will be best considered along with the general topic of the localization of sensory impressions (Chap. XIII.).

Recurrent Sensibility.—Although muscular contraction is the most conspicuous event that follows stimulation of the peripheral end of an anterior nerve-root, it is by no means the only one. It is frequently observed, though not in all kinds of animals, that here, too, pain is caused. That this pain is not due to the muscular contraction is proved by the fact that it can still be elicited when the nerve-trunk is divided between the junction of the roots and the periphery. The real explanation of the phenomenon seems to be that certain fibres from the posterior roots ('recurrent fibres,' see footnote on p. 607) bend up for some distance into the anterior roots, and then turn around again and pursue their course to their peripheral distribution in the mixed nerve, or run on in the motor roots to supply the sheath surrounding them (nervi nervorum), and even the membranes of the spinal cord.

The **afferent impulses** that enter the cord along the pos-

terior roots have the choice of many paths by which they may reach the brain (Fig. 252).

(1) They may pass directly up through the postero-median column. If they take this route, their course will be first interrupted by nerve-cells in the gracile or cuneate nuclei in the medulla oblongata.

(*a*) Thence they may find their way across the middle line by the arcuate fibres of the upper or sensory decussation, and sweeping along the fillet and the longitudinal fibres of the reticular formation of medulla, pons and crus, and the sensory path in the hinder third of the posterior limb of the internal capsule, finally arrive at the cerebral cortex. Between the gracile and cuneate nuclei and the cortex they may pass through nerve-cells in the optic thalamus and the neighbouring region.

(*b*) They may go from the gracile and cuneate nuclei to the restiform body of the same or the opposite side, and thence to the cerebellum, in whose superior or middle peduncles they may cross the middle line and proceed to the cerebral cortex.

(2) They may pass up by the direct cerebellar tract and restiform body to the superficial grey matter of the cerebellar worm. If they take this route their course will be interrupted very soon after their entrance into the cord in the cells of Clarke's column. Since the superficial grey matter of the vermis is connected by association fibres with the dentate nucleus, and the dentate nucleus by the superior peduncle with the opposite cerebral hemisphere, this is also a possible path to the great brain.

(3) They may reach the antero-lateral ascending tract of the same side through its cells of origin in the spinal grey matter, and passing through the medulla and pons to the superior peduncle of the cerebellum, enter the grey matter of the worm.

(4) They may cross the middle line after entering the cord through axons or collaterals (p. 682) which run in the anterior and also in the posterior commissure, enter one of the ascending tracts on the other side—*e.g.*, the tract of Gowers—and continue without further decussation up to their central destination.

(5) They may spread from neuron to neuron in the tangle of the grey matter itself, and pass out again at a different level into one of the white tracts on the same or on the opposite side of the cord.

Efferent impulses, originating in the brain, may travel:

(1) Through the direct or crossed pyramidal tract.

(2) From one side of the cerebral cortex to the other, and then down the pyramidal tracts corresponding to that side (?).

(3) From the frontal part of the cerebral cortex, through the anterior limb of the internal capsule to the grey matter in the pons, and thence to the cerebellum by its middle peduncle.

(4) From the occipital or temporal cortex, in the hinder rim of the internal capsule to the pontine grey matter and through the middle peduncle to the cerebellum. From the cerebellum they may possibly

pass down to the nucleus of Deiters and thence along the antero-lateral descending tract to the anterior horn of the cord, and indirectly to the periphery.

All the paths enumerated, as well as others to which it would be tedious to formally refer, and which the ingenuity of the reader may be profitably employed in constructing for himself, from the data already given, are to be looked upon as *possible* channels for the passage of impulses between the brain and the periphery. But it must be distinctly pointed out that what is certain is in this case much more limited than what is possible. Among the efferent paths it is *certain* that the pyramidal tracts are the conductors of voluntary motor impulses, and that in most individuals the great majority of such impulses decussate in the medulla oblongata, only a small minority in the cord. For a lesion involving the pyramidal tract above the decussation of the pyramids causes paralysis of the opposite side of the body, a lesion below the decussation paralysis of the same side. It is not certain, although it is *possible* that when one pyramidal tract has been destroyed, in some animals at least, the motor cortex from which it leads may to a certain extent place itself again in communication with the paralyzed muscles through its commissural connections with the opposite hemisphere.

Decussation of the Sensory Paths.—On the other hand, it is *certain* that pathological or traumatic lesions, involving the destruction of one lateral half of the cord in man and experimental hemisections in some mammals, are followed by symptoms which suggest that the sensory impulses decussate chiefly in the spinal cord—viz., diminution or loss of sensibility on the opposite side below the level of the lesion, with little or no impairment, and often increase of sensibility (hyperæsthesia) on the same side.

This was first pointed out by Brown-Séquard, although long after he saw cause to retract this interpretation of his experiments. It is a curious circumstance that while clinical observation has on the whole tended more and more to confirm the view that in man an important portion of the sensory path decussates in the cord, experimental physiologists have for the most part obtained contradictory results. Thus Mott, working with monkeys, found that sensation, far from being abolished, is, as a rule, impaired in a smaller degree

on the side opposite to the hemisection than on the same side, while Ferrier and Turner obtained the contrary result. The discovery that no ascending degeneration, or only a trifling amount, is to be found on the opposite side of the cord, either after hemisection or after division of posterior roots, does not of itself enable us to decide the question. For while this latter fact shows that few or none of the afferent *fibres* cross the middle line to enter the long conducting paths before being interrupted by nerve-cells, it by no means proves that afferent *impulses* do not decussate in the cord. And, indeed, we know that some afferent impulses do decussate far below the level of the medulla. For, (1) A part of the negative variation (p. 646) crosses the middle line and ascends in the opposite half of the cord when the central end of one sciatic is stimulated (Gotch and Horsley). (2) Crossed reflex movements are possible; and when excitation of the central end of the sciatic is followed by contraction of the muscles of the opposite fore-limb, the afferent impulses must either decussate in the lumbar cord, and then run up on the opposite side to the level of the brachial plexus, or must ascend on the same side and cross over somewhere between the plane of the sciatic and the brachial nerve-roots. The only other hypothesis on which crossed reflex action can be explained—but a hypothesis for which there is not a tittle of evidence—is that the afferent impulse always acts on motor cells whose axis-cylinder processes pass over to the opposite side, and there enter anterior nerve-roots. But while, for these reasons, it cannot be denied that some afferent impulses decussate in the cord, it would be an error to conclude that all do so in any animal, or that all animals are in this respect alike. It is indeed extremely probable that in different species of animals, and even in individuals of the same species, there are considerable differences in the extent of the sensory decussation in the cord, just as there are in the extent of the motor decussation in the bulb. In some animals the greater part of the sensory path may decussate in the cord; in others (in the monkey, for instance), the greater part may decussate in the bulb, or higher up. The lack of agreement in the experimental results may be due partly to this cause. When it is further remembered how difficult it sometimes is to interpret the account which a man gives of his sensations and to recognise precisely the degree and nature of sensory defects produced by disease in the human subject, it will not be thought surprising that experiments on animals, from the time of Galen onwards, should have yielded evidence which, although perhaps now at length tending to a definite result, is still unfinished and in part conflicting.

If, leaving them out of account, not as valueless but as still difficult of interpretation, we attempt to draw any general conclusion from the clinical observations which, however imperfect, are in such questions our surest guide, it can only be this, that *in man many of the sensory impulses, and particularly those connected with the cutaneous sensations of pain and*

temperature, seem to decussate in the cord. But there is also evidence that some afferent impulses, including those coming from the muscles and related to the muscular sense, decussate not in the cord but in the bulb.

The Paths for Different Kinds of Sensory Impressions. — If this is the state of our knowledge where the problem is merely to determine the crossing-place of afferent impulses which are certainly known to cross, it is only to be expected that we should be still more in the dark as regards the routes by which different kinds of afferent impulses thread their way through the maze of conducting paths in the neural axis to reach their planes of decussation and gain the 'sensory crossway' in the internal capsule. Some authors have indeed cut the Gordian knot by assuming that any kind of sensory impression may travel up any afferent path. Direct stimulation of a naked nerve-trunk, it has been argued in favour of this view, gives rise to a sensation of pain; stimulation of the skin in which the end-organs of the nerve lie gives rise to a sensation of touch or a sensation of temperature, according as the stimulus is a mild mechanical or a thermal one, the contact of a feather or of a hot test-tube. Why, it has been asked, should we imagine that the difference in the result of stimulation depends on a difference in the nerve-fibres excited, and not on a difference in the kind of impulses set up in the same nerve-fibres? This is a question which we shall have again to discuss (p. 757). But apropos of our present problem, we may say that there is very clear proof from the pathological side that a limited lesion in the conducting paths of the central nervous system may be associated with defect or total loss of one kind of sensation, while all the other kinds remain intact. And there seems no other tenable hypothesis than that in such cases the pathological change has picked out a particular group of fibres, either collected into a single strand or scattered among unaltered fibres of different function. For example, in locomotor ataxia, a disease in which inco-ordination of movement and derangement of the mechanism of equilibration are prominent symptoms, degeneration in the posterior column of the cord is a most constant lesion. And there is strong evidence that afferent impulses from muscles and tendons, which give rise to impressions belonging to the group of tactile sensations, and which, according to the most widely accepted doctrine, serve as the basis of the muscular sense, and play an important part in the maintenance of equilibrium (p. 731), pass up in the posterior column, which may also conduct tactile impressions from the skin. A case has been observed where a man received a stab which divided the whole of one side of the cord and the posterior column of the other side. Sensibility to touch was lost on both sides of the body below the level of the injury, sensibility to pain only on the side opposite to the main lesion. In another case, in which some small syphilitic tumours (gummæ) in the lateral column on the left side caused marked degeneration in the left direct

cerebellar tract, the tract of Gowers, and the crossed pyramidal tract, without affecting the posterior columns, tactile sensibility was only slightly impaired in the opposite leg, while the sensibility for pain and temperature was much enfeebled. In the left leg, which was paralyzed, there was slight hyperæsthesia. These observations indicate that impressions of pain and temperature pass up in the antero-lateral column, either in the tract of Gowers, or in the direct cerebellar tract, or in both (Déjerine and Thomas). But it does not follow that they cannot ascend by other paths as well. It appears indeed that the grey matter of the cord is such a path, and that impulses which give rise to pain can be propagated along a cord in which hardly a vestige of white substance remains uncut. The recent observations of Langendorff, who found that when the blood-supply of the lower portion of the spinal cord is temporarily cut off by ligation of the abdominal aorta (Stenson's experiment) tactile stimulation of the posterior portion of the animal causes no rise of blood-pressure and no movements, have led him to the conclusion that the impulses caused by such excitation have also to pass through the grey matter of the cord on their way to the brain. But this conclusion cannot be accepted; for it is based on the assumption that only the grey matter, and not the white, is rendered non-conducting by anæmia. Hering and others have shown that the white suffers as well as the grey, although it may not be so easily destroyed, and may recover more readily when the blood-flow is restored (p. 659).

The posterior columns have nothing to do with the conduction of painful impressions, for division of them causes not anæsthesia, but rather hyperæsthesia, while if they are left intact, and the rest of the cord, including the grey matter, divided, the animal is insensitive to pain below the level of the lesion.

The impulses which descend the cord give token of their arrival at the periphery by causing either contraction of voluntary muscles, or contraction of the smooth muscular fibres of arteries, or secretion in glands. They all pass down in the antero-lateral column, but the path of the voluntary impulses in the pyramidal tracts is the best known and most sharply defined.

2. **Modification of Impulses set up elsewhere (Reflex Action).**—The spinal cord, although it is a conductor of nervous impulses originating elsewhere, is by no means a mere conductor. Many of the impulses which fall into the cord are interrupted in its grey matter. Some of the efferent impulses proceeding from the brain are perhaps modified in the cord, and then transmitted to the muscles. Some of the afferent impulses are modified, and then transmitted to the brain; some are modified, and deflected altogether into an efferent path. These last are the impulses which give rise to reflex effects. Strictly speaking, a reflex action is an action carried

out in the absence of consciousness; not necessarily, however, in the absence of general consciousness, but in the absence of consciousness of the particular act itself. But the term is often used so as to embrace all kinds of actions which are not directly voluntary, whether the individual is conscious of them or not. For example, when the sole of the foot is tickled, the leg is irresistibly and involuntarily drawn up by reflex contraction of its muscles; yet the person is perfectly cognisant both of the movement and of the sensation which accompanies the afferent impulse. Then there is a class of reflex actions in which consciousness is entirely in abeyance; during sleep most of the ordinary reflexes can be elicited.

Normally, it is believed that reflex movements are governed by impulses descending from the higher centres, for (*a*) it is a matter of common experience that a reflex movement may be to a certain extent controlled, or prevented altogether by an effort of the will, and it is worthy of remark that only movements which can be voluntarily produced can be voluntarily inhibited; (*b*) an animal like a frog responds to stimuli by reflex movements more readily after the medulla oblongata has been divided from the spinal cord; (*c*) long-continued muscular contractions may be caused in animals after removal of the cerebral hemispheres by stimulation of sensory nerves, for example by scratching the mucous membrane of the mouth in a 'brainless' frog or Menobranchus; (*d*) by stimulation of certain of the higher centres reflex movements which would otherwise be elicited may be suppressed or greatly delayed. If the cerebral hemispheres are removed from a frog, and one leg of the animal dipped into dilute acid, a certain interval, the (uncorrected reflex time, will elapse before the foot is drawn up (p. 768). If now a crystal of common salt be applied to the optic lobes or the upper part of the spinal cord, and the experiment repeated, it will be found that either the interval is much lengthened, or that the reflex disappears altogether. Strong stimulation of any afferent nerve will also abolish or delay a reflex movement.

Dependence of the Spinal Reflexes on the Brain.—That the brain, in man and the higher animals at least, exerts more than a merely inhibitory influence on the production of reflex movements is suggested by many facts. The knee-jerk, for example, is increased or 'reinforced,' if an instant before the tendon is struck the patient makes a voluntary movement or is acted on by a sensory stimulus. It often disappears in pathological lesions, situated high up in the cord in man, and is markedly impaired after high section of the cord in dogs. In *hemiplegia* (paralysis of one side of the body, caused by disease in the brain) the cutaneous reflexes on the paralyzed side may sometimes be absent for years. Some observers have even

gone so far as to say that, under normal conditions, the so-called spinal reflexes are really cerebral, in other words, that the afferent impulses run up to the cortex of the brain and there discharge efferent impulses, which pass down to the motor cells of the anterior horn and cause their discharge. It may be admitted that there is no physiological ground for supposing that the afferent impulses which have to do with the reflex contraction of the muscles of the leg when the sole is tickled, stop short at the motor cells of those spinal segments from which the efferent nerves come off, while the afferent impulses which have to do with the sensation of tickling pass up to the brain. The probability is that under ordinary circumstances such afferent impulses pass up the cord in long afferent paths, as well as directly towards the motor cells along those fibres of the posterior roots and their collaterals which bend forward into the anterior horn at the level of their entrance into the cord. And the only question is whether, as a matter of fact, the spinal motor cells are most easily discharged by the impulses that reach them directly, or by the impulses that come down to them by the roundabout way of the cortex and the efferent fibres that connect it with the cord. It is evident that the answer to this question need not be the same for all kinds of animals. It may well be that in the higher animals, in which the cortex has undergone a relatively great development, the spinal motor mechanisms are more easily discharged from above than from below, while in lower animals the opposite may be the case. When the cord is cut off from the brain, the afferent impulses may overflow more easily into the spinal motor cells since their alternative path is blocked. In the frog, where there is already a beaten track between the posterior root-fibres and the cells of the anterior horn, this overflow may be established immediately after section of the cord, and may of itself lead to an exaggeration of the reflexes. In animals like the dog a longer time may be necessary before the unaccustomed route from the end arborizations of the afferent axons and their collaterals to the dendrites or the bodies of the motor cells becomes natural and easy; in man a still longer interval may be required. Moore and Oertel have recently made a careful comparative study of reflex action after complete section of the cord in the cervical or upper dorsal region, and conclude that the spinal reflexes in the higher animals are far more dependent on the upper portions of the central nervous system than in the frog.

In order that a reflex action may take place, the reflex arc—afferent nerve, central mechanism, and efferent nerve—must be complete; and in fact a whole series of simple reflex movements exists, the suppression, diminution, or exaggeration of which can be used in diagnosis as tests of the condition of the reflex arc. Such are the *plantar reflex* (the drawing-up of the foot when the sole is tickled), the *cremasteric reflex* (retraction of the testicle when the skin on the inside of the thigh just below Poupart's ligament is stroked, espe-

cially in boys), the *knee-jerk* (a sudden extension of the leg by the rectus femoris muscle when the ligamentum patellæ is sharply struck), the *gluteal, abdominal, epigastric,* and *inter-scapular reflexes* (contraction of the muscles in those regions when the skin covering them is tickled). The *jaw-jerk* (a movement of the lower jaw when, with the mouth open, the chin is smartly tapped) and *ankle-clonus* (a series of spasmodic movements of the foot, brought about by flexing it sharply on the leg) are phenomena of the same class, which can be elicited only in disease. Any condition which impairs the conducting power of the afferent or efferent fibres of the reflex arc necessarily diminishes or abolishes the reflex movement, even if the centre is intact. *E.g.*, in *locomotor ataxia* the disappearance of the knee-jerk is one of the most important diagnostic signs. This disease involves the posterior roots and the fibres that continue them in the posterior column. The anterior nerve-roots are perfectly healthy. The grey matter of the cord—at least, in the earlier stages of the disease—is unaffected. The weak link in the chain is the afferent path. In *anterior poliomyelitis* (p. 686) the afferent link is intact, but the other two are broken, and the reflexes also disappear. Certain lesions which cut off the spinal cord from the higher centres without affecting the integrity of the reflex arcs increase the strength of reflex movements and the facility with which they are called forth. In *paraplegia, e.g.* (paralysis of the legs and the lower portion of the body), caused suddenly by accident to the cord, or more slowly by acute or chronic *transverse myelitis*, or in *hemiplegia*, the knee-jerk can usually be elicited with startling promptitude and exaggeration, and ankle-clonus may also be obtained. In *primary spastic paraplegia*, which is associated with degenerative changes in the lateral columns, a similar increase in the true and pseudo-reflexes may be seen, due either to the cutting off of inhibitory impulses or to an actual increase of excitability in the grey matter of the cord. The position of the centres in the cord for the various simple reflex movements is shown in Fig. 254.

Myotatic Irritability (Muscle Reflex).—Although for convenience of treatment we have included the knee-jerk (with

the jaw-jerk and ankle-clonus) among reflex movements, it might more properly be termed a pseudo-reflex, for there is evidence that the mechanism by which it is produced is different from that concerned in the reflex blinking of the eyelid, or the reflex retraction of the testicle, or the drawing-up of the foot when the sole is tickled. The strongest part of this evidence is the fact that the interval which elapses between the tap and the jerk ($\frac{3}{100}$ to $\frac{4}{100}$ second) is distinctly shorter than the reflex time of the extremely rapid lid-reflex, and is not much greater than the latent period of the quadriceps muscle for direct electrical stimulation, as measured under the ordinary conditions of its contraction. The knee-jerk is obtained in undiminished strength when the nerves of the ligamentum patellæ have been divided. It is therefore not a reflex movement caused by stimulation of afferent nerves coming from the tendon, and the name 'tendon-reflex' is clearly a misnomer. But that it is related in some way or other to afferent impulses is certain, for division of the posterior roots that enter into the anterior crural nerve abolishes the knee-jerk. The phenomenon probably comes under the head of what by some authors is called myotatic irritability—that is, it depends on mechanical stimulation of the slightly-stretched muscle by the pull of the tendon when it is struck. It seems to be necessary for this stimulation that the muscle should be to a certain extent tonically contracted. So that when the afferent fibres are interrupted, or the grey matter

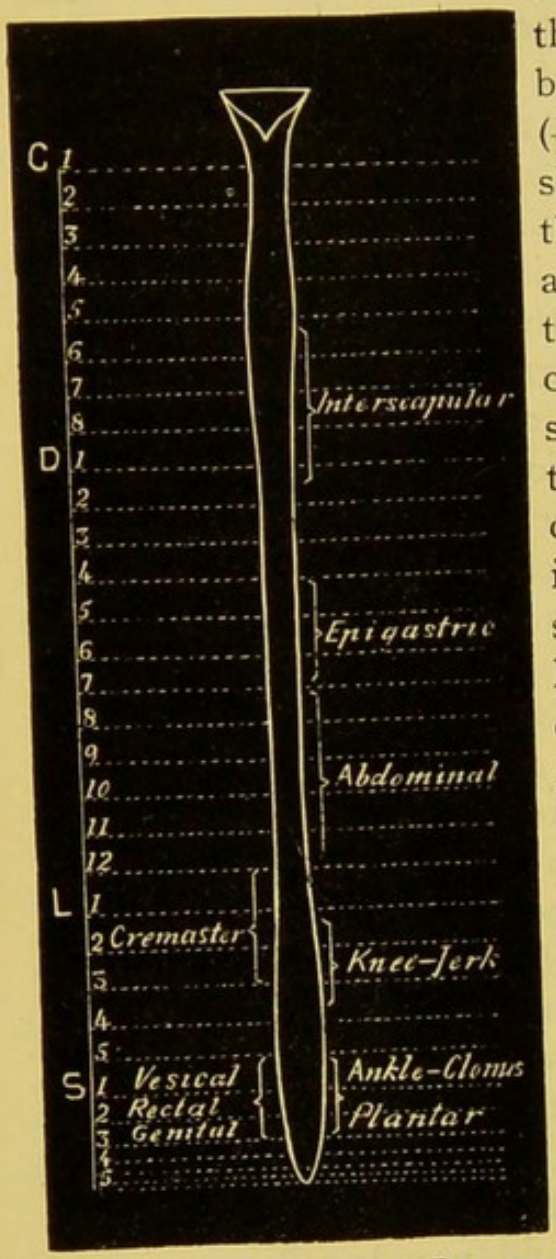

FIG. 254.—DIAGRAM OF REFLEX CENTRES IN CORD (AFTER HILL).

of the cord disorganized, and the reflex tone abolished, the knee-jerk disappears. In addition to the direct stimulation of the muscle on the same side, the tendon-tap may cause also a true reflex knee-jerk on the opposite side, the interval between tap and contraction being about $\frac{1}{8}$ second.

Anatomical Basis of Reflex Action.—Since the essence of reflex action is that the arrival of afferent impulses in the spinal cord causes the discharge of efferent impulses, there must be some connection between the incoming and the outgoing nerve-fibres. When the nervous system is still only a process of an epithelial (sensory) cell joining hands with a muscular cell, the distinction between afferent and efferent fibre does not exist. When development has gone a step further, and the neuro-muscular process is interrupted by a second epithelial cell transformed into a nerve-cell, the afferent fibre enters one pole and the efferent fibre leaves the other pole of the same cell. With increasing complexity of organization the nervous impulse passing up the afferent fibre is offered a choice of many routes when it reaches the spinal cord.

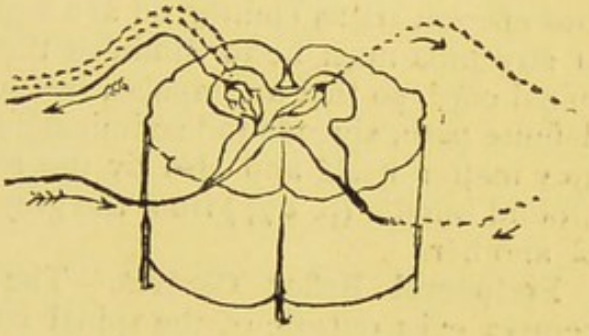

FIG. 255.—DIAGRAM OF A SIMPLE REFLEX ARC.

The arrows indicate the direction of the afferent and efferent impulses.

We have already (p. 681) described the course taken by the fibres of the posterior roots on entering the cord. It is obvious that through the main fibres and their collaterals an extensive connection — partly direct, partly by the link of intermediate neurons—is established with the motor cells on both sides of the cord. But the facts of physiology demonstrate an even ampler connection than the mere anatomical study of the distribution of the root fibres would suggest. Indeed, the phenomena of strychnia-poisoning seem to show that every afferent fibre is potentially connected with the motor mechanisms of the whole cord. For in a frog under the influence of this drug, stimulation of the smallest portion of the skin will cause violent and general convulsions, which are unaffected by destruction of the brain, but cease at once on destruction of the cord (p. 768).

Moderate stimulation of an afferent nerve causes contraction of muscles connected with the same segment of the cord on its own side, and it has been shown that the sensory nerves of a skeletal muscle are derived from the spinal ganglion corresponding to the segment of the cord containing its motor-cells. Stronger excitation, particularly of the end-organs of a nerve, as in stimulation of the skin, will be followed by more extensive movements involving higher or lower segments of the cord, or crossing over to the opposite side. Sometimes the reflex movements are co-ordinated to a high degree,

and even apparently 'purposive' in their action. This also is less true of movements caused by stimulation of naked nerve-trunks than of movements caused by stimulation of sensory surfaces. If a piece of skin in a brainless frog is severed from the rest, but left in connection with its nerves, excitation of the latter will produce simple and comparatively aimless contractions, while pinching of the skin or painting it with dilute acid may cause extensive movements evidently aimed at the removal of the irritation. When a drop of dilute acid is applied to the flank of a 'reflex' frog, it will attempt to wipe it off with the foot which is situated most conveniently for the purpose. If this foot be held, it will use the other.

Under ordinary conditions we must suppose that the resistance to the passage of impulses is greater for certain paths than for others, that it is easier, *e.g.*, in a brainless frog for an impulse travelling up a posterior root to reach the anterior root-fibres of the same segment on the same side than to cross the middle line and tap the opposite efferent tract, or to extend longitudinally along the cord and flow over into efferent tracts coming off at a higher or lower level. The action of strychnia must be to diminish the resistance in the whole of the spinal cord, so that an impulse, instead of being confined to a fairly definite path, spreads indiscriminately from neuron to neuron in the grey matter itself, and also by the short paths of the antero-lateral ground bundle (p. 677) from the grey matter of one segment to that of another.

Peripheral Reflex Centres.—The question whether any reflex centres exist outside of the spinal cord and brain, and especially in the sympathetic ganglia, has been the subject of a lengthy controversy. That the spinal ganglia cannot act as reflex centres is generally acknowledged, and it is not difficult to see why, for anatomical reasons, this must be so. A reflex arc must, so far as we know, in all highly-organized animals, include at least two neurons. There is no proof that an afferent impulse can ascend an axon to a cell-body and there excite an efferent impulse, which, descending the same axon in a separate set of fibrils, gives rise to a reflex contraction, or a reflex secretion. Now, the cells of a spinal ganglion represent the original neuroblasts from which the posterior root-fibres grew out as processes towards the cord on the one side and the periphery on the other. A sensory fibre passing into the ganglion makes connection with a cell by a T-shaped junction and passes on its course again. No afferent fibres run from the nerve-trunk into the ganglion, to end in arborizations around the ganglion cells, and no efferent fibres arise from nerve-cells in the ganglion to pass out into the trunk. For although a slightly greater number of medullated fibres of small calibre is found in a spinal nerve-trunk immediately distal to the junction of the roots than in both roots taken together, this appears to be due to the passage into the nerve (from the grey ramus communicans) of medullated fibres which end in the bloodvessels or other tissue of the ganglion (Dale). Here it is evident that there is no possibility of a complete reflex arc. Indeed, it is not certain that the normal afferent impulses pass through the bodies of the spinal ganglion cells at all. For (1) a negative variation can be observed in the posterior

roots above the ganglia on stimulation of the trunk of a frog's sciatic nerve more than two days after the death of the animal, when the ganglion cells may be supposed to have completely lost their vitality. (2) When the blood-supply of the posterior root-fibres and the ganglion is cut off without killing the frog, the nerve impulse is still conducted by the fibres, as is shown by the reflex movements elicited on stimulation of the central end of the sciatic, at a time when the nerve-cells show marked histological alterations. (3) Prolonged excitation of the posterior roots or the mixed nerve causes no noticeable microscopical changes in the ganglion cells (Steinach).* In the ordinary sympathetic ganglia,† also, it is doubtful whether the anatomical foundation for a reflex arc exists, and the most careful physiological experiments have failed to connect them with any reflex function. Sokownin, indeed, observed that stimulation of the central end of the hypogastric nerve caused contractions of the bladder, and he considered these movements to be reflex, the centre being the inferior mesenteric ganglion. Langley and Anderson have also found that when all the nervous connections of the inferior mesenteric ganglion, except the hypogastric nerves, are cut, stimulation of the central end of one hypogastric causes contraction of the bladder, the efferent path being the other hypogastric. In addition, they have observed an apparent reflex excitation of the nerves which supply the erector muscles of the hairs (pilo-motor nerves) through other sympathetic ganglia. But they believe it likely that in neither case is the action truly reflex, but that it is caused by stimulation of the central ends of motor fibres, which come off from the spinal cord, and in passing through the ganglion give off collateral branches to some of its cells. In the case of the inferior mesenteric ganglion the spinal fibres passing down in the left hypogastric would send branches to arborize around ganglion cells which give origin to fibres of the right hypogastric, and *vice versâ*. When the central end of the left hypogastric is stimulated the excitation is conducted up the spinal fibres, and so reaches their branches, and, through the ganglion cells, the sympathetic fibres of the right hypogastric, which convey it to the muscles of the bladder (see sartorius or gracilis experiment of Kühne, p. 602).

Reflex Time.—When a reflex movement is called forth, a measurable period elapses between the application of the stimulus and the commencement of the movement. This interval may be called the uncorrected reflex time. A part of the interval is taken up in the transmission of the afferent impulse to the reflex centre, a part in the transmission of the efferent impulse to the muscles, a part represents the

* Hodge obtained changes. In such experiments it is necessary that the ganglion should not be directly excited by electrotonic currents or escape of the stimulating current.

† The ganglion cells of Auerbach's and Meissner's plexus in the intestine are not of ordinary sympathetic type, and, as we have already seen, it is probable that they, or some of them, are true reflex centres for the stomach and intestines.

latent period of muscular contraction, and the remainder is the time spent in the centre, or the true reflex time. When the conjunctiva or eyelid is stimulated on one side both eyelids blink. This is a typical reflex action reduced to its simplest expression, and the true reflex time is correspondingly short—only about $\frac{1}{20}$ second. An additional $\frac{1}{100}$ second is consumed in the passage of the afferent impulse along the fifth nerve to the medulla oblongata, of the efferent impulse from the medulla to the orbicularis palpebrarum along the seventh nerve, and in the latent period of the muscle. When a naked nerve, like the sciatic, is stimulated, the true reflex time is reduced to $\frac{1}{100}$ to $\frac{1}{50}$ second. As estimated by Türck's method (p. 768), the uncorrected reflex time is greatly lengthened, it may be to several, or even many, seconds. For here it is evident that the time taken by the acid to soak through the skin and reach the nerve-endings in strength sufficient to stimulate them is included. But even when the peripheral factors remain constant, the central factor may vary. With strong stimulation, *e.g.*, the reflex time is shorter than with weak stimulation. Fatigue of the nerve centres delays the passage of impulses through them; and strychnia, while it increases the excitability of the cord, also lengthens the reflex time.

3. The Origination of Impulses in the Spinal Cord.

Automatism.—A physiological action is termed automatic when it depends upon a nervous outburst which seems to be spontaneous, in the sense that it is not brought about by any evident reflex mechanism, or, in other words, is not discharged by afferent impulses falling into the centre where it arises. An action known to be caused or conditioned by such afferent impulses is called a reflex action. Automatic actions being thus defined in a negative manner by the defect of a quality, there is always a possibility that some day or other it may be demonstrated that any given action which at present seems automatic in its origin depends on afferent impulses hitherto unnoticed. As a matter of fact, the supposed proofs of spinal automatism have in more than one case vanished with the advance of knowledge, and as

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the domain of purely automatic action has been narrowed, that of reflex action has extended, until the controversy as to the boundaries between the two seems not unlikely to be ended by the absorption of the automatic in the reflex. And as we seem almost driven to conclude that from the anatomical standpoint the nervous system is essentially a vast collection of looped conducting paths, each with an afferent portion, an efferent portion, and connections between them formed by the end arborizations of the axons and their collaterals, the dendrites and the cell-bodies, so it may be that no true physiological automatism really exists either in cord or brain, that every form of physiological activity—muscular movement, secretion, intellectual labour, consciousness itself—would cease if all afferent impulses were cut off from the nervous centres. But there are certain groups of actions so widely separated from the most typical reflex actions that, provisionally at least, they may be distinguished as automatic. Such are the voluntary movements, and certain involuntary movements, like the beat of the heart. And we may proceed to inquire whether the spinal cord has any power of originating movements or other actions of this high degree of automatism.

Muscular Tone.—So long as a muscle is connected with the spinal segment from which its nerves arise, it is never completely relaxed; its fibres are in a condition of slight tonic contraction, and retract when cut. If a frog whose brain has been destroyed is suspended so that the legs hang down, and one sciatic nerve is cut, the corresponding limb may be observed to elongate a little as compared with the other. At one time this tone of the muscles was supposed to be due to the continual automatic discharge of feeble impulses from the grey matter of the cord along the motor nerves. But it has been proved that if the posterior roots be cut, or the skin removed from the leg, its tone is completely lost although the anterior roots are intact. So that the tone of the skeletal muscles depends on the passage of afferent impulses to the cord, and must be removed from the group of automatic actions and included in the reflexes.

The 'rigidity' of the muscles, often observed in paralysis

from lesions of the central system, and denominated 'early' or 'late' according as it comes on within a few days or a few weeks after the occurrence of the lesion, is also probably in part a reflex phenomenon, although possessing some of the characters of a tonic contraction due to automatic discharge from the spinal centres. For in such cases myotatic irritability is increased; the knee-jerk is exaggerated; a finger-jerk may be elicited by tapping the wrist, an arm-jerk by striking the skin over the insertion of the biceps or triceps, ankle-clonus by flexing the foot (Gowers). Now, myotatic irritability depends on reflex muscular tone (p. 708).

It is probable that the tone of such visceral muscles as the sphincters of the anus and bladder has also a reflex element, and possible that the same is true of the tone of the smooth muscular fibres of the bloodvessels on which the maintenance of the mean blood-pressure so largely depends. And it may be that if all afferent impulses could be cut off from the vaso-motor centre, as by section of the whole of the posterior spinal roots and other centripetal paths to the medulla, general dilatation of the arterioles would take place, and the blood-pressure be greatly diminished. But, as has been already more than once pointed out, there exist peripheral mechanisms which, after a time, make good to some extent the loss of tone caused by destruction of the spinal centres (p. 694).

Trophic Tone.—The degenerative changes that occur in muscles, nerves, and other tissues when their connection with the central nervous system is interrupted have been already referred to (p. 605). It is possible to explain these changes in some cases without the assumption that tonic impulses are constantly passing out from the brain and cord to control the nutrition of the peripheral organs; and we have seen that there is no real evidence of the existence of specific trophic fibres. But the degeneration of muscles after section of their motor nerves is difficult to understand except on the hypothesis that impulses from the cells of the anterior horn influence their nutrition. The only question is whether these are the impulses to which muscular

tone is due, and therefore reflex, or different in nature and automatically discharged. Now, degeneration of a muscle is not usually caused, or at least not for a long time, by interruption of its afferent nerve-fibres, as in locomotor ataxia, or after section of the posterior nerve-roots (Mott and Sherrington). We can hardly suppose that in any case the trophic influence of the cells of the spinal or sympathetic ganglia to which all other reflex powers have been denied, is of reflex nature. And there is, indeed, more evidence in favour of trophic tone being an automatic action of the cord than for any of the other tonic functions hitherto considered.

Respiratory Automatism.—But the evidence upon which the spinal cord has been credited with true automatic action is chiefly connected with the central respiratory mechanism. It is known (p. 211) that a section above a certain level in the medulla oblongata does not abolish the respiratory movements. The respiratory centre, then, must be continually sending out impulses which are not originated by impulses reaching it from the brain. But this is far from being a proof of definite automatic action by the spinal cord, for although afferent impulses do not, under the conditions of that experiment, reach the respiratory centre from the brain, they may and do reach it from the periphery; and the only true test of automatic activity would be to sever the whole of the afferent paths leading to the centre, and then to observe whether or no the respiratory movements continued. This is an experiment which it is difficult, if not almost impossible, to carry out. But to say this is merely to confess that, in the present state of experimental physiology, it is difficult or impossible to apply a crucial test to the doctrine of respiratory automatism.

The 'Centres' of the Cord and Bulb.—We have frequently used the word 'centre' in describing the functions of the spinal cord, but the term, although a convenient one, is apt to convey the idea that our knowledge is far more minute and precise than it really is. When we say that a centre for a given physiological action exists in a definite portion of the spinal cord, all that is meant is that the action can be called out experimentally, or can normally go on, so long as this portion of the cord and the nerves coming to it and leaving it are intact, and that destruction of the 'centre' abolishes the action. For example, a part of the medulla oblongata on each side of the

middle line in the floor of the fourth ventricle above the calamus scriptorius is so related to the function of respiration that when it is destroyed the animal ceases to breathe. But this respiratory centre, the 'nœud vital' of Flourens, does not correspond in position with any definite collection of grey matter, although it includes the nuclei of origin of several cranial nerves, and forms an important point of departure for efferent, and of arrival for afferent, fibres connected with the respiratory act. Its destruction involves the cutting off of the impulses constantly travelling up the vagus to modify the respiratory rhythm, and of the impulses constantly passing down the cord to the phrenics and the intercostal nerves. And just as the traffic of a wide region can be paralyzed at a single blow by severing the lines in the neighbourhood of a great railway junction, or more laboriously, though not less effectually, by separate section of the same tracks at a radius of a hundred miles, so destruction of the respiratory centre accomplishes by a single puncture what can be also performed by section of all the respiratory nerves at a distance from the medulla oblongata. But while nobody speaks of the destruction of a 'centre' when a reflex action is abolished by division of the peripheral nerves concerned in it, there is a tendency, when the same effect is brought about by a lesion in the brain or cord, to invoke that mysterious name, and to forget that the cerebro-spinal axis is at least as much a stretch of conducting paths as a collection of discharging nervous mechanisms.

It is, perhaps, a profitless task to enumerate all the so-called centres in the bulb and cord with which the perverse ingenuity of investigators and systematic writers has encumbered the archives and text-books of physiology. In addition to the great vaso-motor, respiratory, cardio-inhibitory and cardio-augmentor centres in the bulb, which, perhaps, have more right than the rest to be regarded as distinct physiological mechanisms, if not as definitely bounded anatomical areas, there have been distinguished ano-spinal, vesico-spinal, and genito-spinal centres in the lumbar cord, a cilio-spinal centre for dilatation of the pupil in the cervical cord, and in the medulla centres for sneezing, for coughing, for sweating, for sucking, for masticating, for swallowing, for salivating, for vomiting, for the production of general convulsions, for closure of the eyes. It would be just as correct, and more practically useful (for it would perhaps encourage the student who has lost his way amidst these interminable distinctions), to say that the cerebral cortex contains a centre for learning sense, and another for forgetting nonsense, and that in a healthy brain it is the latter which is generally thrown into activity in the study of this portion of modern physiology.

The Cranial Nerves.

Unlike the spinal nerves, which arise at not very unequal intervals from the cord, the nuclei of the cranial nerves, with the exception of the olfactory and optic, are crowded together in the inch or two of grey matter of the primitive neural axis in the immediate neighbourhood of the fourth ventricle and the Sylvian aqueduct. Of these nuclei some are the end nuclei or 'nuclei of reception' of sensory fibres, that is to say, collections of nerve-cells around which the sensory fibres break up into terminal arborizations. Such are the sensory nucleus of the fifth, both nuclei of the eighth, and probably the common nucleus of the ninth, tenth, and eleventh. The nuclei of origin of the motor fibres lie, upon the whole, in two longitudinal rows—a median row, which consists of the nuclei of the third and fourth nerves in the floor of the aqueduct, and those of the sixth and twelfth nerves in the floor of the fourth ventricle; and a lateral row comprising the motor nuclei of the fifth, tenth, and eleventh nerves, and the nucleus of the seventh. The clumps of grey matter which make up these nuclei may be considered as homologous with the grey matter of the ventral or anterior (including the lateral) horn of the spinal cord; and the motor fibres of the nerves themselves as homologous with the anterior spinal roots. Without going further into the thorny subject of the homologies of the cranial and spinal nerves, we may point out that while all the spinal nerves contain both motor and sensory fibres, some of the cranial nerves are purely motor, some purely sensory, and others mixed. So that if we are to look upon the motor nerves as the homologues of the ventral roots, the dorsal (posterior) root-fibres corresponding to them must be represented in the other cranial nerves. Thus the sensory portion of the mixed fifth nerve, and the purely sensory auditory nerve, must be supposed to contain fibres corresponding to several dorsal roots.

The first or olfactory nerve consists of fine fibres, each of which is a process of an olfactory cell (Fig. 257). The olfactory cells, which are really peripheral nerve-cells, lie among the epithelial cells in the olfactory region of the Schneiderian membrane, the common lining of the nostrils. Each olfactory cell gives off two processes, a short one, representing a dendrite, which runs out to the surface of the mucous membrane, and a longer but more slender process, representing an axon, which as a fibre of the olfactory nerve pierces the cribriform plate of the ethmoid bone, and plunges into the olfactory bulb.

In the *olfactory bulb* at least four layers can be distinguished—(1) on the surface, beneath the pia mater, the layer of entering olfactory nerve-fibres; (2) the layer of *olfactory glomeruli*, peculiar structures, each of which is made up of an intricate basket-like arborization formed by an olfactory nerve-fibre, or, it may be, more than one, and a brush-like arborization belonging to a dendrite of one of the mitral cells of the next layer; (3) the molecular layer, which contains a number of large nerve-cells called *mitral cells*, along with smaller nerve-cells and neuroglia; (4) the nuclear layer, containing numerous small nerve-cells or 'granules' intermingled with white fibres. The mitral cells

give off axons, which pass through the fourth layer, and then as fibres of the olfactory tract to the grey matter at the base of the brain. The course of the impulses from the olfactory mucous membrane to the brain is shown in Fig. 257. The olfactory tract, as it runs back, divides into portions called its 'roots.' Of these the lateral is the most important, and it terminates in the uncinate gyrus of the same side. The median root crosses to the opposite side of the brain, and

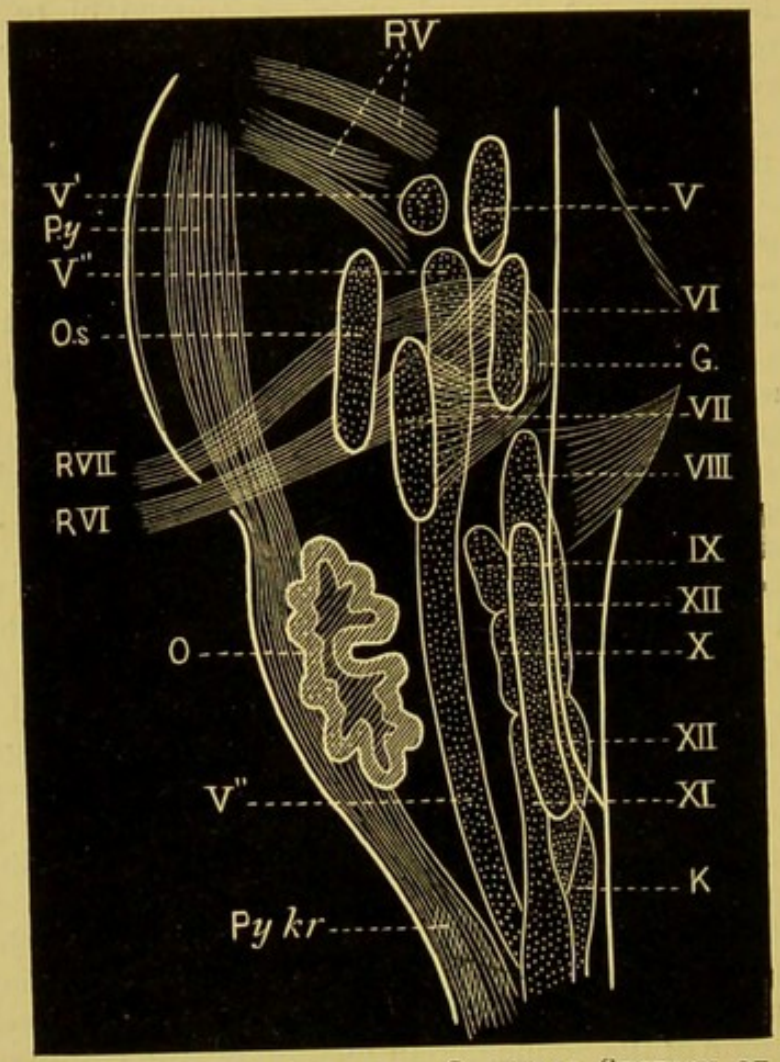


FIG. 256.—SCHEMATIC TRANSPARENT SAGITTAL SECTION OF MEDULLA OBLONGATA.

The numerals V to XII refer to the nuclei of origin of the respective cranial nerves. V is the motor nucleus of the fifth nerve ; RV, the roots, and V', the sensory nucleus ; V'', sensory nucleus and ascending or spinal root of the fifth ; RVI, root of sixth nerve ; RVII, root of seventh nerve ; Py, pyramidal fibres. Py. kr., decussation of the pyramids ; O.s., superior olive ; O, olive ; G. genu of the facial nerve ; K, clavate nucleus ; VIII, inner auditory nucleus.

some, though not all, of its fibres go to the opposite uncinate gyrus. Excessive stimulation of the olfactory nerve by exposure to a strong odour has been known to cause complete and permanent loss of smell.

The second or optic nerve contains mainly afferent fibres, which arise from the ganglion cells of the retina and terminate by forming synapses with nerve-cells in the lateral geniculate body, the pulvinar (or posterior portion) of the optic thalamus, and the anterior corpus quadrigeminum. This visual path is continued by the axons of

these nerve-cells, which proceed in the optic radiation (p. 692) to the occipital cortex (Figs. 258, 271, and 288). In young animals all these structures undergo atrophy after extirpation of the eyeball. At the chiasma the fibres of the optic nerve decussate, partially in man and some mammals, as the rabbit, dog, cat, and monkey, completely in animals whose visual field is entirely independent for the two eyes, as in fishes and birds. In man the fibres for the nasal halves of both retinæ cross the middle line at the chiasma, those for the temporal halves do not. The chiasma also contains fibres in its posterior portion, which extend from one optic tract to the other, but are not connected with the retinæ or the optic nerves. They are commissural fibres which connect the two mesial geniculate bodies across the middle line, and are called Gudden's commissure. A lesion involving the occipital cortex on one side, or the posterior

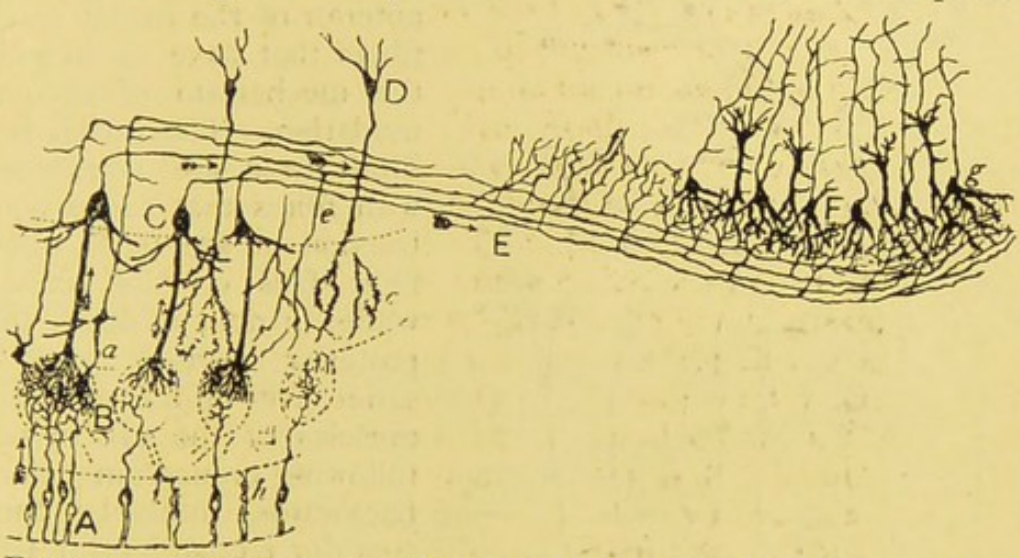


FIG. 257.—SCHEME OF THE OLFACTORY NERVOUS APPARATUS (HALLIBURTON AFTER CAJAL).

A, olfactory cells; B, glomeruli; C, mitral cells; D, olfactory granule cell; E, lateral root of olfactory tract; F, cortex of brain in the region of the uncinate gyrus; *a*, small cell of mitral layer; *b*, brush of dendrite of a mitral cell ending in a glomerulus; *c*, thorns or spines on the processes of an olfactory granule; *e*, collateral coming off from the axon of a mitral cell; *f*, collaterals ending in the molecular layer of the uncinate gyrus; *g*, pyramidal cells of the cortex; *h*, supporting epithelial cells of the olfactory mucous membrane.

portion of the optic thalamus, or the optic tract, causes hemianopia* (blindness of the corresponding halves of the two retinæ) on the side of the lesion. Thus, a lesion equivalent to complete section of the right optic tract would cause blindness of the nasal half of the left, and of the temporal half of the right eye, and the left half of the field of vision would be blotted out—the patient would be unable, with his eyes directed forwards, to see an object at his left. A lesion, *e.g.*, a tumour of the pituitary body, involving the

* The terms 'hemiopia,' 'hemianopia,' 'hemianopsia,' are sometimes used with reference to the blind side of the retinæ, sometimes to the dark half of the visual field. We shall always use the word 'hemianopia' with reference to the retina.

whole of the optic nerve in front of the chiasma, would cause complete blindness of the corresponding eye. Sometimes in disease of the optic nerve vision is not totally destroyed in the eye to which it belongs, but the field is narrowed by a circumference of blindness. In this case the pathological change involves the circumferential fibres of the nerve. When the chiasma is affected by disease, a very frequent symptom is nasal hemianopia, blindness of the nasal halves of the retinæ, with loss of the outer or temporal half of each field of vision. The optic nerve contains a few efferent fibres for the retina, whose cell-bodies are situated in the anterior corpus quadrigeminum.

The third nerve, or oculo-motor, arises from a series of nuclei in the floor of the Sylvian aqueduct below the anterior corpora quadrigemina. The root-bundles coming off from the most anterior of the nuclei carry fibres that have to do with the mechanism of accommodation. The nuclei behind these are connected with fibres that cause contraction of the pupil when light falls on the retina; while, in dogs at least, the posterior portion of the series gives off fibres for the muscles of the eye in the following order from before backwards: internal rectus, superior rectus, levator palpebræ superioris, inferior rectus, inferior oblique. Complete paralysis of the third nerve causes loss of the power of accommodation of the corresponding eye, dilatation of the pupil by the unopposed action of the sympathetic fibres, diminution of the power of moving the eyeball, ptosis, or drooping of the upper lid, external squint, and consequent diplopia, or double vision.

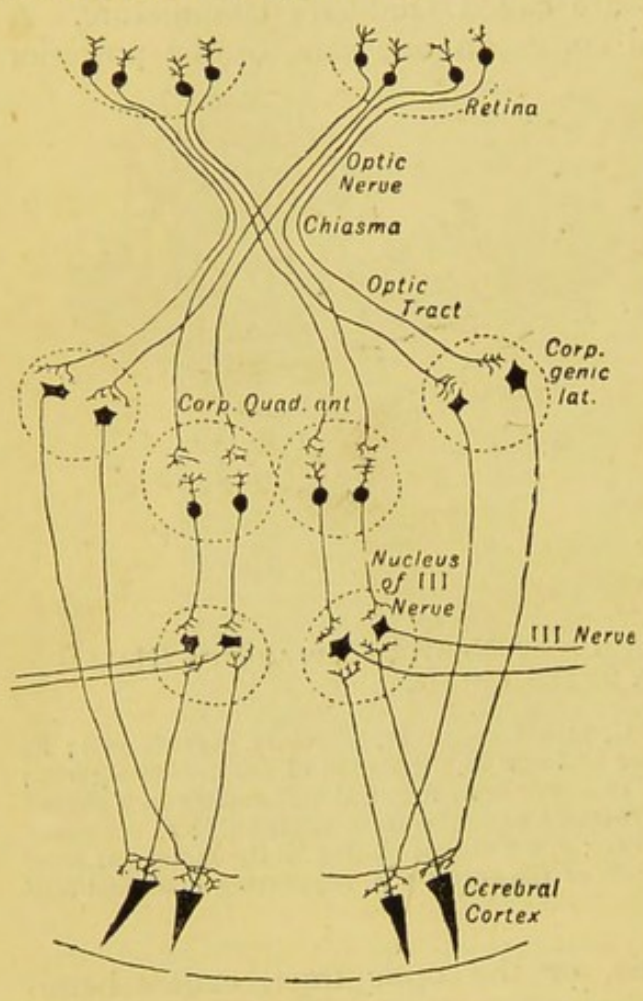


FIG. 258.—SCHEME OF THE VISUAL PATH (HALLIBURTON, AFTER SCHÄFER).

In Fig. 258, optic nerve-fibres are represented as forming synapses with cells in the anterior corpus quadrigeminum whose axons pass to the nucleus of the third nerve and arborize around some of its cells. It is possible that this is the path of the impulses which cause contraction of the pupil when light falls on the retina.

The fourth or trochlear nerve arises from the posterior part of the same tract of grey matter which gives origin to the third nerve. It supplies the superior oblique muscle. Paralysis of the nerve causes internal squint when an object below the horizontal plane is

looked at, owing to the unopposed action of the inferior rectus There is also diplopia on looking down. Unlike the other cranial nerves, the two trochlear nerves decussate completely *after* they emerge from their nuclei of origin.

The fifth or trigeminus nerve appears on the surface of the pons as a large sensory root and a smaller motor root. Its deep origin is more extensive than that of any of the other cerebral nerves, stretching as it does from the level of the anterior corpus quadrigeminum above to the upper part of the spinal cord below. Its sensory root, in fact, seems to include the sensory divisions of several motor cranial nerves.

The motor root arises partly from a nucleus in the floor of the fourth ventricle below the pons, partly as the so-called descending

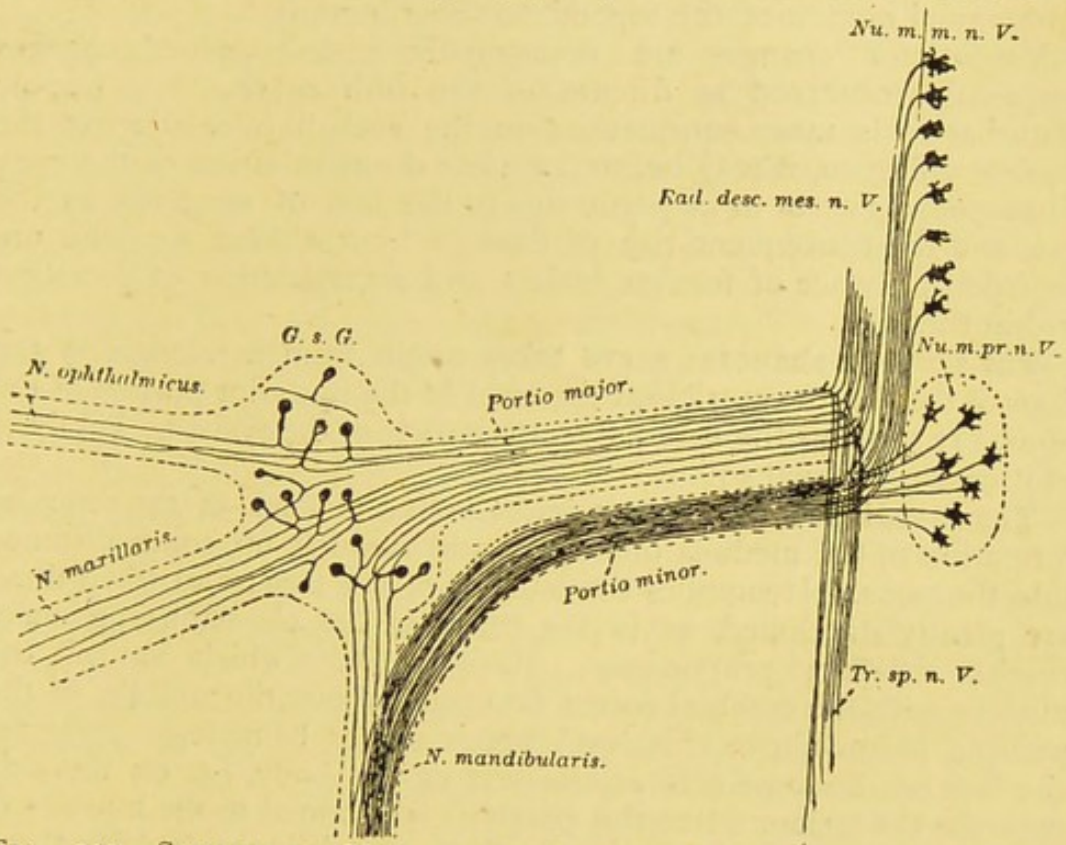


FIG. 259.—SCHEME OF MOTOR AND SENSORY NEURONS OF TRIGEMINUS (BARKER, AFTER GEHUCHTEN).

G. s. G., Gasserian ganglion; *Nu. m. m. n, V.*, nucleus of the descending root; *Nu. m. pr. n. V.*, chief motor nucleus of the fifth nerve; *Rad. desc. mes. n. V.*, descending root; *Tr. sp. n. V.*, tractus spinalis, or ascending root of the fifth.

root from large nerve-cells scattered in the grey matter around the aqueduct of Sylvius all the way from the anterior quadrigeminate body to the point at which the motor root is given off.

The sensory root has likewise two nuclei of reception: a nucleus in the neighbourhood of the motor nucleus in the floor of the fourth ventricle, and a long tract of scattered cells, the so-called spinal root, extending upwards from the level of the second cervical nerve through the medulla oblongata and the tegmentum of the pons, where it lies external to the descending root. The sensory fibres of the fifth have their cells of origin in the Gasserian ganglion.

The motor fibres of the fifth nerve supply the muscles of mastica-

tion and the tensor tympani. The sensory fibres confer common sensation on the face, conjunctiva, the mucous membranes of the mouth and nose, and the structures contained in them, and, according to Gowers, special sensation, through branches given off to the facial and glosso-pharyngeal nerves, on the organs of taste.* Complete paralysis of the nerve causes loss of movement in the muscles of mastication, sometimes impaired hearing, and loss of common sensation in the area supplied by it. Loss or impairment of taste in the corresponding half of the tongue is also often seen in disease involving the sensory root, although not in affections of the trunk of the nerve, since the taste fibres leave it near its origin (Gowers). Both taste and touch are lost in the monkey in the anterior two-thirds of the tongue after intracranial section of the trigeminus (Sherrington).

Vaso-motor changes are occasionally, and 'trophic' changes frequently, observed in disease of the fifth nerve. The trophic disturbance is most conspicuous in the eyeball (ulceration of the cornea, going on, it may be, to complete disorganization of the eye). These effects seem to be partly due to the loss of sensation in the eye, and the consequent risk of damage from without, and the unregarded presence of foreign bodies and accumulation of secretion within the lids.

The sixth or abducens nerve takes origin from a nucleus in the floor of the fourth ventricle at the level of the posterior portion of the pons. It supplies the external rectus muscle of the eyeball. Paralysis of it causes internal squint.

The seventh or facial nerve arises from a nucleus in the reticular formation of the medulla oblongata, and running up some distance into the pons. It supplies the muscles of the face; and when these are greatly developed, as in the trunk of the elephant, the nerve reaches very large proportions. Since the fibres which connect the nucleus with the cerebral cortex decussate about the middle of the pons, a lesion above this level which causes hemiplegia paralyzes the face on the same side as the rest of the body, *i.e.*, on the side opposite the lesion. But the paralysis is confined to the muscles of the lower portion of the face, and affects especially the muscles about the mouth. Sometimes the pyramidal tract and the facial nerve, or nucleus, are involved in a common lesion. In this case paralysis of the face is on the side of the lesion, and is total, while the rest of the body is paralyzed on the opposite side. Complete facial paralysis is often caused by an inflammatory process in the nerve itself (neuritis). The symptoms of complete facial paralysis are very characteristic. The face and forehead on the paralyzed side are smooth, motionless, and devoid of expression. The eye remains open even in sleep, owing to paralysis of the orbicularis palpebrarum. A smile becomes a grimace. An attempt to wink with both eyes

* It should be stated that some physiologists believe that the glosso-pharyngeal is the nerve of taste, and that none of the taste fibres go to the sensory nuclei of the fifth nerve. Others suppose that the glosso-pharyngeal supplies the posterior third, and the chorda tympani and lingual the anterior two-thirds of the tongue with gustatory fibres.

results in a grotesque contortion. The mouth appears like a diagonal slit in the face, its angle being drawn up on the sound side, and the patient cannot bring the lips sufficiently close together to be able to blow out a candle or to whistle. Liquids escape from the mouth, and food collects between the paralyzed buccinator and the teeth. The labial consonants are not properly pronounced. Taste may be lost in the anterior two-thirds of the tongue when the nerve is injured between the entrance of the gustatory fibres from the trigeminus and their exit by the chorda tympani, but not when the lesion is in the nucleus of origin, or anywhere above it. Hearing is sometimes impaired because the auditory and facial nerves, lying close together for part of their course, are apt to suffer together, but perhaps also because the stapedius muscle is supplied by the seventh.

The eighth or auditory nerve arises from the medulla oblongata by two roots (a dorsal and a ventral), one of which passes in on each side of the restiform body. The auditory nucleus in the floor of the fourth ventricle consists of two parts, a lateral, or outer, and a median, or inner, nucleus. The lateral nucleus we have already recognised, under the name of the nucleus of Deiters, as a possible origin of the antero-lateral descending tract. It is also a nucleus of reception for some of the fibres of the ventral auditory root, the axons of which, and especially their collaterals, form synapses with some of its cells. The median auditory nucleus is also a nucleus of reception for the ventral root. Through the nucleus of Deiters the ventral root is connected with the cerebellum. At the junction of the dorsal and ventral roots on the ventral surface of the restiform body lies a swelling, the accessory nucleus, into which, and into another smaller swelling, the tuberculum acusticum, the fibres of the dorsal root pass, and with whose cells they come into contact by their end arborizations. The nerve-cells of the accessory nucleus and the acoustic tubercle, therefore, constitute the nucleus of reception for the dorsal root-fibres. The cells of origin, both of the dorsal and of the ventral root, are situated in the internal ear, the former in the ganglion spirale, or ganglion of Corti, which is embedded in the bony spiral of the cochlea, the latter in the ganglion vestibulare, which lies in the vestibule. These cells seem to correspond to the ganglion cells on the posterior root of a spinal nerve, but, unlike them, they remain, even in mammals, bipolar throughout life. Their central processes form the axons of the auditory nerve. Their peripheral processes are distributed in the case of the dorsal root to the organ of Corti, in the case of the ventral root to the semicircular canals and the vestibule. For this reason the dorsal root is often called the cochlear division, and the ventral root the vestibular division of the auditory nerve. And it is believed that the cochlear and vestibular roots are physiologically as well as anatomically distinct. For, as we shall see (p. 732), it is extremely probable that the cochlea subserves the function of hearing, the semicircular canals and vestibule the function of equilibration. We must assume, from clinical and experimental data, that the dorsal root is connected through its nuclei with the first, or first and second temporo-sphenoidal convolutions on the opposite side. The *striæ*

acusticæ, a series of prominent strands that run transversely across the floor of the fourth ventricle, consist of fibres arising in the accessory nucleus and the acoustic tubercle, and form a portion of this central path. Two prominent symptoms may be associated with disease of the auditory nerve—(*a*) disturbance or loss of hearing; (*b*) loss or impairment of equilibration.

The ninth, or glosso-pharyngeal, the tenth, or vagus, and the eleventh, or spinal accessory nerves, may be considered together. They are connected with an elongated nucleus in the medulla oblongata, the upper portion of which is especially related to the glosso-pharyngeal, the middle to the vagus, and the lower to that division of the spinal accessory which arises from the medulla, and which may, therefore, be called the bulbar accessory. Since the fibres of the nerves related to this nucleus pass into it from the nerve-roots to form synapses with its cells, it must be looked upon not as a nucleus of origin for these fibres, but as a nucleus of reception. An additional nucleus of reception for some of the afferent fibres is supplied by scattered cells in the lateral grey matter of the cord as far down as the fourth cervical nerve, and in the formatio reticularis of the medulla. The fibres passing down to arborize around these cells form a bundle, called the fasciculus solitarius, or, since they belong mainly to the ninth nerve, the ascending root of the glosso-pharyngeal. The cells of origin of these afferent fibres are unipolar ganglion cells of somewhat the same type as those of the spinal ganglia. They are situated in various ganglia connected with the vagus (ganglion jugulare and ganglion nodosum) and with the glosso-pharyngeal (ganglion petrosum and ganglion superius). Their central processes become the afferent axons of the nerve-roots, their peripheral processes pursue their course as the axons of sensory fibres to the structures to which the nerves are distributed. A motor nucleus of origin is the nucleus ambiguus, which lies in the reticular formation of the bulb. The axons of its cells proceed mainly to the vagus, although some of them may enter the other two nerves. The spinal portion of the spinal accessory is a purely motor nerve. Its cells of origin lie in the lateral horn of the cord from about the level of the first to the sixth or seventh cervical nerves. Some authors consider that the bulbar accessory is also entirely motor, but this is probably erroneous.

The glosso-pharyngeal has both sensory and motor fibres—sensory for the posterior third of the tongue and the mucous membrane of the back of the mouth, motor for the middle constrictor of the pharynx and the stylo-pharyngeus. It also contains the nerves of taste for the posterior third of the tongue, but these reach it from the fifth nerve.

The vagus contains both sensory and motor fibres, the latter partly derived from the accessory, whose internal branch joins it not far from its origin. The distribution of the nerve is more extensive than that of any other in the body. The œsophagus receives both motor and sensory branches from the œsophageal plexus. The pharyngeal branch of the vagus is the chief motor nerve of the pharynx and soft palate (including the tensor palati). The superior laryngeal branch is the nerve of common sensa-

tion for the larynx above the vocal cords, and the motor nerve of the crico-thyroid muscle. The inferior or recurrent laryngeal supplies the rest of the laryngeal muscles, and the sensory fibres for the mucous membrane of the trachea and the larynx below the glottis. The superior laryngeal contains afferent fibres, stimulation of which gives rise to coughing, slows respiration, or stops it in expiration. Reflex movements of deglutition are also caused. The vagus supplies the lung both with motor and sensory filaments through the pulmonary plexus. The motor fibres when stimulated cause constriction of the bronchi; excitation of the afferent fibres causes reflex changes in the rate or depth of respiration. The cardiac branches contain inhibitory fibres probably derived from the spinal-accessory, and depressor fibres which pass up in the vagus trunk (dog), or as a separate nerve to join the vagus or its superior laryngeal branch or both (rabbit). The gastric and intestinal branches contain both motor and sensory nerves for the stomach and intestines. The sensory are probably large medullated fibres (7 μ to 9 μ). The afferent vagus fibres from the stomach carry up impulses which excite the action of vomiting. Lesions of the vagus, its nuclei of origin, or its branches, are associated with many interesting forms of paralysis and other symptoms. Paralysis of the pharynx is generally caused by disease of the nucleus in the medulla. From its anatomical relation to the nuclei of the glosso-pharyngeal and hypoglossal, it will be easily understood that these nerves are often involved in localized central lesions along with the vagus. But the fact that in glosso-labio-laryngeal palsy—a condition characterized by progressive paralysis and atrophy of the muscles of the tongue, lips, larynx, and pharynx —the orbicularis oris is paralyzed, while the other muscles supplied by the facial remain intact, would seem to show that in system diseases it is not so much anatomical groups of nerve-cells which are liable to simultaneous degeneration and failure, as physiological groups normally associated in particular functions. Such functional groups of cells, occupied with the same kinds of labour at the same times and under the same conditions, may be supposed to take on a similar bias or tendency to degeneration, a tendency not indicated, it may be, by any structural peculiarity, but traced deep in the molecular activity of the cells. Difficulty in swallowing is the chief symptom of pharyngeal paralysis. The symptoms of *laryngeal paralysis* have been already described under 'Voice' (p. 270). Tachycardia, or a permanent increase in the rate of the heart, has been stated to occur in certain cases of paralysis of the vagus, caused by disease or accidental interference; and a persistent slowing of the respiration has been occasionally attributed to the same cause. But it is difficult to reconcile many of these cases with experimental results, for in most of them the lesion only involved one vagus; and in animals section of one vagus has no permanent effect on the rate of the heart or of the respiratory movements.

Destruction of the nerve near its origin has been sometimes found associated with disappearance of the food-appetites, hunger and thirst, and it has been assumed that this was due to loss of afferent

impulses from the stomach. But clinical testimony is by no means unanimous on this point, and experiments on animals show that other factors are involved in these sensations.

The spinal accessory nerve, soon after the junction of its bulbar and spinal portions, divides into two branches, an internal and an external. The external branch passes out to supply the trapezius and sterno-mastoid muscles with motor fibres. The internal branch passes bodily into the vagus.

The twelfth or hypoglossal nerve is exclusively an efferent nerve. Its nucleus of origin is an elongated collection of large nerve-cells lying in the bulb close to the median line and parallel to it. It contains the motor supply of the intrinsic and extrinsic muscles of the tongue and of the thyro- and genio-hyoid. Paralysis of it causes deficient movement of the corresponding half of the tongue. When the tongue is put out, it deviates towards the paralyzed side, being pushed over by the unparalyzed genio-hyoglossus of the opposite side, which is thrown into action in protruding the tongue.

The Functions of the Brain.

The paths by which the various parts of the central nervous system are connected with each other and with the periphery have been already described, and we have completed the examination of the functions of the spinal cord and medulla oblongata. The events that take place in the upper part of the central nervous stem and in the cortex of the cerebellum and cerebrum now claim our attention.

From very early times the brain has been popularly believed to be the seat of all that we mean by consciousness—sensation, ideation, emotion, volition. And he who loves to trace the roots of things back into the past may see, if he choose, running through the whole texture of the older speculations a belief that the brain does not act as a whole, but is divided into mechanisms, each with its special work—a foreshadowing, often in grotesque outlines, of the doctrine of localization so widely held to-day. But until comparatively recent times, cerebral physiology remained a kind of scientific terra incognita; and no notable additions were made for a thousand years to the doctrines of Galen. Even to-day the utmost limit of our knowledge is reached when in certain cases we have connected a particular movement or sensation with a more or less sharply defined anatomical area. How the cerebral processes that lead to sensations and movements, to emotions and intellectual acts, arise and die out; what molecular changes are associated with them; above all, how the molecular changes are translated into consciousness—how, for example, it is that a series of nerve-impulses flickering across the labyrinth of the occipital cortex should light up there a visual sensation—these are questions to which we can as yet give no

answer, and the answers to some of which must for ever remain hidden from us.

Functions of the Upper Part of the Central Stem and Basal Ganglia.—The function of the *pons* is sufficiently indicated by its name. The grey matter so plentifully scattered, especially in its ventral portion, may exercise a not unimportant influence on the impulses that traverse it. But on the whole its main office is to provide a bridge along which impulses may travel between other portions of the nervous system. We have already seen that many of its transverse fibres are the cerebellar segments of commissural arcs interrupted by pontine grey matter, and continued by fibres of

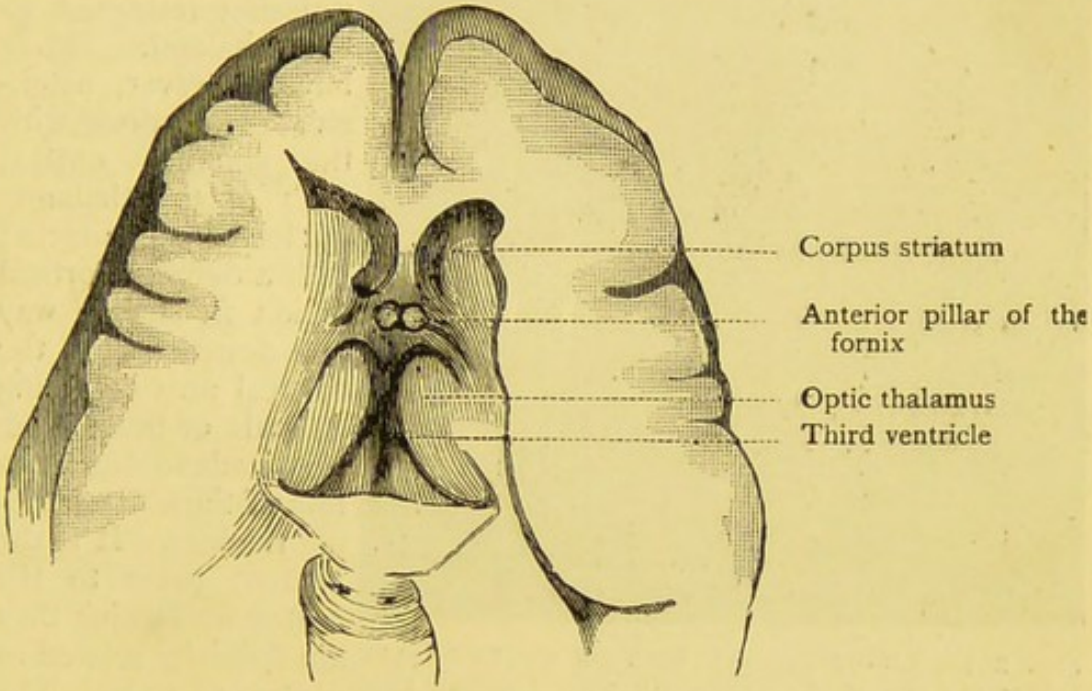


FIG. 260.—HORIZONTAL SECTION THROUGH BRAIN TO SHOW THE BASAL GANGLIA AND THIRD VENTRICLE (HUMAN).

the crura cerebri, internal capsule and corona radiata to the prefrontal, temporal and occipital portions of the cerebral cortex (p. 690).

The *posterior corpora quadrigemina* (testes) and internal geniculate bodies are connected with the cochlear division of the auditory nerves, and therefore have some relation to the sense of hearing. Stimulation of the testes causes a peculiar cry, and the pupils dilate.

The *anterior corpora quadrigemina* (nates) and the *lateral corpora geniculata* are connected with the optic tracts. Their development is arrested after extirpation of the eyeball in young animals, and they may therefore be assumed to be concerned in vision, athough the size of their homologues, the optic lobes or corpora bigemina, in animals below the rank of mammals (birds, reptiles, amphibians), does not seem to be related to the development of the organs of sight. The Proteus and the Hag-fish, *e.g.*, have large optic lobes, rudimentary eyes and optic tracts. The optic nerve, the anterior

corpus quadrigeminum, the nucleus of the oculo-motor nerve in the wall of the Sylvian aqueduct, and the fibres which it carries to the iris, form a reflex arc for the contraction of the pupil to light, as represented in Fig. 258, p. 720.

The *functions of the optic thalami* have not been satisfactorily defined either by experiment or pathological observation. Lying as they do in the isthmus of the brain, begirt by the great motor and sensory paths, it is to be expected that lesions of the thalami should affect also the internal capsule, and give rise to the symptoms of motor and sensory paralysis. But no definite defect of motor power or common sensation has ever been unequivocally connected with a lesion restricted to the thalami. They have, however, extensive connections with the cerebral cortex, each of the thalamic nuclei being connected with a definite cortical region in such a way that destruction of the cortical area in young animals or human beings leads to degeneration of the corresponding nucleus. It is the afferent paths to the cortex with which they are specially related as centres of relay. The posterior portion of the thalamus, or pulvinar, forms part of the central visual apparatus; for (*a*) it is found to be undeveloped in animals from which the eyeballs have been removed soon after birth; (*b*) a portion of the optic tract is certainly connected with it; (*c*) in some cases of atrophy of the occipital cortex, which, as we shall see, is undoubtedly a central area for visual sensations, atrophy of the pulvinar has also been noticed; (*d*) a lesion of the pulvinar may give rise to hemianopia (p. 719).

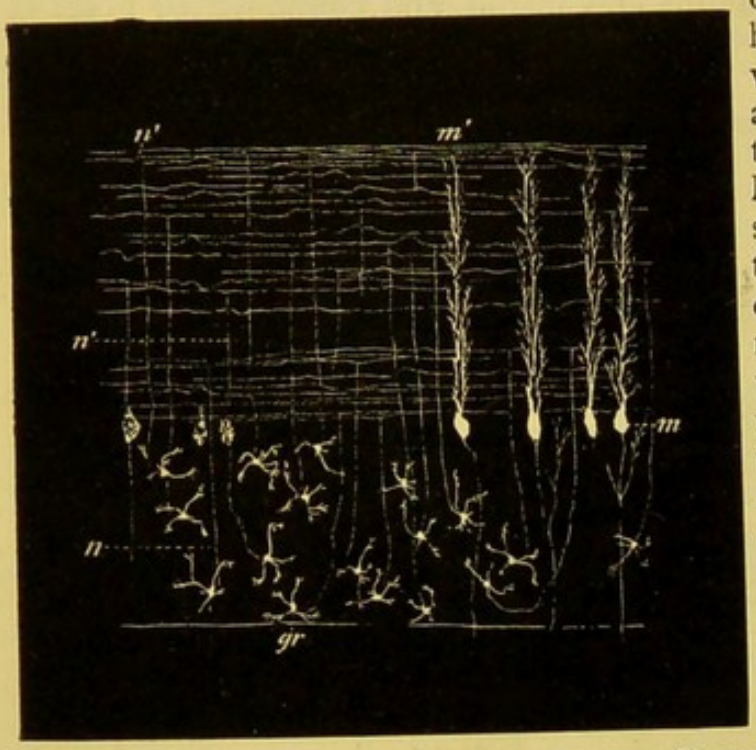


FIG. 261.—LONGITUDINAL SECTION OF THE GREY MATTER OF A LAMELLA OF THE CEREBELLUM (DIAGRAMMATIC, AFTER KÖLLIKER).

gr, a 'granule' cell with its axon, *n*; *n'*, bifurcation of *n*, in the molecular layer, into two fine longitudinal branches; *m*, a Purkinje's cell; *m'*, dendritic antler process (Golgi's method).

Hæmorrhage into the caudate or lenticular nucleus of the *corpus striatum* often causes hemiplegia, but this is always due to implication of the internal capsule. Experimental lesions in dogs and rabbits are followed by disturbances of the heat-regulating mechanism and rise of temperature.

Certain structures, belonging to the primary fore-brain, which have now no functional importance, may nevertheless be mentioned as

milestones in the march of development. The *pineal* body is made up of the vestiges of the unpaired mesial eye of such animals as the ancient labyrinthodonts, which resembled the eye of invertebrates in having the retinal rods directed towards the cavity instead of towards the circumference of the eyeball. In many living forms, especially in certain lizards, this pineal or parietal eye is found in a more perfect condition, though covered by a thin membrane. The *ganglia habenulæ* seem to represent the optic ganglia of this cyclopean eye. The *infundibulum* is probably what remains of the gullet of the ancestors of the vertebrates. The *pituitary body* consists of two portions, the anterior lobe, or hypophysis, derived from the buccal cavity, the posterior lobe, or infundibular body, from the primary fore-brain. We have already spoken of the action of extracts of the pituitary (p. 489).

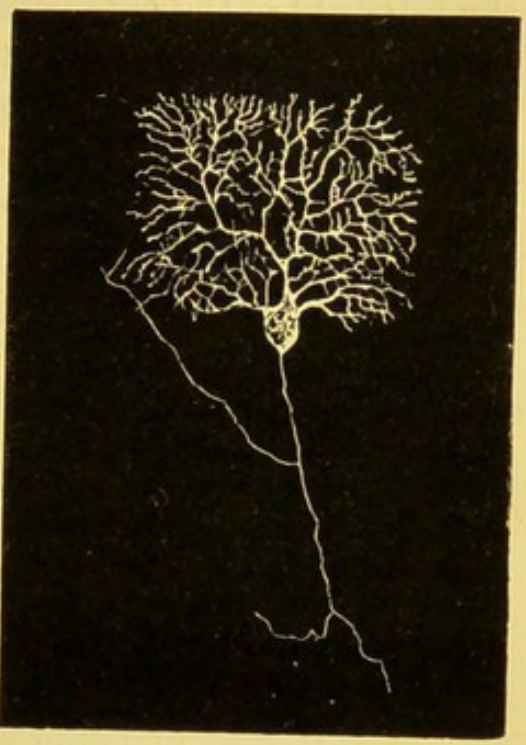


FIG. 262.—A PURKINJE'S CELL FROM THE CEREBELLUM OF A CAT (AFTER CAJAL; GOLGI'S METHOD).

Functions of the Cerebellum.—The elaborate pattern of the arbor vitæ, the appearance given by the branched laminæ in a section of the cerebellum, excited the speculation of the old anatomists. A structure so marvellous must be matched, they thought, with functions as unique. At a time when the discoveries of Galvani and Volta were fresh, and the world ran mad on electricity, the hypothesis of Rolando, that 'nerve-force' was generated by the lamellæ of the cerebellum as electrical energy is generated by the plates of the voltaic pile, ridiculous as it now appears, was not unnatural. The speculation of Gall, who connected the cerebellum with the development of sexual emotions and the action of the generative mechanisms, was based on no fact. It has been definitely disproved by the observations of Luciani, who found that a bitch deprived of its cerebellum showed all the phenomena of heat or 'rut,' was impregnated, whelped at full term in an entirely normal manner, and manifested the maternal instincts in their full intensity. Flourens put forward the doctrine that the cerebellum is an

organ especially concerned in the co-ordination of movements and the maintenance of equilibrium, supporting his conclusions by an elaborate series of experiments. Notwithstanding the very large amount of experimental and clinical study which has been devoted to the cerebellum since the time of Flourens, our knowledge of its functions has hardly advanced beyond the point then reached. Indeed, it may be said that the tendency has been rather to abridge than to extend the field of current physiological doctrine on this subject. For while it has been shown that the integrity of the cerebellum is essential to equilibration, it is by no means certain that it is essential for the co-ordination of movements other than those concerned in the maintenance of equilibrium and in locomotion. Animals entirely deprived of the cerebellum have shown, after the primary effects of the operation have passed away, no impairment in general co-ordinative power; and cases are on record in which the human cerebellum has been found at death to be utterly disorganized, and yet in which many classes of movements have been well co-ordinated during life. But what has been noticed in such cases is a marked inability to maintain the upright posture, a staggering gait, twitching movements of the eyes (nystagmus)—in a word, a general disorder of the mechanism of equilibration. In cases of congenital defect of the cerebellum, the power of walking, and even of standing, is late in being acquired, and usually imperfect. The connections of the cerebellum with other parts of the central nervous system and with the periphery corroborate the direct results of experiment. For the most important afferent impulses concerned in equilibration are those from the muscles, the skin, the semicircular canals and vestibule of the internal ear, and the eyes. And the cerebellum, as we have seen (p. 689), is linked with all of these, and has besides an extensive crossed connection through the middle and superior peduncles with the opposite cerebral hemisphere. The importance and extent of this crossed connection with the great brain is illustrated by the facts that in disease atrophy or deficient development of one cerebellar hemisphere is associated with a similar condition of the

opposite cerebral hemisphere, and that a lesion in one half of the cerebellum affects chiefly the co-ordination of the movements of the same side of the body, that is to say, of the side connected with the opposite cerebral hemisphere.

We do not as yet know the full significance of this extraordinarily free communication of the grey matter of the cerebellum with every part of the central nervous system. But it is evident that by the broad highway of the restiform body, or the cross-country routes from cerebral cortex to cerebellum, impulses may reach it from every quarter; while impulses passing out from it along its peduncles may influence the motor discharge either indirectly through the Rolandic cortex and the pyramidal tract, or more directly through a descending spinal path that brings it into relation with the nuclei of origin of the motor nerves. It is an organ so connected that is suited to take cognizance of the multitudes of afferent impressions concerned in the co-ordination of movements and the maintenance of equilibrium, and to regulate the outflow of efferent impulses in correspondence with the inflow of afferent. This is a convenient place to consider a little more in detail the nature and peripheral sources of the most important of these afferent impressions.

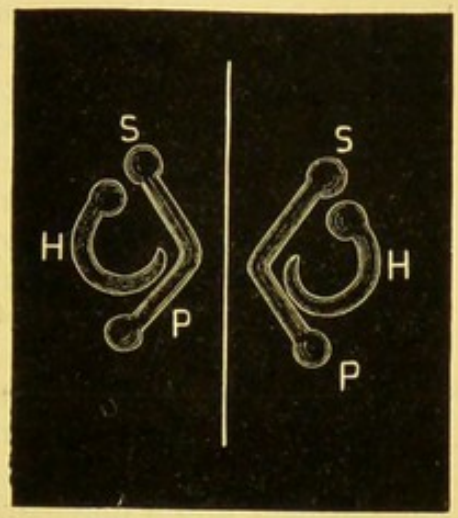


FIG. 263.—THE SEMICIRCULAR CANALS (DIAGRAMMATIC).

H, horizontal or external; S, superior; P, posterior.

(1) **Afferent Impressions from the Muscles.**—Muscles are richly supplied with afferent fibres, for about half of the fibres in the nerves of skeletal muscles degenerate after section of the posterior roots beyond the ganglia (Sherrington). Various kinds of impressions may pass up these muscular nerves: (*a*) Impressions giving rise to pain, as in muscular cramp and in experimental excitation of even the finest muscular nerve-filament; (*b*) impulses causing a rise of blood-pressure; (*c*) impulses which are not associated with a distinct impression in consciousness, but enable us to localize the position of the limbs, head, eyes, and other parts of the body; (*d*) impulses which inform us as to the extent and force of muscular contraction, and seem to underlie the so-called muscular sense. It is the last two kinds—if, indeed, they are distinct—which must be concerned in equilibration. In locomotor ataxia such impressions are blocked by degeneration in a part of the afferent path (p. 703), and disorders of equilibrium are the result.

(2) **Afferent Impressions from the Skin.**—Of the various kinds of nerve-impulses that arise in the nerve-endings of the skin, only those of touch and pressure seem to be concerned in the maintenance of

equilibrium. When the soles of the feet are anæsthetized by chloroform or by cold, and the person is directed to close his eyes, he staggers and sways from side to side. The disturbance of equilibrium in locomotor ataxia must be partly attributed to the loss of these tactile sensations, for numbness of the feet is a frequent symptom, and the patient asserts that he does not feel the ground. An interesting illustration of the importance of afferent impulses from the skin in the maintenance of equilibrium is afforded by the behaviour of a frog deprived of its cerebral hemispheres. Such a frog will balance itself on the edge of a board like a normal animal, but if the skin be removed from the hind-legs, it will fall like a log.

(3) **Afferent Impulses from the Semicircular Canals.**—The semicircular canals are three in number, and lie nearly in three mutually rectangular planes: the external canal in the horizontal plane, the superior canal in a vertical longitudinal plane, and the posterior canal in a vertical transverse plane. Each canal bulges out at one end into a swelling, or ampulla, which opens into the utricular division of the vestibule (Figs. 263, 324). The other extremities of the superior and posterior canals join together, and have a common aperture into the utricle, but the undilated end of the external or horizontal canal opens separately. The utricle and the semicircular canals are thus connected by five distinct orifices. The greater part of the internal surface of the membranous canals, utricle and saccule, is lined by a single layer of flattened epithelium. But at one part of each ampulla projects a transverse ridge, the crista acustica, covered not with squamous, but with long columnar epithelium. Hair-like processes (auditory hairs) are borne by some of the columnar cells, between which lie more elongated fibre-like supporting cells. The hairs project into a mucus-like mass, sometimes containing otoconia, or crystals of calcium carbonate. The ampullæ, like the rest of the membranous labyrinth, is filled with a watery fluid called endolymph. The utricle and saccule have each a somewhat similar but broader elevation, the macula acustica, covered with epithelium and hair-cells of the same character, and the hairs project into a similar mass in which otoconia are constantly present. In some animals, as fishes, the calcareous matter in the utricle and saccule forms masses of considerable size (*otoliths*). Fibres of the auditory nerve end in arborizations around the bodies of the hair-cells of the maculæ and cristæ acusticæ. We have already seen that it is the vestibular division of the nerve which is especially related to the vestibule (p. 723).

There is very strong evidence that the semicircular canals are concerned, not in hearing, but in equilibration. A pigeon from which the membranous canals have been removed still hears perfectly well so long as the cochlea is intact, but exhibits the most profound disturbance of equilibrium. If the horizontal canal is destroyed or divided the pigeon moves its head continually from side to side around a vertical axis; if the superior canal is divided, the head moves up and down around a horizontal axis. The power of co-ordination of movements is diminished, but not to the same extent in all kinds of animals. Thrown into the air, the pigeon is

helpless; it cannot fly; but a goose with divided semicircular canals can still swim. The condition is only temporary, even when the injury involves the three canals on one side; but if the canals on both sides are destroyed, recovery is tardy, and often incomplete. In mammals the loss of co-ordination is much less than in birds; and movements of the eyes, the direction of which depends on the canal destroyed, take to a large extent the place of movements of the head. The effects of destructive lesions have their counterpart in the phenomena caused by stimulation; excitation of a posterior canal, for example, in the pigeon causes movements of the head from side to side.

Lee's results in fishes are, on the whole, of similar tenor. Mechanical stimulation of the ampullæ in the dogfish, by pressing on them with a blunt needle, calls forth characteristic movements of the eyes and fins, and electrical stimulation of the auditory nerve causes movements compounded of the separate movements obtained by stimulation of the ampullæ one by one. Lee concludes that the semicircular canals are the sense-organs for dynamical equilibrium (*i.e.*, equilibrium of an animal in motion), and the utricle and saccule for statical equilibrium (*i.e.*, equilibrium of an animal at rest).

The evidence from all sources points strongly to the conclusion that afferent impulses are actually set up in the fibres of the auditory nerve, through the hair-cells, by alterations of pressure or by streaming movements of the endolymph when the position of the head is changed. Rotation of the head to the right may be supposed to cause the endolymph in the right external canal, in virtue of its inertia, to lag behind the movement, and to press upon the anterior surface of the ampulla. The disorders of movement after lesions of the canals may be explained as the result of the withdrawal of certain of these afferent impulses, and the consequent overthrow of that equipoise of excitation necessary for the maintenance of equilibrium. Even in man there is evidence of the existence of some mechanism not depending on the muscular sense or on impressions passing up the channels of ordinary or special sensation, by which orientation (the determination of the position of the body in space) is rendered possible. For a man lying perfectly still, with eyes shut, on a horizontal table which is made to rotate uniformly, can not only judge whether, but also in what direction, and approximately through what angle, he is moved (Crum Brown). The phenomena of pathology afford weighty additional testimony in favour of the equilibratory function of the semicircular canals. For many cases of vertigo are associated with changes in the internal ear (Menière's disease). And while nearly every normal individual becomes dizzy when rapidly rotated, 35 per cent. of deaf-mutes are entirely unaffected (James), and the proportion seems to be much higher among congenital deaf-mutes. Kreidl and Bruck, too, have found that abnormalities of locomotion and equilibration are much more common in deaf and dumb children than in others. Now, in these cases the defect is usually in the internal ear. We must conclude, then, that the co-ordination of muscular movements necessary for equilibrium is achieved in

some centre, to which afferent impulses pass from the internal ear by the vestibular branch of the auditory nerve, and from which efferent impulses pass out to the muscles. If, as there is strong reason to believe, this centre is situated in the cerebellum, the efferent path is in all probability an indirect one (perhaps by commissural fibres to the Rolandic area, and then out along the pyramidal tract). Ewald has made a curious observation which illustrates the peculiar relation of the semicircular canals to the muscular system, namely, that the labyrinth (in rabbits) influences the course of rigor mortis in the striped muscles. Rigor does not come on so soon on the side from which the labyrinth has been removed.

It is the middle lobe of the cerebellum which seems to be concerned in the co-ordination of movements and maintenance of equilibrium. In birds and lower vertebrates the worm is alone present. The cerebellar hemispheres become more prominent the higher we ascend, and it cannot be doubted that they have important functions, but what these are is entirely unknown. The fact that they are connected chiefly with those parts of the cerebral cortex which are supposed to be concerned in psychical and sensory processes suggests that, at any rate, the superficial grey matter of the cerebellum is not motor, and no movements can be obtained on stimulating it; while stimulation of the worm may cause movements of the eye. Excitation of the line of junction of the superior worm with the lateral lobe in animals which exhibit tonic contraction of extensor muscles after excision of the cerebral hemispheres (acerebral tonus, as it is called) causes relaxation of the extensors accompanied by contraction of the antagonistic flexors—for example, relaxation of the triceps and contraction of the biceps (Horsley and Löwenthal). But this can scarcely be considered a reaction specific to the cerebellum. For Sherrington, who finds that the tonus or spasm is largely due to centripetal impulses coming from the rigid limb, has been able to inhibit it by stimulation of various regions, among others the motor cortex around the fissure of Rolando.

Forced Movements.—We have incidentally mentioned that in fishes injuries to the semicircular canals may give rise to movements which seem to be beyond the control of the animal, and which have consequently received the name of 'forced movements.' It may be added that when the internal ear of a Menobranchus (one of the tailed amphibia) is destroyed on one side, rapid movements of rotation around a longitudinal axis are observed. The animal spins round and round apparently without voluntary control, purpose, or fatigue. The direction of rotation is towards the side of the lesion, the observer being supposed to look down upon the animal as it lies in its normal position. After a time it becomes quiescent; but the forced movements can be again produced by pinching or exciting it in other ways. In man, too, during the passage of a galvanic current through the head by electrodes applied just behind the ears, a tendency to move the head towards the anode is experienced. The person may resist the tendency, but if the current be strong enough his resistance will be overcome; he will execute a forced movement.

When the head turns towards the anode the eyes move in the same direction, and then undergo jerking movements towards the kathode. There is at the same time a feeling of vertigo. Complex as such an experiment is, involving as it does stimulation of so many structures within the cranium, there is reason to believe that it is the excitation of the semicircular canals, or their cerebellar connections, that is responsible for these forced movements. For when the experiment is performed on a pigeon, forced movements are caused so long as the membranous canals are intact, but not after they have been destroyed (Ewald). The observation of Rawitz, that the peculiar rotatory movements of the so-called Japanese dancing mice are associated with marked anatomical peculiarities in the labyrinth, is a new fact in favour of the connection of the canals with the maintenance of equilibrium and the sense of rotation. So is the relation between the degree of development of the canals in different species of birds and the degree of agility in the co-ordination of their movements (Laudenbach).

But forced movements may also follow injuries (especially unilateral) to many portions of the brain—*e.g.*, the pons, crus cerebri, posterior corpora quadrigemina, corpus striatum, even the cerebral cortex, but above all the cerebellum. The movements are of the most various kinds. The animal may run round and round in a circle (circus movements); or, with the tip of its tail as centre and the length of its body as radius, it may describe a circle with its head, as the hand of a clock does (clock-hand movement); or it may rush forward, turning endless somersaults as it goes. Intervals of rest alternate with paroxysms of excitement, and the latter may be brought on by stimulation. In man forced movements associated with vertigo have been sometimes seen in cases of tumour of the cerebellum—*e.g.*, involuntary rotation of the body in tumour of the middle peduncle. No entirely satisfactory explanation of these forced movements has been given. They are evidently connected with disturbance of the mechanism of co-ordination, leading to a loss of proportion in the amount of the motor discharge to muscles or groups of muscles accustomed to act together in executing definite movements. For instance, in circus movements the muscles of the outer side of the body contract more powerfully than those of the inner side, and the animal is therefore constrained to trace a circle instead of a straight line, the excess of contraction on the outer side being analogous to the acceleration along the radius in the case of a point moving in a circle.

Co-ordination of Movements.—The capacity of executing some co-ordinated movements, occasionally of considerable complexity, seems to be inborn in man, and to a still greater extent in many of the lower animals. The new-born child brings with it into the world a certain endowment of co-ordinative powers; it has inherited, for example, from a long line of mammalian ancestors the power of performing those movements of the cheeks, lips, and tongue, on which sucking depends; perhaps from a long, though somewhat shadowy, race of arboreal ancestors the power of clinging with hands and feet, and thus suspending itself in the air. Many movements,

such as walking and the co-ordinated muscular contractions involved in standing, and even in sitting, which, once acquired, appear so natural and spontaneous, have to be learnt by painful effort in the hard school of (infantile) experience. Most people learn, and are willing to confess that they have learnt, to execute a considerable number of co-ordinated movements with the arms, and especially with the fingers; but few have considered that the extreme dexterity of jaws, tongue, and teeth displayed by a hungry mouse or schoolboy is the result of the much practice which maketh perfect. The exquisite co-ordination of the muscles of the eyeball, which we shall afterwards have to speak of, and the no less wonderful balance of effort and resistance, of power put forth and work to be done, of which we have already had glimpses in studying the mechanism of voice and speech, become to a great extent the common property of all fully-developed persons. But the technique of the finished singer or musician, of the swordsman or acrobat, and even the operative skill of the surgeon, are in large part the outcome of a special and acquired agility of mind or body, in virtue of which highly-complicated co-ordinated movements are promptly determined on and immediately executed.

With such special and elaborate movements it is impossible to occupy ourselves in a book like this. Their number may be almost indefinitely extended, and their nature almost infinitely varied, by the needs and training of special trades and professions. It will be sufficient for our purpose to sketch in a few words the mechanism of one or two of the most common and fundamental co-ordinations of muscular effort, passing over the rest with the general statement that the more refined and complex movements are in general brought about not by the abrupt contraction of crude anatomical groups of muscles, but by the contraction of portions of muscles, perhaps even single fibres or small bundles of fibres, while the rest remain relaxed. The excitation may gradually wax and wane as the different stages of the movement require. Antagonistic muscles may be called into play to balance and tone down a contraction which might otherwise be too abrupt.

A most interesting illustration of this process of 'give and take' between opposing muscles has been reported by Sherrington. In the cortex cerebri, as we shall see (pp. 743, 747), there is an area in the frontal region, and another in the occipital region, stimulation of which gives rise to conjugate deviation of the eyes—that is, rotation of both eyes—to the opposite side. Sherrington divided the third and fourth cranial nerves in monkeys—say on the left side. The external rectus, which is supplied by the sixth nerve, caused now by its unopposed contraction external squint of the left eye. When either of the cortical areas referred to, or even the subjacent portion of the corona radiata, was stimulated on the left side, both eyes moved towards the right, the left eye, however, only reaching the middle line—that is, the position in which it looked straight forward. The same thing was observed when the animal, after complete recovery from the operation, was caused to voluntarily turn its eyes to

the right by the sight of food. Here an inhibitory influence must have descended the fibres of the abducens, the only nervous path connected with the extrinsic muscles of the left eye, and the relaxation of the left external rectus must have kept accurate step with the contraction of the right internal rectus. Hering has made an exhaustive analysis of the co-ordinated movements concerned in opening and closing the hand in monkeys. These movements can be produced by stimulation of the cortex or the internal capsule, but not by stimulation of the anterior spinal roots. When the hand is opened the muscles that open it are excited, and those which close it are inhibited from the cortex. (See also p. 734.)

Standing.—In the upright posture the body is supported chiefly by non-muscular structures, the bones and ligaments. But muscles also play an essential part, for it is only peculiarly-gifted individuals like some of the fishermen of the North Sea who can go to sleep on their feet, and a dead body cannot be made to stand erect. The condition of equilibrium is that the perpendicular dropped from the centre of gravity to the ground should fall within the base of support —that is, within the area enclosed by the outer borders of the feet and lines joining the toes and heels respectively. The centre of gravity alters its position with the position of the body, which tends to fall whenever the perpendicular cuts the ground beyond the base of support.

The centre of gravity of the head is a little in front of the vertical plane passing through the occipital condyles. A slight degree of contraction of the muscles of the nape of the neck is required to balance it. When these muscles are relaxed, as in sleep, the head must fall forward, and this is the reason why Homer or any lesser individual nods. In animals which go upon all fours, none of the weight of the head bears directly upon the occipito-atloid articulation; its support by muscular action alone would be an intolerable fatigue, and the ligamentum nuchæ is specially strengthened to hold it up

The vertebral column is kept erect by the ligaments and muscles of the back. The centre of gravity of the trunk lies between the ensiform cartilage and the eighth or tenth dorsal vertebra. The perpendicular dropped from it passes a little behind the horizontal line joining the two acetabula; but the body is prevented from falling backward by the tension of the ileo-femoral ligament and the fascia lata, and perhaps by slight contraction of some of the muscles on the front of the thigh. The perpendicular let fall from the centre of gravity of the whole of the body above the knee passes very slightly behind the axis of rotation of that joint, so that but little muscular action is required to keep the knee-joints rigid. The whole weight of the body is finally transferred to the astragalus on each side, the perpendicular from the centre of gravity of the whole, which is situated near the sacral promontory, falling a little in front of these bones. By means of the muscular sense, and the tactile sensations set up by the pressure of the soles on the ground, alterations in the position of the centre of gravity, and consequent deviations of the

perpendicular passing through it, are detected, and equilibrium is maintained by adjustment of the amount of contraction of this or the other muscular group.

In standing at 'attention,' the heels are close together, the legs and back straightened to the utmost, and the head erect; the weight falls equally upon both legs, but the advantage is much more than counterbalanced by the considerable muscular exertion required to maintain this more ornamental than useful position. In 'standing at ease,' practically the whole weight is supported by one leg, the perpendicular from the centre of gravity passing through the knee and ankle-joints. The centre of gravity is brought over the supporting leg by flexure of the body to the corresponding side, and comparatively little muscular effort is required. The other foot rests lightly on the ground, the weight of the leg itself being almost balanced by the atmospheric pressure acting upon the air-tight and air-free cavity of the hip-joint. The light touch of this foot varies slightly from time to time, so as to maintain equilibrium.

When the arms or head are moved, or the body swayed, the centre of gravity is correspondingly displaced, and it is by such movements that tight-rope dancers continue to keep the perpendicular passing through it always within the narrow base of support.

In *sitting*, the base of support is larger than in standing, and the equilibrium therefore more stable. The easiest posture in sitting without support to the back or feet is that in which the perpendicular from the centre of gravity passes through the horizontal line joining the two tubera ischii.

Locomotion.—In walking, the legs are alternately swung forward and rested on the ground. In military marching, it is directed that toe and heel be simultaneously set down. But with most persons the swinging foot first strikes the ground by the heel; then the sole comes down, the heel rises, the leg is extended, and, with a parting push from the toe, the leg again swings free. By this manœuvre the body is raised vertically, tilted to the opposite side, and also pushed in advance.

The forward swing of the leg is only slightly, if at all, due to muscular action; it is more like the oscillation of a pendulum displaced behind its position of equilibrium, and swinging through that position, and in front of it, under the influence of gravity. For this reason the natural pace of a tall man is longer and slower than that of a short man; but it may be modified by voluntary effort, as when a rank of soldiers of different height keeps step.

The lateral swing of the body is illustrated by the everyday experience that two persons knock against each other when they try to walk close together without keeping step. In step, both swing their bodies to the same side at the same moment, and there is no jarring.

Even in the fastest walking there is a short time during which both feet are on the ground together, the one leg not beginning its swing until the other foot has been set down. In running, on the other hand, there is an interval during which the body is completely in the air.

Functions of the Cerebral Cortex.—When an animal, like a frog, is deprived of its cerebral hemispheres, the power of automatic voluntary movement appears to be definitively and entirely lost. The animal, as soon as the effects of the anæsthetic and the shock of the operation have passed away, draws up its legs, erects its head, and assumes the characteristic position of a normal frog at rest. So close may be the resemblance, that if all external signs of the operation have been concealed, it may not be possible for a casual observer to tell merely by inspection which is the intact and which the 'brainless' frog. The latter will jump if it be touched or otherwise stimulated. It will croak if its flanks be stroked or gently squeezed together. It will swim if thrown into water. If placed on its back, it will promptly recover its normal position. But it will do all these things as a machine would do them, without purpose, without regard to its environment, with a kind of 'fatal' regularity. Every time it is stimulated it will jump, every time its flanks are squeezed it will croak, and, in the absence of all stimulation, it will sit still till it withers to a mummy, even by the side of the water that might for a while preserve it.

A Menobranchus, without its cerebral hemispheres, will, like the frog, refuse to lie on its back. On stimulation it moves its feet or tail, or its whole body; but if not interfered with, it lies for an indefinite time in the same position. Its gills are seen to execute rhythmic movements, which never stop, and rarely slacken, except for an instant, when some part of the skin, particularly in the region of the head, is mechanically or electrically stimulated. The normal Menobranchus, on the other hand, lies for long periods with its gills at perfect rest, and when stimulated moves for a considerable distance. After a time, two months or more, it is true the 'brainless frog,' if it be kept alive, as may be done by careful attention, will recover a certain portion of the powers which it has lost by removal of the cerebral hemispheres; and, indeed, the longer it lives, the nearer it approximates to the condition of a normal frog. A brainless frog has been seen to catch flies and to bury itself as winter drew on. A fish even three days after the destruction

of its cerebrum has been seen to dart upon a worm, seize it before it had time to sink to the bottom of the aquarium, and swallow it. Even in the pigeon the loss of the hemispheres, which at first induces a state of profound and seemingly permanent lethargy, is to a great extent compensated for, as time passes on, by the unfolding in the lower centres of capabilities previously dormant or suppressed. A brainless pigeon has been known to come at the whistle of the attendant and follow him through the whole house.

In the mammal the removal of the whole or the greater part of the cerebral hemispheres at a single operation is uniformly and speedily fatal; even rabbits or rats, which bear the operation best, survive but a few hours. During those hours they manifest phenomena similar to those observed in the bird and the frog. In the dog the entire cortex has been removed piecemeal by successive operations. In this case, of course, the change in the condition of the animal is more gradually produced, and an opportunity is afforded for a certain recovery of function in the intervals between the operations. On the whole, however, as might be expected from its greater intellectual development, recovery is more imperfect in the dog than in the bird, much more imperfect than in the frog. But even in the dog wonderful resources lie hidden in the grey matter of the central neural axis, and are called forth by degrees to replace the lost powers of the cerebral cortex. It is true that a 'brainless' dog is a less efficient animal than a brainless fish, or even than a brainless frog; but in favourable cases even in the dog, the movements of walking may still be carried out with tolerable precision in the absence of the cerebral hemispheres. The animal can swallow food pushed well back into the mouth, although it cannot feed itself. Stupid and listless as it is compared with the normal dog, it seems to be by no means devoid of the power of experiencing sensations as the result of impressions from without, nor of carrying on mental operations of a low intellectual grade. Goltz had a dog which lived more than a year and a half practically without its cerebral hemispheres, and another which lived thirteen weeks. He believes that they had lost understanding,

reflection, and memory, but not sensation, special or general, nor emotions and voluntary power. Their condition may be best described as one of general imbecility. Hunger and thirst are present. They experience satisfaction when fed, become angry when attacked, see a very bright light, avoid obstacles, hear loud sounds, such as those produced by a fog-horn, and can be awakened by them. They are not completely deprived of sensations of taste and touch. But it ought to be remembered that the interpretation of the objective signs of sensation in animals is beset with difficulties; and although everybody admits the accuracy of Goltz's description of what is to be seen, his interpretation of the facts has been severely criticised, particularly by H. Munk.

To the monkey there can be no doubt that the loss of the cerebral hemispheres would be a still heavier and more irremediable blow than to the dog. But nobody has yet succeeded in keeping a monkey alive after complete removal of even one hemisphere.

In man the destruction of considerable masses of brain-substance, particularly if gradual, is not necessarily fatal. How great a loss is compatible with life cannot be exactly stated. It depends to a large extent on the position of the lesion. But it is possible that one cerebral hemisphere may be rendered functionally useless without immediately putting a term to existence. In the fœtus, however, no portion of the great brain is absolutely indispensable for life and movement. An anencephalous fœtus (in which the brain has remained undeveloped) may be born alive, and live for a short time.

We see, then, that homologous organs are not necessarily, nor indeed usually, of the same physiological value in different kinds of animals. A loss which perhaps hardly narrows the range of the psychical, and certainly restricts only to a slight extent the physical powers of a fish, impairs in a marked degree the voluntary movements of a dog, in addition to cutting off from it a great part of its intellectual life, and is in man incompatible with life altogether.

The results of the removal of the entire cerebral hemispheres help us to fix their position as a whole in the

physiological hierarchy. A more minute analysis shows us that the cerebral cortex itself is not homogeneous in function, that certain regions of it have been set aside for special labours. Our knowledge of this localization of function in the cerebral cortex has been derived partly from clinical, coupled with pathological observations on man, and partly from the results of the removal or stimulation of definite areas in animals. And so varied and extensive have been the contributions from both of these sources, that it is difficult to decide to which we owe most.

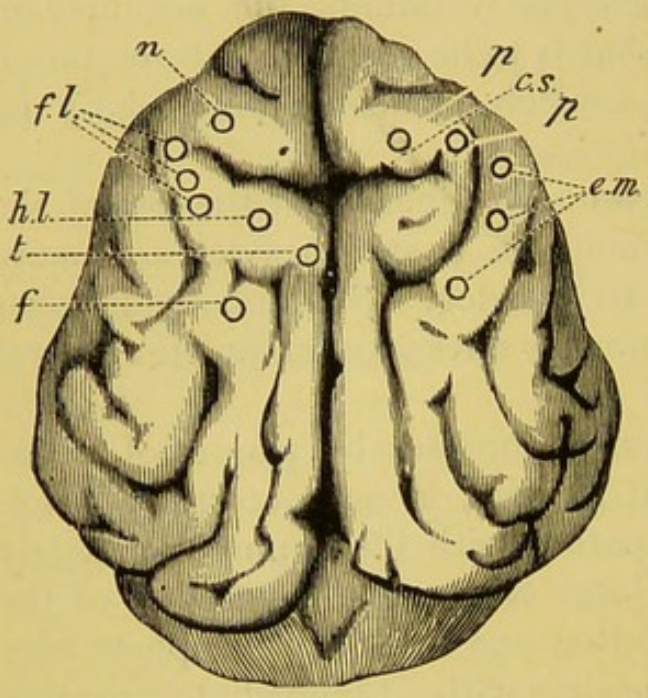


FIG. 264.—MOTOR AREAS OF DOG'S BRAIN.

n, neck; *f.l.*, fore-limb; *h.l.*, hind-limb; *t*, tail; *f*, face; *c.s.*, crucial sulcus; *e.m.*, eye movements; *p*, dilatation of the pupil in both eyes, but especially in the opposite eye. All the areas are marked in the figure only on the left side except the eye areas, whose position, to avoid confusion, is indicated on the right hemisphere.

It is a fact which might appear strange and almost inexplicable did the history of science not constantly present us with the like, that thirty years ago the universal opinion among physiologists, pathologists, and physicians was that the cerebral cortex is inexcitable to artificial stimuli, that no visible response can be obtained from it. The great names of Flourens and Magendie stood sponsors for this error, and repressed research. In 1870, however, Hitzig and Fritsch showed that not only was it possible to elicit muscular contractions by stimulation of the cortex of the brain in the dog with voltaic currents, but that the excitable area occupied a definite region in the neighbourhood of the crucial sulcus, which runs out over the convexity of the hemispheres nearly at right angles to the longitudinal fissure. In this region they were further able to isolate several distinct areas, stimulation of which was followed by movements respectively of the head, face, neck, hind-leg, and fore-leg. This was the starting-point of a long series of researches by Ferrier, Munk, Horsley, Schäfer, Heidenhain, and many others, on the brains of monkeys, as well as dogs—researches which have formed the basis of an exact cortical localization in the brain of man, and have enriched surgery with a new province. In these later experiments the interrupted current from an induction machine has been

found the most suitable form of stimulus (see Practical Exercises, p. 769). For certain purposes the method of Ewald has advantages. He fixes in a trephine hole in the skull an ivory plug, through which pass the electrodes. When the animal has recovered from the operation, the region of the brain in contact with the electrodes can be stimulated without fastening the animal.

Motor Areas.—Lying around the fissure of Rolando, and lapping over on the mesial surface of the hemisphere in this region, are the so-called motor areas (Figs. 264 to 270). They occupy the whole of the ascending frontal and parietal convolutions, running forward a little into the horizontal frontal convolutions, backward a little into the superior parietal convolution, and turning over on the mesial surface into the marginal convolution. Highest of all on the convexity of the hemisphere lies the area of the leg; below this, in order, the areas for the arm, face, mouth, pharynx, and larynx. In front of the leg and arm areas lies the area of the head, neck, and eyes, passing out into the posterior portions of the first and second frontal convolutions. On the mesial surface in the marginal convolution lie areas for the head, arm, trunk, and leg in order from before backwards.

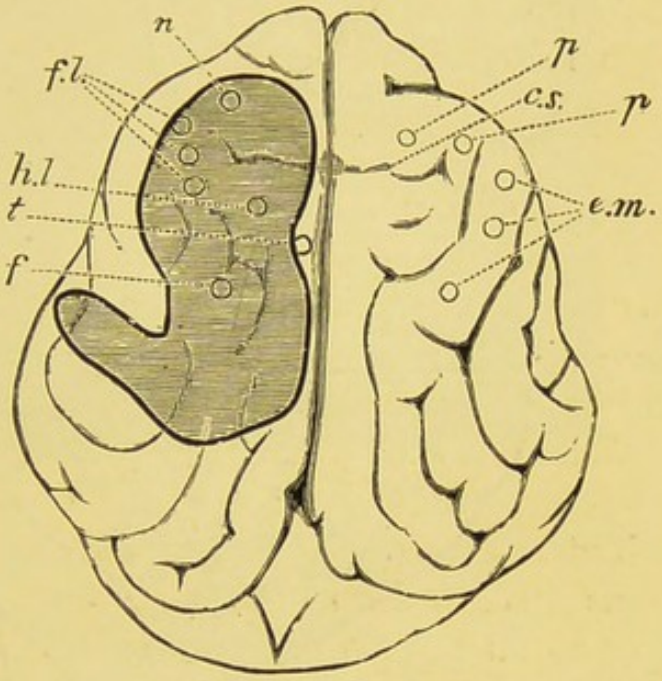


FIG. 265.—DOG'S BRAIN WITH LESION.

A portion of the cortex indicated by the shaded area was destroyed by cauterization. The symptoms were complete blindness of the opposite eye (in this case the right); weakness of the muscles of the limbs and of the neck on the right side; slight weakness of the limbs on the left side. When the animal walked there was a tendency to turn to the left in a circle. In eating or drinking the head was turned to the left, so that the mouth was oblique, and the right angle of the mouth was lower than the left. The tail movements were normal, and there was no deviation of the tail to one side.

It is to be particularly noted (1) that within the larger areas, such as those of the arm and leg, smaller foci can be mapped off which are related to movements of the separate

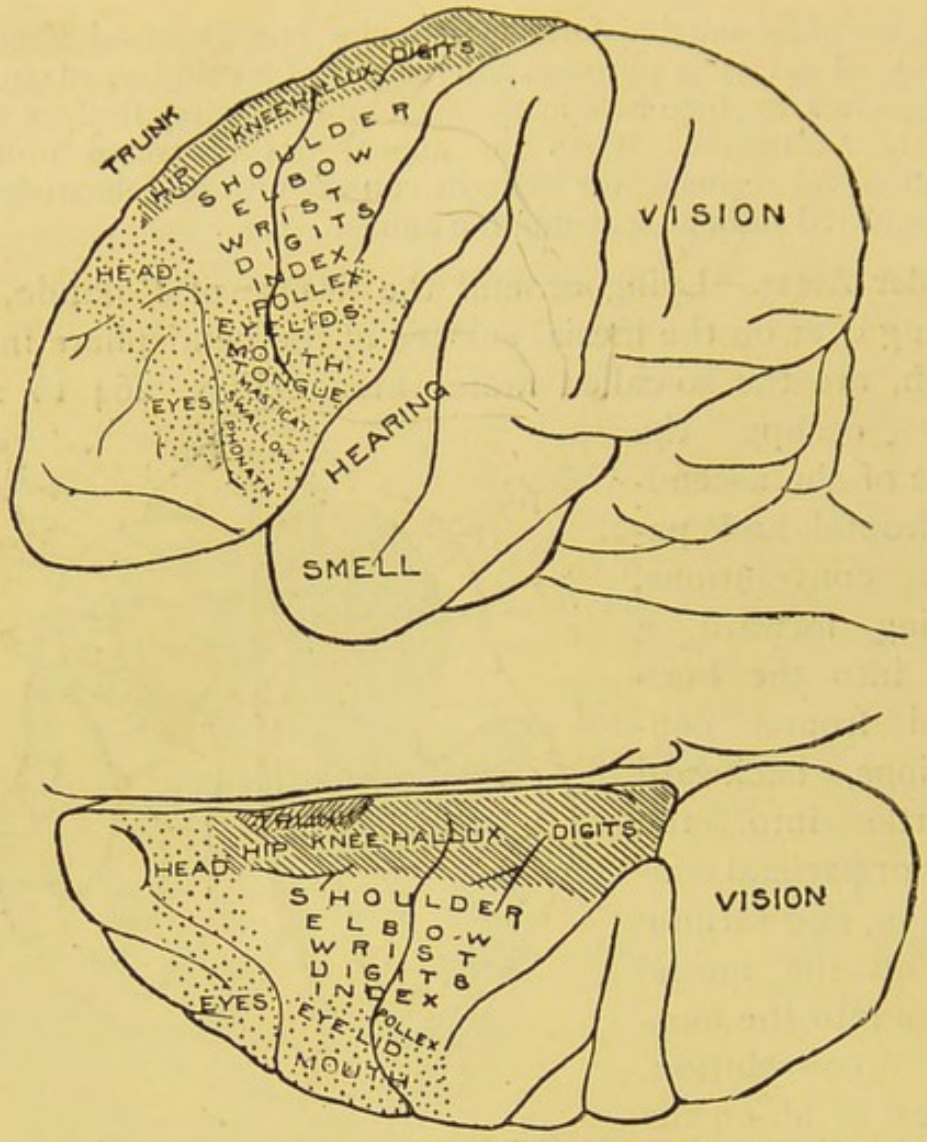


FIG. 266.—BRAIN OF MACAQUE MONKEY (BEEVOR AND HORSLEY).
The upper figure shows the lateral aspect of the left hemisphere, and the lower figure its upper (or dorsal) surface. The motor and sensory areas are indicated.

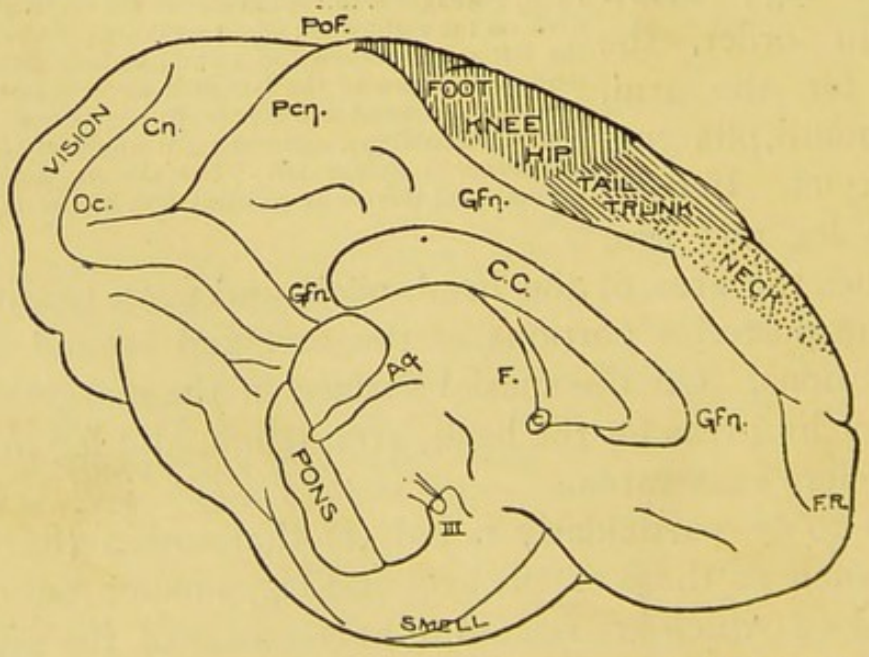
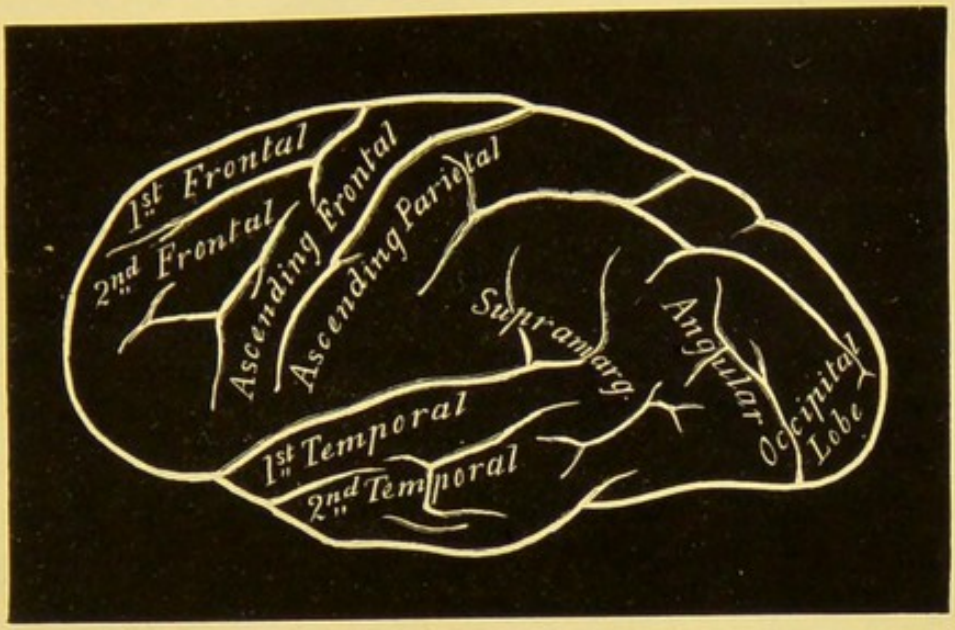


FIG. 267.—MESIAL SURFACE OF LEFT HEMISPHERE OF MACAQUE MONKEY (HORSLEY).

joints—thus, in the leg area, the hip, knee, and ankle joints, and the great toe, are represented by separate and special centres; (2) that stimulation of any one of these areas leads, not to contraction of individual muscles, but to contraction



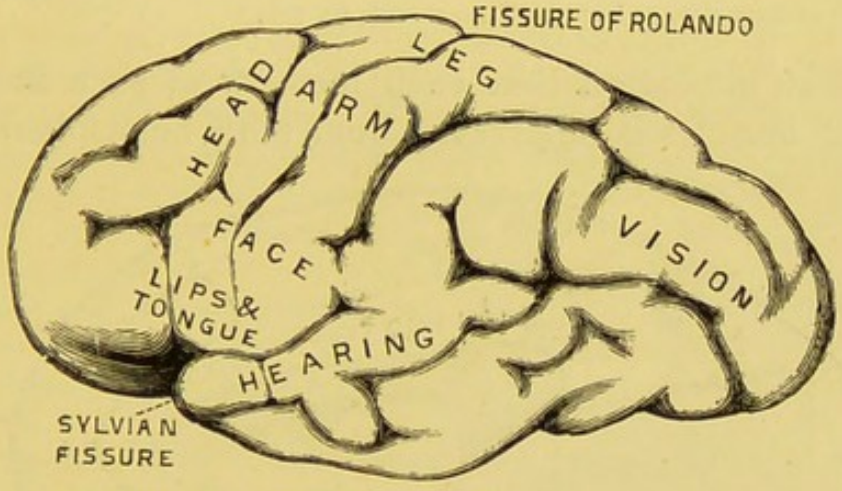


FIG. 268.—LATERAL VIEW OF LEFT HEMISPHERE (MAN), WITH MOTOR AND SENSORY AREAS.

The front of the brain is towards the left.

of muscular groups which have to do with the execution of definite movements.

Removal of the whole of the motor cortex of one hemisphere causes paralysis of movement on the opposite side of the body. The paralysis is less marked in the case of bilateral muscles that habitually act together than in the

case of those which ordinarily act alone. Thus the muscles of respiration and the muscles of the trunk in general are, although perhaps weakened, never completely paralyzed.

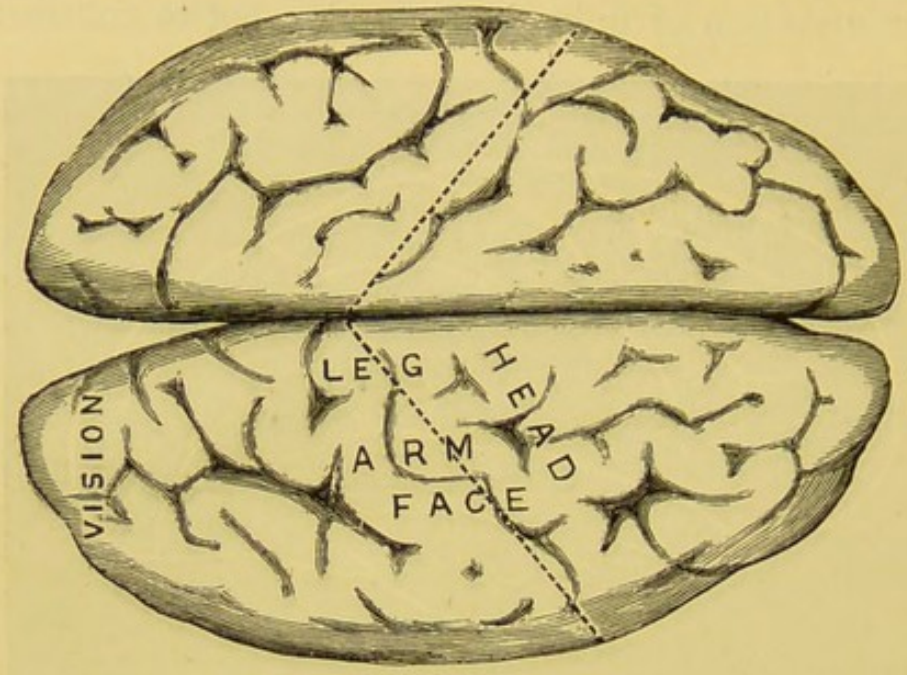


FIG. 269.—CEREBRAL CORTEX (MAN) SEEN FROM ABOVE.

The front of the brain is towards the right. The dotted line shows the position of the fissure of Rolando, as fixed by Thane's rule (p. 748).

This is an indication that each member of such functional pairs of muscles is innervated from both hemispheres; and

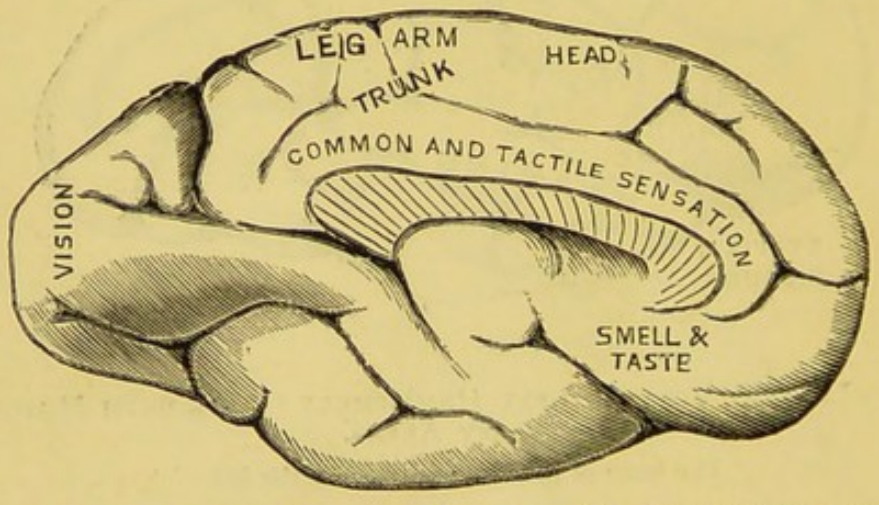


FIG. 270.—MOTOR AND SENSORY AREAS OF MESIAL SURFACE OF HUMAN BRAIN.

The front of the brain is towards the right. The words 'smell and taste' are wrongly placed in the figure. They should be placed just behind the Sylvian fissure instead of in front of it. The location of 'common and tactile sensation' in the gyrus fornicatus is purely hypothetical.

this physiological deduction is supported by the anatomical fact already referred to, that after removal of the motor

cortex, or injury to the pyramidal tracts in the internal capsule or crus, some degenerated fibres (homolateral fibres) are found in the crossed pyramidal tract on the side of the lesion (p. 688).

Removal of a single motor region leads to paralysis only of the corresponding limb, or part of a limb, on the opposite side. In the dog after a time the paralysis may more or less completely disappear, the loss of the cortical centres on one side being perhaps compensated by increased activity of those that are left. In the monkey restoration is less complete; in man it is more imperfect still.

Goltz has lately reported some interesting observations on a monkey, which was carefully watched for eleven years after the removal by two operations of the cortex of the greater portion of the frontal and parietal lobes on the left side. The character of the animal, which had been studied for months before the operations, was entirely unaffected, All its traits remained unaltered. There was no loss of memory or intelligence. On the other hand, disturbances of movement on the right side were very noticeable up till its death. It learned again to use the right limbs in locomotion; but, although they were not markedly weaker than those of the left side, their movements had a certain clumsiness, which was associated with a permanent diminution in the sensibility of the skin of these limbs. Muscular sensibility was also lessened. In acts requiring the use of only one hand, the right was never willingly employed, and it evidently cost the animal a great effort to use it in such movements, but by special training it learnt again to give the right hand when asked for it, and to make use of it for other purposes. The movements with which the motor areas are concerned are essentially skilled movements, and we may suppose that it is more difficult for a monkey to educate again a centre for such complex and elaborate manœuvres as are performed by its hand than for a dog to regain cortical control of the comparatively simple movements of its paw. In man in cases of hemiplegia, when the patient lives for some time a certain amount of recovery usually takes place, especially in young persons, in the paralyzed leg, but much less in the paralyzed arm.

It is in the light of the results obtained in monkeys, and by the aid of clinical and pathological observations, that the motor areas in man have to a great extent been mapped out. An extensive hæmorrhage involving the cerebral cortex on both sides of the fissure of Rolando, or an embolus blocking the middle cerebral artery, causes paralysis of the opposite side of the body. An embolus of a branch of the middle cerebral artery causes paralysis of the muscles, or rather movements, represented in the area supplied by it. A tumour causes symptoms of irritation, motor or sensory—convulsions beginning in, or sensations referred to, the parts represented in the regions on which it presses. In connection with the localization

of lesions in the motor area of the cortex, and operative interference for their cure, the exact position of the fissure of Rolando becomes important; and Thane has given the following simple method for fixing it: The point midway between the root of the nose and the occipital protuberance is fixed by measuring the distance with a tape. The upper end of the fissure of Rolando lies half an inch behind this middle point. The fissure makes an angle of 67° with the longitudinal fissure (Fig. 269).

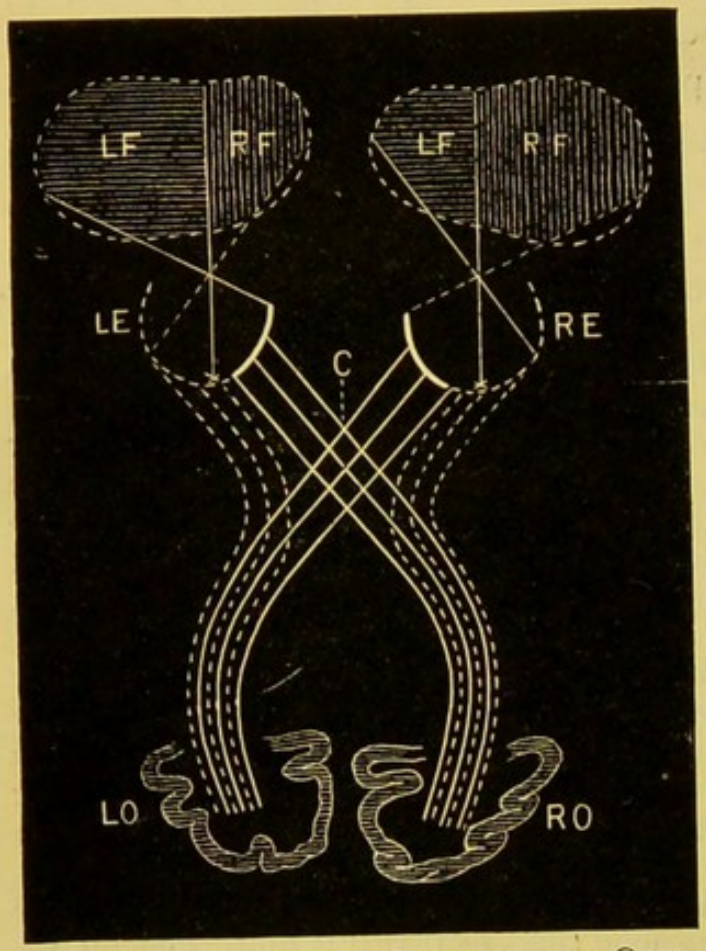


FIG. 271.—DIAGRAM OF RELATIONS OF OCCIPITAL CORTEX TO THE RETINÆ.

RO, LO, right and left occipital cortex; RE, LE, right and left retina; C, optic chiasma; RF, LF, right and left visual fields. The continuous lines passing back from the retinæ to the occipital cortex represent the crossed, the broken lines the uncrossed, fibres of the optic nerves and tracts.

Sensory Areas—Visual Centres. — In the occipital lobe an area of considerable extent has been found, destruction of which causes hemianopia, *i.e.*, loss of vision in the corresponding halves of the retinæ. Thus, if the right occipital cortex is destroyed, the right halves of the two retinæ are paralyzed, and the left half of the field of vision is a blank. There is *conjugate deviation* of the head and eyes to the same side as the lesion; in other words, the animal turns its head and eyes to the right. Destruction of this region on both sides causes complete blindness. When the same region is stimulated, the eyes and head are turned to the left—that is, there is conjugate deviation to the opposite side. The movements differ from those produced by stimulation of the Rolandic area. They are not so certain, their latent period is longer, and they are considered to be not direct, but reflex movements. It cannot be doubted that the occipital

region is concerned in vision, and it is a very natural suggestion that the movements are the result of visual sensations in the excited occipital cortex. The right occipital lobe is concerned with vision in the right halves of the two retinæ (Figs. 271 and 258). Now, under normal conditions a visual image would be cast on the two right retinal halves by an object placed towards the left of the field. The movements of the head and eyes to the left may therefore be plausibly explained as an attempt to look at, and a rotation towards, the supposed object.

The pathological evidence is very clear that disease of the occipital lobe, especially of the cuneus, a triangular area on its mesial surface, causes hemianopia in man. A limited lesion may even be associated with an incomplete hemianopia, and cases have been recorded in which colour hemianopia (blindness of the corresponding halves of the two retinæ for coloured objects) co-existed with normal vision for white light. Sometimes dimness of vision in the whole of the opposite eye (crossed amblyopia), and not hemianopia, is caused by a lesion of the occipital cortex. It seems impossible to explain this and other facts without postulating the existence of more than one visual centre; and it has been supposed that in the angular gyrus a higher visual centre exists which is connected with the lower occipital centres for the two halves of the opposite eye. Thus, the right angular gyrus would be in connection with the part of the right occipital cortex which has to do with vision in the nasal half of the left eye, and with the part of the left occipital cortex which has to do with vision in the temporal half of that eye. It has been stated that after complete removal of the occipital lobes in young monkeys, the power of vision, lost for a time, is gradually regained, the growth of new nerve-cells and nerve-fibres having made good the deficiency (Vitzou).

Auditory Centre.—On the outer surface of the temporo-sphenoidal lobe, in the hinder portion of the first and second temporal convolutions, lies an area associated with the sense of hearing. Stimulation in the region of the first temporal convolution may cause the animal to prick up its ear on the opposite side. Destruction of this area on both sides is followed by complete and irremediable loss of hearing. If it is destroyed only on one side there is partial deafness of the opposite ear, and also to some extent of the ear on the same side. This is gradually recovered from. If it is destroyed on the left side there is also the peculiar condition

called 'word deafness,' which will be referred to directly (p. 753). In deaf-mutes the first temporal convolution may be atrophied. There is evidence that the posterior corpora quadrigemina and the mesial geniculate body form an inferior relay on the route between the fibres of the auditory nerve and the temporal cortex. There are indications that within the auditory area so-called 'musical centres' exist—that is, an orderly arrangement of the cell-bodies of the neurons that have to do with the perception of pitch, so that a limited lesion may cause deafness to notes of a particular pitch when it is situated in one part of the area, and deafness to notes of a different pitch when it is situated elsewhere (Larionow).

Centre for Smell.—As to the position of the centre for smell, direct experiment on animals cannot teach us much, for if the outward tokens of visual and auditory sensations are dubious and fluctuating, still more is this the case with the signs of sensations of smell. A further source of fallacy is the fact that other sensations than those of smell are caused by stimulation of the mucous membrane of the nose. Substances like ammonia, for example, affect entirely the endings of the trigeminus, which is the nerve of common sensation for the nostrils. Pathological and clinical evidence would be of great value, but it is as yet scanty, and of itself indecisive. So far as it goes, however, it undoubtedly supports the view derived from the anatomical connections of the olfactory tracts, that the centre for smell is situated in the uncinate gyrus on the mesial aspect of the temporal lobe, for the olfactory tract may be traced into this region. In animals with a very acute sense of smell, this gyrus is magnified into a veritable lobe, called from its shape the pyriform lobe; from its supposed function, the rhinencephalon. The centre for taste is supposed to be situated in the same region as the centre for smell.

Ordinary and **tactile sensation** have been located by some observers on the mesial surfaces of the hemispheres—in the hippocampal convolution and the gyrus fornicatus. But this cannot be considered as settled, and in any case this is not the only region where common sensibility is represented.

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For example, it is certain that the Rolandic area has sensory as well as motor functions; and there are good grounds for believing that the sensory fibres from the muscles and the skin terminate here in arborizations which come into contact either with those of the motor pyramidal cells, or with those of intermediate cells which link them to the pyramidal cells.

Pathological evidence in man agrees, upon the whole, with wonderful precision with the results of experiments on animals; and, indeed, before any experimental proof of the minute and elaborate subdivision of the cortex had been obtained, Broca had already, from the phenomena of the sick-bed and the post-mortem room, located a centre for speech in the left inferior frontal convolution, and Hughlings Jackson had associated pathological lesions of the Rolandic area with certain cases of epileptiform convulsions.

Aphasia.—In most persons the inferior frontal convolution on the left side is concerned in the expression of ideas in spoken or written language. It is even said that oratorical powers have been found associated with marked development of this convolution (as in the case of Gambetta, the French statesman). Words are, at bottom, arbitrary signs by which certain ideas are expressed. The power of intelligent communication by spoken or written language may be lost: (1) by paralysis of the muscles of articulation or the muscles which guide the pen; (2) by inability to hear or see the spoken or written word, *i.e.*, by deafness or blindness; (3) by inability to comprehend the meaning of spoken or written language, although sensations of hearing and sight may not be abolished—that is to say, by inability to *interpret* the auditory or visual symbols by which ideas are conveyed; (4) by inability to clothe ideas in words, although the ideas conveyed by speech or writing may be perfectly comprehended. Neither (1) nor (2) is considered to constitute the condition of aphasia; (3) represents what is called amnesia, or *sensory aphasia;* (4) is aphasia in the ordinary restricted sense, or *motor aphasia.* It is this last condition which is associated with a lesion in the left inferior frontal convolution. The portion of the convolution concerned is the posterior extremity, where it borders on the fissure of Sylvius, and it either completely coincides with or largely overlaps the centre for the movements of the tongue, lips, and larynx concerned in articulation. In motor aphasia the patient understands quite well what is said to him, and also knows quite well what to reply, but the words necessary to express his meaning do not come to him. He makes no answer whatever, or strings together a series of words each correctly articulated but having no

meaning, or utters a jargon not composed of known words at all. The failure does not lie in the articulatory mechanism. The patient uses the same muscles of articulation, without any marked impairment of function, for chewing and swallowing his food. It is only when the corresponding area in the right inferior frontal convolution, or the path from it to the internal capsule, is also destroyed, that articulation is greatly and permanently interfered with. An aphasic may sometimes sing a song without a single slip in words or measure, and yet be unable to speak or write it. In a case recorded by Larionow an aphasic could speak only one syllable, 'tan,' but could sing the Marseillaise. In certain cases the change is confined to loss of the power of spontaneous speech, and the patient may be able to read intelligently. Sometimes he can express his ideas in speech but not in writing (*agraphia*). Sometimes the loss is restricted to certain sets of ideas. For example, a boy was injured by falling on his head. Typical symptoms of motor aphasia developed, but the power of dealing with ideas of number was not interfered with, and the boy continued to learn arithmetic as if nothing had happened. Proper names and nouns are more easily lost than adjectives and verbs. Motor aphasia is generally accompanied by paralysis, frequently transient, of voluntary movement on the right side, sometimes amounting to complete hemiplegia, but more often involving the right arm alone. This association is explained by the proximity of the inferior frontal convolution to the motor area of the arm, and their common blood-supply.

Why, now, is it that motor aphasia is commonly due to a lesion in the left hemisphere alone? The answer to this question is partly supplied by the important and curious observation that in left-handed individuals damage to the right inferior frontal convolution may cause aphasia. In the right-handed man the motor areas of the left hemisphere may be supposed to be more highly educated than those of the right hemisphere. The movements of the right side which they initiate or control are stronger and more delicate and precise than those of the left side. It is only necessary to assume that this process of specialization, of selective training, has been carried on to a still greater extent in the left frontal convolution, that in most men the speech-centre there has taken upon itself the whole, or the greater part, of the labour of clothing ideas in words, leaving to the right centre only its primitive but undeveloped powers. In left-handed persons the speech-centre on the right side may be supposed to share in the general functional development of the right hemisphere. That great capabilities are lying dormant in the right speech-centre of the ordinary right-handed individual is indicated by the fact that after complete destruction of the left inferior frontal convolution the power of speech may be to a considerable extent, though slowly and laboriously, regained; and it is said that this second accumulation may be swept away, and without remedy, by a second lesion in the right inferior frontal convolution. But frail is the tenure of life in a person who has twice suffered from such a lesion; and we do not know whether recovery might not take place

to some extent even after destruction of both inferior frontal convolutions, if the patient only lived long enough.

Temporary aphasia may occur without any structural change in the speech-centre—for example, during an attack of migraine. In children it may even be caused by some comparatively slight irritation in the digestive tract, such as that due to the presence of a tape-worm.

Sensory Aphasia.—In typical motor aphasia spoken and written words convey to the patient their ordinary meaning. They call up in his mind the usual sequence of ideas, but the chain is broken at the speech-centre, and the outgoing ideas cannot be clothed in words. In another class of cases the patient may be perfectly capable of rational speech; he may talk to himself or on a set topic with fluency and sense, but he may be unable to respond to a question or read a single line of print. Damage to two regions of the left hemisphere of the brain has been found associated with this strange condition, (1) the upper portion of the temporo-sphenoidal lobe, (2) the angular gyrus and the occipital lobe. When the temporal region is alone affected, it is the spoken word that is missed, the written that is understood (*word-deafness*). When, as occasionally happens, the lesion is confined to the occipital region, spoken language is perfectly understood, written language not at all (*word-blindness*). Sensory, like motor aphasia, may exist in any degree of completeness, from absolute word-deafness or word-blindness, in which no spoken or printed word calls up any mental image, to a condition not amounting to much more than a marked absence of mind or unusual obtuseness. Motor and sensory aphasia may be present together. In well-marked word-deafness speech is always interfered with to some extent.

Cortical Epilepsy.—While it was still believed that the cortex was inexcitable, epilepsy was supposed to be exclusively due to morbid conditions, structural or functional, of the medulla oblongata (Kussmaul and Tenner). Some more recent writers have put forward precisely the opposite opinion, that the disease is always cortical in origin (Unverricht, etc.). What we know for certain is that some cases, but only a minority, are associated with irritative lesions in or near the Rolandic area (cortical or Jacksonian epilepsy). It has even been found possible to localize the position of the lesion from the part of the body in which the fit, or the aura (the sensation or group of sensations peculiar to each case, which precedes and announces it), begins. For example, if the convulsions commence with a twitching of the right thumb and extend over the arm, or if the aura consists of sensations beginning in the thumb, there is a strong presumption that the seat of the lesion is the part of the arm-area known as the 'thumb-centre' in the left cerebral hemisphere. It is the seat of the convulsion at its commencement, not the regions to which it may afterwards spread, that is important in diagnosing the position of the lesion. For just as strong or long-continued electrical stimulation of a given 'centre' of the motor cortex may give rise to contractions of muscles associated with other 'centres,' so the excita-

tion set up by localized disease may spread far and wide from its original focus, involving area after area of the Rolandic region first in the one hemisphere and then in the other. The part of the body to which a sensory aura is referred is as significant an indication of the seat of the discharging lesion as is the part of the body which first begins to twitch.

Sensory Functions of the Rolandic Area.—This is one of the proofs that the Rolandic region is not a purely motor, but a *sensori-motor*, or *kinæsthetic*, area. Histological studies on the course of the sensory paths support this conclusion. We have already mentioned that, according to Goltz's observations (p. 747), removal of the Rolandic cortex causes defects of sensation as well as of movement. From the field of experiment further evidence is forthcoming.

(1) It has been found that if the posterior roots of the nerves supplying one of the limbs be cut in a monkey, all the most delicate and skilled movements of the limb are either greatly impaired or totally abolished (Mott and Sherrington). The limb is not used for progression or for climbing, but hangs limp, and apparently helpless, by the side of the animal. That this condition is not due to any loss of functional power by the peripheral portion of the motor path may be assumed, since the anterior roots remain intact. That it is not due to any want of capacity on the part of the motor centres to discharge impulses when stimulated may be shown by exciting the cortical area of the limb—either electrically or by inducing epileptic convulsions by intravenous injection of absinthe—when movements of the affected limb take place just as readily as movements of the sound limbs. The cause of the impairment of voluntary motion, then, can only be the loss of the afferent impulses which normally pass up to the brain, and presumably to the motor cortex. When only one sensory nerve-root is cut, no defect of movement can be seen; and this is evidently in accordance with the fact already mentioned (p. 698), that complete anæsthesia of even the smallest patch of skin is never caused by section of a single posterior root. And that it is the loss of impulses from the skin which plays the chief part is shown by the fact that after division of the posterior roots supplying the muscles of the hand or foot, which only partially interferes with the sensory supply of the skin, joints, sheaths of tendons, etc., movement is unimpaired; while section of the nerve-roots supplying the skin, those of the muscles being left intact, causes extreme loss of motor power.

(2) If a strength of stimulus be sought which will just fail to cause contraction of the muscular group related to a given motor area, and a sensory nerve, or, better, a sensory surface (best of all, the skin over the corresponding muscles), be now stimulated, contraction will occur—that is to say, the excitability of the motor centres will be increased. This shows that the motor region is *en rapport* not only with efferent, but also with afferent fibres, that it receives impulses as well as discharges them.

The same experiment is a proof that the results of excitation of the motor cortex are due to stimulation of the grey matter, and not,

as has been asserted, of the white fibres of the corona radiata. It is undoubtedly possible to excite these fibres by electrodes directly applied to the motor cortex, but in the latter case the current has to be made stronger than is sufficient to excite the grey matter alone. Further evidence is afforded by the following facts: (*a*) The 'period of delay,' that is, the period which elapses between stimulation and contraction, is greater by nearly 50 per cent. when the cortex is stimulated than when the white fibres are directly excited. (*b*) Morphia greatly increases the period of delay for stimulation of the cortex, and at the same time renders the resulting contractions more prolonged than normal, while the results of direct stimulation of the white fibres are much less, if at all, affected. (*c*) Mechanical stimulation of the motor areas also causes appropriate movements. (*d*) Stimulation of the grey matter, when separated from the subjacent white matter by the knife but left in position, is without effect unless the strength of stimulus be increased, although twigs of the current ought, of course, to pass into the corona radiata as easily as before.

Evidence that the phenomena are not due to accidental excitation of the corona radiata is *a fortiori* evidence that they are not caused by escape of current to the basal ganglia, for the distance of the basal ganglia from the larger part of the motor cortex is much greater than the thickness of the grey matter; and, indeed, that portion of the grey matter at the bottom of the Sylvian fissure which lies nearest to the basal ganglia does not respond to stimulation by motor effects.

When we have deducted from the cortex of the hemisphere the whole Rolandic region and the sensory centres, there still remains a large territory unaccounted for. Considerable portions of the occipital, parietal and temporal lobes, nearly the whole of the island of Reil and the greater part of the frontal lobe anterior to the ascending frontal convolution are 'silent areas,' and respond to stimulation by neither motor nor sensory sign. By a process of exclusion it has been supposed that they are the seat of intellectual operations. This function has been more particularly assigned to the frontal lobes, but we have little real knowledge to guide us to a decision. Extensive destruction and loss of substance of the pre-frontal region may occur without any marked symptoms, except some restriction of mental power or loss of moral restraint. Thus in the famous 'American crowbar case,' an iron bar completely transfixed the left frontal lobe of a man engaged in blasting. Although stunned for the moment, he was able in an hour to climb a

long flight of stairs, and to answer the inquiries of the surgeon. Finally, he recovered, and lived for nearly thirteen years without either sensory or motor deficiency, except that he suffered occasionally from epileptic convulsions. But his intellect was impaired; he became fitful and vacillating, profane in his language and inefficient in his work, although previously decent in conversation and a diligent and capable workman.

Localization of Function in the Central Nervous System.—Let us now consider a little more closely the real meaning of this localization of function. Scattered all over the grey matter of the primitive neural axis, and, as we have seen, over the grey mantle of the brain as well, are numerous 'centres' which seem to be related in a special way to special mechanisms, sensory, secretory or motor. The question may fitly be asked whether those centres are really distinct from each other in quality of structure or action, or whether they owe their peculiar properties solely to differences in situation and anatomical connection. It is clear at the outset that the nature of the work in which a centre is engaged must be largely determined by its connections. The kind of activity which goes on in the vaso-motor centre in the bulb, for example, may in no essential respect differ from that which goes on in the respiratory centre. The calibre of the bloodvessels will alter in response to a change of activity in the one because it is anatomically connected with the muscular coat of the bloodvessels. The rate or depth of the respiratory movements will alter in response to a change of activity in the other because it is connected with muscles which can act upon the chest-walls.

Some recent experiments afford a very interesting illustration of the determining influence of their peripheral connections on the function of nerve-fibres. Langley divided (in cats) the vagus nerve and the cervical sympathetic. The peripheral end of the former degenerated, of course, below the section, and the peripheral (cephalic) end of the latter degenerated above the section, up to the terminations of its axons in the superior cervical ganglion. The central end of the cut vagus was subsequently sutured to the peripheral end of the cut sympathetic. After a time the vagus-fibres grew along the course of the degenerated sympathetic up to the ganglion, where some of them formed arborizations around the ganglion cells. It was now found that stimulation of the vagus produced the effects usually caused by stimulation of the cervical sympathetic; for example, dilatation of the pupil and constriction of the bloodvessels of the head and neck. From these experiments it follows that the functions of the various groups of fibres in the cervical sympathetic do not depend on anything peculiar to the fibres; any fibre which can make connection with one of the ganglion-cells that send axons to the dilator muscle of the iris will, when stimulated, act as a pupillo-dilator fibre, just as well as a cervical sympathetic fibre.

The results of Budgett and Green carry us a step farther and indicate that the function of an efferent, may even be taken on by an afferent nerve. They divided the vagus centrally to the trunk-ganglion, and sutured the peripheral cut end to the peripheral end of the divided hypoglossal. After two or three months, stimulation of the peripheral end of the vagus caused contractions of the muscles of the tongue, apparently due to the excitation of the muscular fibres by impulses reaching them along the formerly afferent vagus fibres.

The localization of function in the cerebral cortex has been likened to the localization of industries in the multiplex commercial life of the modern world. The barbarian household in which cloth is woven and worked into garments, sandals or moccasins cobbled together, rough pottery baked in the kitchen fire, and all the rude furniture of the lodge fashioned by the hands which built it, and which rest beneath its roof at night—this state of things where centralization has not yet begun, it has been said, is a picture of what goes on in the undeveloped brains of the frog, the pigeon, and the rabbit. The 'diffusion' of industries which is characteristic of a primitive state has given place among the most highly civilized men to extreme centralization and concentration. Manchester spins cotton and Liverpool ships it. Chicago handles wheat and pork that have been produced on the prairies of Minnesota and Illinois. Amsterdam cuts diamonds. Munich brews beer. Lyons weaves silk. New York and London are centres of finance. This, it is said, is the picture of the highly specialized brain of a monkey or a man. But ingenious and alluring though such analogies are, they do not rest upon a sufficient basis of fact.

It has never been shown—nor is it likely that the proof will soon be forthcoming—that there is any difference whatever in the physical, chemical or psychical processes which go on in the various centres of the Rolandic cortex. It may be supposed, indeed, that the so-called sensory areas of the cortex differ more widely in their internal activity from the motor areas than the latter do among themselves, and that the activity of the anterior portion of the brain, the portion which has been credited *par excellence* with psychical functions, differs in kind, not merely in degree, from that of all the rest. But, as we have just seen, even the motor areas have sensory functions. A cast-iron physiology may explain this by the assumption of 'sensory' as well as 'motor' cells in the Rolandic area, and may find support for such an assumption in the well known fact that the large pyramidal cells whose axons form the pyramidal tract make up but a small proportion of the total number of pyramidal cells in this region, which, besides, contains numerous cells of Golgi's second type (p. 665). Yet there is absolutely nothing to contradict the supposition that the discharge of energy from the most circumscribed motor area or element may be accompanied not only with consciousness, but with a high degree of psychical activity. And, indeed, some writers have supposed that such a consciousness of, or even conscious measurement of, the discharge from the motor areas is the basis of the muscular sense (Bain, Wundt).

So far, at least, as the Rolandic region and the grey matter immediately around the neural canal are concerned, the analogy of an electrical switch-board connected with machines of various kinds might be more correct. Touch one key or another, and an engine is set in motion to grind corn, or to saw wood, or to light a town. The difference in result lies not in any difference of material or workmanship in the switches, but solely in the difference in their connections.

Grey matter in the upper part of the Rolandic cortex is excited, and the muscles of the leg contract. Grey matter around the lower part of the fissure is excited, and there are movements of the face and mouth. Grey matter in the medulla oblongata is excited, and the salivary glands pour forth a thin, watery fluid, poor in proteids, and containing an amylolytic ferment. Another portion of grey (?) matter in the medulla is thrown into activity, and the pancreatic ducts become flushed with a thick secretion, rich in proteids and in ferments which act on proteids, starch, and fat. Here, too, there is a variety in result according as one or another nervous switch is closed; here, too, the variety is due, not to essential differences in the structure or the activity of the nervous centres, but to their connection, by nervous paths, with peripheral organs of different kinds. There is, indeed, a specialization, a localization, of function, but the localization is at the periphery, the specialization is in the peripheral organs.

It may be asked whether, if this is the case for the peripheral organs of efferent nerves, the converse does not hold true for the afferent nerves—in other words, whether the localization here is not at the centre. And that there is in some degree a central localization of sensation may be considered proved by the well-known clinical fact, already referred to, that sensations of various kinds may be produced by pathological changes in the cortex. For example, a tumour involving the upper part of the temporal lobe may give rise to epileptiform convulsions preceded by an auditory aura, a sound, it may be, resembling the ringing of bells; a tumour involving the occipital region may cause a visual aura, and so on. Central sensory localization is the fundamental idea of the old doctrine of the *specific energy* of nerves, which, in modern phraseology, expresses the fact that excitation of the central end of a sensory nerve by various kinds of stimuli causes always, or at least very often, the particular kind of sensation appropriate to the nerve. The observation so frequently made in surgery before the days of anæsthetics, that when the optic nerve was cut in removing the eyeball the patient experienced the sensation of a flash of light, was long looked upon as the strongest prop of the law of specific energy, and well illustrates the meaning of the term. Here a mechanical excitation of the optic fibres in their course gives rise to the same sensation as excitation of the retina by the natural or *homologous* stimulus of light. Since a similar mechanical stimulus applied to the auditory nerve gives rise to a sensation of sound, and, applied to the trigeminal nerve, to a sensation of pain, many physiologists have assumed that the impulses

set up in the auditory nerve when sound impinges on the tympanic membrane do not differ essentially from those set up in the optic nerve when a ray of light falls upon the retina, or from those set up in the fifth nerve by the irritation of a carious tooth, or from those set up in certain fibres of all cutaneous nerves when a warm body comes in contact with the skin. Since the results in consciousness are very different, this assumption has necessitated the further conclusion that somewhere or other in the central nervous system there exist organs that are differently affected by the same kinds of afferent impulses—in other words, that sensory localization is at the centre. On this view, the visual areas in the cortex respond to all kinds of stimuli by visual sensations; the auditory areas by sensations of sound, and so on.

But while it cannot be doubted that special sensory regions exist in the grey matter of the brain, there is no reason to suppose that the nerve-impulses which travel up to them are absolutely similar until they have reached the centres, and there suddenly become, or produce, sensations absolutely different. There is, indeed, evidence of a certain amount of sensory specialization at the periphery. For example, when an ordinary nerve-trunk is touched, the resultant sensation is not one of touch. If there is any sensation at all, it is one of pain. Heating or cooling a naked nerve-trunk gives rise to no sensations of temperature. When the ulnar nerve is artificially cooled at the elbow, the first effect is severe pain in the parts of the hand supplied by the nerve. The pain disappears somewhat abruptly as cooling goes on, and is succeeded by gradual loss of all sensation in the ulnar area of the hand; but the cooling of the nerve-trunk does not give rise to any sensation of cold (Weir Mitchell). Stimulation of the end organs is essential in order that sensations of touch and temperature should be experienced. Such facts indicate that the afferent impulses are to some extent differentiated before they reach their centres. One reason, then, why excitation of the temporal cortex by impulses falling into it along the auditory nerve-fibres causes a sensation different from that caused by impulses reaching the occipital cortex through the fibres of the optic nerve may be a difference in the nature of the impulses. If this were the only reason, it would follow that were it possible to physiologically connect the fibres of the optic radiation with the temporal cortex, and those of the temporal radiation with the occipital cortex, sights and sounds would still be perceived and discriminated in a normal manner, although now the integrity of the occipital lobe would be bound up with the perception of sound, the integrity of the temporal lobe with visual sensation. This state of affairs would correspond to complete specialization for sensation in the peripheral organs, complete absence of specialization in the centres. On the other hand, it is conceivable that, after such an ideal experiment, sound-waves falling on the auditory apparatus might cause visual sensations, and luminous impressions falling on the retina sensations of sound. This would correspond to complete specialization of sensation in the centres, complete absence of specialization at the periphery. A third possibility would be that

the 'transposed' centres, responding at first feebly or not at all to the new impulses, might, by slow degrees, become more and more excitable to them. This would correspond to a peripheral specialization, combined with a tendency to development of central specialization. And, indeed, it is not easy to conceive in what way, except as the result of differences in the nature of impulses coming from the periphery, specialization of sensory areas in the central nervous system could have at first arisen.

Degree of Localization in Different Animals.—Before leaving this subject, two points ought to be made clear: (1) The degree of localization of function on the cortex goes hand in hand with the general development of the brain. In man and the monkey, the motor localization is more elaborate than in the dog, that is to say, a greater number of movements can be associated with definite cortical areas. In the rabbit, whose motor centres have been particularly studied in recent years by Mann and Mills, localization is still less advanced than in the dog. Towards the bottom of the mammalian group certain motor areas can still be demonstrated, though they are rather ill-defined, for instance, in the hedgehog (Mann), opossum (Cunningham), and ornithorhynchus (Martin). In general the movements of the anterior limb are easier to obtain than those of the posterior. In birds Mills found no evidence of the existence of any motor centres.

(2) Areas of the same name (homologous areas) in different groups of animals do not necessarily have the same function; that is, in the case of the motor areas, are not necessarily associated with the same movements. Taking the position of the centre for the orbicularis oculi as a test, Ziehen has lately come to the conclusion that in the anthropomorphous apes and in man, this centre has been pushed forward by the encroachment of the centres behind it, and especially of the visual centre, the arm centre, and the speech centre, which have undergone a great functional development.

Reaction Time.—Just as in a reflex act a certain measureable time (*reflex time*) is taken up by the changes that occur in the lower nervous centres, so we may assume that in all psychical processes the element of time is involved. And, indeed, when the interval that elapses between the application of a stimulus and the signal which announces that it has been felt (*reaction time*) is measured, it is found that the cerebral processes associated with the perception of the simplest sensation and the production of the simplest voluntary contraction is longer than the time which the spinal centres require for the elaboration of even complex and co-ordinated reflex movements. Suppose, *e.g.*, that the stimulus is an induction shock applied to a given point of the skin, and that the signal is the closing of

the circuit of an electro-magnet, then, if both events are automatically recorded on a revolving drum, the interval can be readily determined. It is evident that this includes, not only the time actually consumed in the central processes, but also the time required for the afferent impulse to reach the brain, and the efferent impulse the hand, along with the latent period of the muscles. The time taken up in these three events can be approximately calculated, and when it is subtracted, the remainder represents the reduced or corrected reaction time; that is, the interval actually spent in the centres themselves. This is by no means a constant. It is influenced not only by the degree of complexity of the psychical acts involved, and the mental attitude of the person (whether he expects the stimulus or is taken by surprise, whether he has to choose between several possible kinds of stimuli and respond to only one, etc.), but it varies also for different kinds of sensation, for the same sensation at different times, and as is recognised in the *personal equation* of astronomers, in different individuals. For sensations of touch and pain it may be taken as one-ninth to one-fifth, for hearing one-eighth to one-sixth, and for sight one-eighth to one-fifth of a second. So that the proverbial quickness of thought is by no means great, even in comparison with that of such a gross process as the contraction of a muscle (one-tenth of a second). Nor is it the case that the man 'of quick apprehension' has always a short reaction time, or the dullard always a long one, although in all kinds of persons practice will reduce it.

Sleep.—Certain gland-cells, certain muscular fibres, and the epithelial cells of ciliated membranes, never rest, and perhaps hardly ever even slacken their activity. But in most organs periods of action alternate at more or less frequent intervals with periods of relative repose. In all the higher animals the central nervous system enters once at least in the twenty-four hours into the condition of rest which we call sleep. What the cause of this regular periodicity is we do not know. It is accompanied by changes in the microscopical appearance of the nerve-cells. Thus Hodge found differences between the cells of certain portions of the cerebral cortex in birds, and of certain ganglia in the honey bee after a long day of work and after a night's rest; and Mann and other observers in the cells of the cerebral cortex and the anterior horn in dogs fatigued by muscular exercise as compared with rested dogs (Fig. 272). The most

constant changes in fatigue are a diminution in size and irregularity in outline of the nucleus (which also stains more deeply than before), a shrinking of the protoplasm, a diminution in the amount of the stainable substance of Nissl, with the breaking up of some of the Nissl bodies (p. 662) and the diffusion of their stainable material through the cell. The shrinking of the protoplasm is preceded by an increase in its volume, and this is the sole change in moderate activity. It is only when activity begins to pass into fatigue that other alterations occur. Histological alterations may also be caused in sympathetic ganglion cells by prolonged artificial stimulation of the nerves connected with the ganglia. Experiments on fatigue changes in the cells of the spinal ganglia after electrical excitation of the posterior root-fibres are less decisive, some observers having obtained positive, others negative results (p. 711).

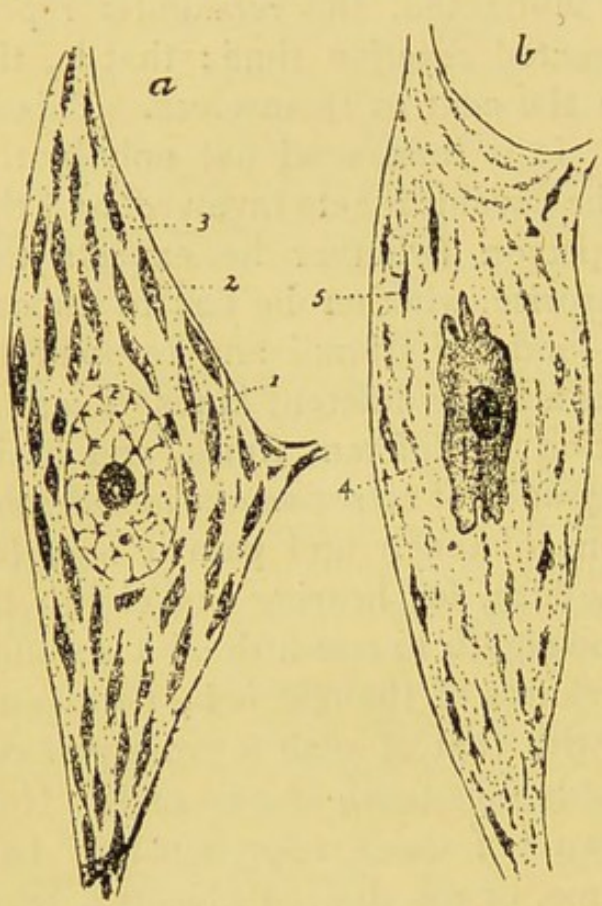

FIG. 272.—EFFECT OF FATIGUE ON NERVE-CELLS (BARKER, AFTER MANN).

Two motor cells from lumbar cord of dog fixed in sublimate and stained with toluidin blue; *a*, from rested dog: 1, pale nucleus, 2, dark Nissl spindles; 3, bundles of nerve fibrils. *b*, from the fatigued dog: 4, dark shrivelled nucleus; 5, pale spindles.

Theories of the Causation of Sleep.—(1) Some have suggested that sleep is induced by the using up of substances necessary for the functional activity of the neurons, *e.g.*, the stored-up or intramolecular oxygen, or by the action of the waste products of the tissues, and especially lactic acid, when they accumulate beyond a certain amount in the blood, or in the nervous elements themselves.

(2) Others have looked for an explanation to vascular changes in the brain, but so far are the possible causes of such changes from being understood, that it is even yet a question whether in sleep the brain is congested or anæmic. Certain writers have settled this question by the summary statement that when the brain rests the quantity of blood in it *must* be supposed to be diminished, as in other resting organs. But this is a fallacious argument. For when the whole body rests, as it does in sleep, it has as much blood in it as when it works; in sleep, therefore, if some resting organs have less blood than in waking life, other resting organs must have more; and it is the province of experiment to decide which are congested

and which anæmic. In coma, a pathological condition which in some respects has analogies to profound and long-continued sleep, the brain is congested, and the proper elements of the nervous tissue presumably compressed. And artificial pressure (applied by means of a distensible bag introduced through a trephine hole into the cranial cavity) may cause not only unconsciousness, but absolute anæsthesia. But it is possible that this artificial increase of intracranial pressure may produce its effects by rendering the brain anæmic, and it has been actually observed that the retinal vessels, as seen with the ophthalmoscope and the vessels of the pia mater exposed to direct observation in man by disease of the bones of the skull, or in animals by operation, shrink during sleep. In sleeping children the fontanelle sinks in, an indication that the intracranial pressure is reduced. Observations with the plethysmograph have shown that the arm swells in sleep, and shrinks when the sleeper awakes, or even when he is subjected to sensory stimuli not sufficient to arouse him, *e.g.*, a tune played by a musical-box (Howell). The tone of the vasomotor centre is therefore diminished, and the arterial pressure falls during sleep. But a fall of general arterial pressure is usually accompanied by a diminution of the quantity of blood passing through the brain. So that the balance of evidence is decidedly in favour of the view that *sleep is associated with cerebral anæmia.*

As to the nature of the relation between the two conditions, it has been suggested that the anæmia is produced by fatigue of the vasomotor centre, which causes it to relax its grip upon the peripheral bloodvessels, and that the condition of the cortical nerve-cells which we call sleep is directly produced by the lack of blood. But there does not appear to be any good reason for believing that the vasomotor centre is more susceptible of fatigue than the higher cerebral centres. On the contrary, it is probable that the bulbar centres are less delicately organized and more resistant than the higher centres. In any case, if the cerebral nerve-cells 'go to sleep' because their blood-supply is diminished, ought we not to look for a similar cause for diminished activity of the vasomotor centre? Or if the answer is made that the activity of the vaso-motor cells is directly lessened by fatigue, or by the cessation of external stimuli, why should not this be the case also for the cortical cells? Hill has indeed shown by means of the sphygmometer (p. 104) that the fall of arterial pressure is not essentially connected with sleep, but is produced by the bodily rest and warmth which accompany it. Further, even a great diminution in the supply of blood going to the brain is not necessarily followed by sleep. For example, both carotid and both vertebral arteries may frequently be tied in dogs at the same time without producing any symptoms, the anastomosis of the superior intercostal arteries with the anterior spinal artery providing a sufficient channel for the blood absolutely required by the brain. The same is true of monkeys after ligation of one carotid and one vertebral. We must, therefore, conclude that *although sleep is normally associated with anæmia of the brain,*

it is not directly caused by it. The cortical centres go to sleep because they are 'tired,' or because the stimuli which usually excite them have ceased, and not because their blood-supply is diminished.

(3) The idea that the dendrites are contractile, and by pulling themselves in, and thus breaking certain nervous chains, cause sleep, still remains a mere theory, unsupported by any real evidence. The same is true of the notion that the fibrils of the neuroglia insinuate themselves into the 'joints,' by which one neuron comes into contact with another, and acting as insulating material, block the nerve-impulses.

In general, the depth of sleep, as measured by the intensity of sound needed to awaken the sleeper, increases rapidly in the first hour, falls abruptly in the second, and then slowly creeps down to its minimum, which it reaches just before the person awakens. As to the amount of sleep required, no precise rules can be laid down. It varies with age, occupation, and perhaps climate. An infant, whose main business is to grow, spends, or ought to spend, if mothers were wise and feeding-bottles clean, the greater part of its time in sleep. The man, whose main business it is to work with his hands or brain, requires his full tale of eight hours' sleep, but not usually more. The dry and exhilarating air of some of the inland portions of North America, and perhaps the plains of Victoria and New South Wales, incites, and possibly enables a new-comer to live for a considerable period with less than his ordinary amount of sleep. Idiosyncrasy, and perhaps to a still greater extent habit, have also a marked influence. The great Napoleon, in his heyday, never slept more than four or five hours in the twenty-four. Five or six hours or less was the usual allowance of Frederick of Prussia throughout the greater part of his long and active life.

Hypnosis is a condition in some respects allied to natural slumber; but instead of the activity of the whole brain—or perhaps we should rather say, the whole activity of the brain—being in abeyance, the susceptibility to external impressions remains as great as in waking life, or may be even increased, while the critical faculty, which normally sits in judgment on them, is lulled to sleep. The condition can be induced in many ways—by asking the subject to look fixedly at a bright object, by closing his eyes, by occupying his attention, by a sudden loud sound or a flash of light, etc. The essential condition is that the person should have the idea of going to sleep, and that he should surrender his will to the operator. In the hypnotic condition the subject is extremely open to suggestions made by the operator with whom he is *en rapport.* He adopts and acts upon them without criticism. If, for example, the hypnotizer raises the subject's arm above his head, and suggests that he cannot bring it down again, it stays fixed in that position for a long time without any appearance of fatigue; or the whole body may be thrown, on a mere hint, into some unnatural pose in which it remains rigid as a statue. Suggested hemiplegia or hemianæsthesia, or paralysis of motion and sensation together or apart in limited areas, can also be realized; and surgical operations have been actually performed on hypnotized persons without any appearance of suffering. If, on the other

hand, the operator suggests that the subject is undergoing intense pain, he will instantly take his cue, writhing his body, pressing his hands upon his head or breast, and in all respects behaving as if the suggestion were in accord with the facts. If he is told that he is blind or deaf, he will act as if this were the case. If it is suggested that a person actually present is in Timbuctoo, the subject will entirely ignore him, will leave him out if told to count the persons in the room, or try to walk through him if asked to move in that direction. What is even more curious is that the organic functions of the body are also liable to be influenced by suggestion. A postage-stamp was placed on the skin of a hypnotized person, and it was suggested that it would raise a blister. Next day a blister was actually found beneath it. The letter K, embroidered on a piece of cloth, was suggested to be red-hot. The left shoulder was then 'branded' with it, and on the right shoulder appeared a facsimile of the K as if burnt with a hot iron. The secretions can be increased or diminished, subcutaneous hæmorrhages, veritable stigmata,* can be caused, and many of the 'miracles' of Lourdes and other shrines, ancient and modern, repeated or surpassed by the aid of hypnotic suggestion. Hypnotism has also been practically employed in the treatment of various diseases, and particularly in functional derangements of the nervous system. But care and judgment are necessary on the part of the operator, and although as a rule there is no difficulty in putting an end to the condition by a suitable suggestion, it is said that in rare instances grave mischances have occurred. There seems to be no ground for the opinion that women are more easily hypnotized than men. Out of more than a thousand persons, Liébault found only seventeen absolutely refractory.

Relation of Size of Brain to Intelligence.—While it is the case that some men of great ability have had remarkably heavy and richly convoluted brains, it would seem that in general neither great size nor any other obvious anatomical peculiarity of the cerebrum is constantly associated with exceptional intellectual power. In the animal kingdom as a whole, there is undoubtedly some relation between the status of a group and the average brain development within the group. But that this is a relation which is complicated by other circumstances than the mere degree of intelligence is sufficiently shown by the fact that a mouse has more brain, in proportion to its size, than a man, and thirteen times more than a horse; while both in the rabbit and sheep the ratio of brain-weight to body-weight is nearly twice as great as in the horse, in the dog only half as great as in the cat, and not very much more than in the donkey. The following tables, too, which illustrate the weight of the brain in

* *I.e.*, bleeding spots on the skin generally corresponding to the wounds of Christ. In the well-known case of Louise Latour, which excited great interest in France in 1868, blisters first appeared; they burst and then there was bleeding from the true skin. The probable explanation is that she concentrated her attention on these parts of her body and so influenced them, perhaps by causing congestion through the vaso-motor centre.

man at different ages, show that, although we might give 'the infant phenomenon' an anatomical basis, we should greatly overrate the intellectual acuteness of the average baby if we were to measure it by the ratio of brain to body-weight alone.

Age.	Brain-weight.
1 year.	885 grm.
2 years.	909 ,,
3 ,,	1071 ,,
4 ,,	1099 ,,
5 ,,	1033 ,,
6 ,,	1147 ,,
7 ,,	1201 ,,
8 years.	1045 grm.
10 ,,	1315 ,,
11 ,,	1168 ,,
12 ,,	1286 ,,
13 ,,	1505 ,,
14 ,,	1336 ,,
15 ,,	1414 ,,

(Bischoff.)

Age.	Men.	Women.
10—19	1411 grm.	1219 grm.
20—29	1419 ,,	1260 ,,
30—39	1424 ,,	1272 ,,
40—49	1406 ,,	1272 ,,
50—59	1389 grm.	1239 grm.
60—69	1292 ,,	1219 ,,
70—79	1254 ,,	1129 ,,
80—90	1303 ,,	898 ,,

(Huschke.)

In some small birds the ratio is as high as 1 : 12, in large birds as low as 1 : 1,200 ; in certain fishes a gramme of brain has to serve for over 5 kilos of body. As a rule, especially within a given species, the brain is proportionally of greater size in small than in large animals. It is to be supposed that quality as well as quantity of brain substance is a potent factor in determining the degree of mental capacity. Such investigations as those of Berkley, who states that he has made out in a case of dementia in a man addicted to alcohol and opium, changes in the dendrites of pyramidal cells in the cerebral cortex (diminution in their diameter, and in the number of gemmules and branches), are of interest in this connection.

The Cerebral Circulation.—The arrangement of the cerebral bloodvessels has certain peculiarities which it is of great importance to remember in connection with the study of the diseases of the brain, many of which are caused by lesions in the vascular system—hæmorrhage or embolism. Four great arterial trunks carry blood to the brain, two internal carotids and two vertebrals (Plate V., 4). The vertebrals unite at the base of the skull to form the single mesial basilar artery, which, running forward in a groove in the occipital bone, splits into the two posterior cerebral arteries. Each carotid, passing in through the carotid foramen, divides into a middle and an anterior cerebral artery ; the latter runs forward in the great longitudinal fissure, the former lies in the fissure of Sylvius. A communicating branch joins the middle and posterior cerebrals on each side, and a short loop connects the two anterior cerebrals in front. In this way a hexagon is formed at the base of the brain, the so-called circle of Willis. While the anastomosis between the large arteries is thus very free, the opposite is true of their branches. All the arteries in the substance of the brain and cord are 'end-arteries'; that is to say, each terminates within its

area of distribution without sending any communicating branches to make junction with its neighbours. The consequence of these two anatomical facts is: (1) that interference with the blood-supply of the brain between the heart and the circle of Willis does not readily produce symptoms of cerebral anæmia; (2) that the blocking of any of the arteries which arise from the circle or any of their branches leads to destruction of the area supplied by it. The basal ganglia are fed by twigs from the circle of Willis and the beginning of the posterior, middle, and anterior cerebral arteries. Of these the most important are the lenticulo-striate and lenticulo-optic branches of the middle cerebral, which are given off near its origin, and run through the lenticular nucleus into the internal capsule, and thence to the caudate nucleus and optic thalamus respectively. The chief part of the blood from the circle of Willis is carried by the three great cerebral arteries over the cortex of the brain. The white matter, with the exception of that in the immediate neighbourhood of the basal ganglia, is nourished by straight arteries which penetrate the cortex. The middle cerebral supplies the whole of the parietal as well as that portion of the frontal lobe which lies immediately in front of the fissure of Rolando and the upper part of the temporal lobe. The rest of the frontal lobe is supplied by the anterior cerebral, and the occipital lobe, with the lower part of the temporal lobe, by the posterior cerebral. The medulla oblongata, cerebellum, and pons are fed from the vertebrals and the basilar artery before the circle of Willis has been formed.

Cerebro-spinal Fluid.—The cerebro-spinal fluid, which fills the ventricles of the brain and the central canal of the cord, is continuous with that contained in the subarachnoid space through the foramen of Magendie, an opening in the piece of pia mater that helps to roof in the fourth ventricle. It is secreted in part by the cubical cells covering the choroid plexus, a fold of pia mater which projects into each lateral ventricle. It is a thin watery fluid, faintly alkaline in reaction to litmus, and with a specific gravity of about 1010. It contains the ordinary salts, a very small amount of proteids (usually about ·1 per cent.), and a little glucose (Nawratzki). Its composition is evidently very different from that of ordinary lymph.

PRACTICAL EXERCISES ON CHAPTER XII.

1. **Section and Stimulation of the Spinal Nerve-roots in the Frog.**—Select a large frog (a bull-frog, if possible). Pith the brain. Fasten the frog, belly down, on a plate of cork. Make an incision in the middle line over the spinous processes of the lowest three or four vertebræ, separate the muscles from the vertebral arches, and with strong scissors open the spinal canal, taking care not to injure the cord by passing the blade of the scissors too deeply. Extend the opening upwards till two or three posterior roots come into view. Pass fine silk ligatures under two of them, tie, and divide one root central to the ligature, the other peripheral to it. Stimulate the central

end, and reflex movements will occur. Stimulate the peripheral end: no effect is produced. Now cut away the exposed posterior roots and isolate and ligature two of the anterior roots, which are smaller than the posterior. Stimulate the central end of one: there is no effect. Stimulation of the peripheral end of the other causes contractions of the corresponding muscles.

2. **Reflex Action: Inhibition of the Reflexes.**—Pith a frog (brain only). Pass a hook through the jaws. Holding the frog by the hook, dip one leg into a dilute solution of sulphuric acid (·2 to ·5 per cent.), and note with the stop-watch the interval which elapses before the frog draws up its leg (Türck's method of determining the reflex time). Wash the acid off with water. Now touch the skin of one thigh with blotting-paper soaked in strong acetic acid. The leg is drawn up, and the foot moved as if to get rid of the irritant. If the leg is held, the other is brought into action. Immerse the frog in water to wash away the acid. Again dip one leg into the dilute sulphuric acid, and estimate the reflex time. Then apply a crystal of common salt to the upper part of the spinal cord. If the opening made for pithing the frog is not large enough to enable the cord to be clearly seen, enlarge it. Again dip the leg in the dilute acid. It will either not be drawn up at all, or the interval will be distinctly longer than before.

3. **Action of Strychnia.**—Pith a frog (brain only). Inject into one of the lymph-sacs three or four drops of a 0·1 per cent. solution of strychnia. In a few minutes general spasms come on, which have intermissions, but are excited by the slightest stimulus. The extensor muscles of the trunk and limbs overcome the flexors. Destroy the spinal cord; the spasms at once cease, and cannot again be excited.

4. **Excision of Cerebral Hemispheres in the Frog** (Fig. 273).—Anæsthetize a frog lightly by putting it under a bell-jar or tumbler with a small piece of cotton-wool soaked in ether. Then, holding it in a cloth, make an incision through the skin over the skull in the mesial line. With scissors open the cranium about the position of a line drawn at a tangent to the posterior borders of the two tympanic membranes. Remove the roof of the skull in front of this line with forceps, scoop out the cerebral hemispheres, and sew up the wound. As soon as the animal has recovered from the ether, the phenomena described at p. 739 should be verified. The frog will still swim when thrown into water, will refuse to lie on its back, and will not fall if the board on which it lies be gradually slanted. Let the frog live for a day, keeping it in a moist atmosphere; then expose the brain again, determine the reflex time by Türck's method; apply a crystal of common salt to the optic lobes, and repeat the observation. The reflex movements will be completely inhibited or delayed. Remove the salt, wash with normal saline, excise the optic lobes, and see whether the frog will now swim.

5. **Excision of the Cerebral Hemispheres in a Pigeon.**—Feed a pigeon for two or three days on dry food, etherize it by holding a piece of cotton-wool sprinkled with ether over its beak, or inject into the rectum ¼ gramme chloral hydrate. The pigeon being wrapped up in a cloth, and the head held steady by an assistant, the feathers

are clipped off the head, an incision made in the middle line through the skin, and the flaps reflected so as to expose the skull. Cut through the bones with scissors, and make a sufficiently large opening to bring the cerebral hemispheres into view. They are now rapidly divided from the corpora bigemina and lifted out with the handle of a scalpel. The bleeding is very free, but may be partially controlled by stuffing the cavity with the vegetable fibre known as Pengavar Djambi, which should be removed in a few minutes, the wound cleansed with iodoform gauze wrung out of normal salt solution at 50° C., and sewed up. Study the phenomena described on p. 740.

6. **Stimulation of the Motor Areas in the Dog.**—(*a*) Study a hardened brain of a dog, noting especially the crucial sulcus (Fig. 742), the convolutions in relation to it, and the areas mapped out around it by Hitzig and Fritsch and others. (*b*) Inject morphia under the skin of a dog. Set up an induction-coil arranged for tetanus, with a single Daniell in the primary circuit. Connect a pair of fine but not sharp-pointed electrodes through a short-circuiting key with the secondary. Fasten the dog on the holder, belly down, and put a large pad under the neck to support the head. Clip the hair over the scalp. Feel for the condyles of the lower jaw, and join them by a string across the top of the head. Connect the outer canthi of the eyes by another thread. The crucial sulcus lies a little behind the mid-point between these two lines. Now give the dog ether if necessary, make a mesial incision through the skin down to the bone, and reflect the flaps on either side. Detach as much of the temporal muscle from the bone as is necessary to get room for two trephine holes, the internal borders of which must be not less than ¼ inch from the middle line, so as to avoid wounding the longitudinal sinus. Carefully work the trephine through the skull, taking care not to press heavily on it at the last. Raise up the two pieces of bone with forceps, connect the holes with bone forceps, and enlarge the opening as much as may be necessary to reach all the motor areas. At this stage only enough ether should be given to prevent suffering. Now unbind the hind and fore limbs on the side opposite to that on which the brain has been exposed, apply blunt electrodes successively to the areas for the fore and hind limbs, and stimulate.* Contraction of the corres-

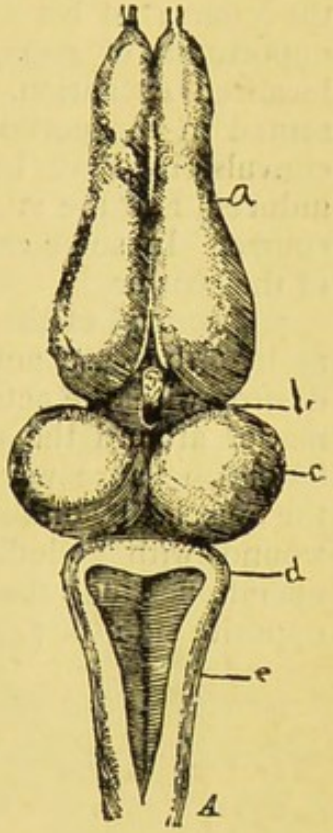

FIG. 273.—BRAIN OF FROG. (AFTER STEINER.)

a, cerebral hemispheres; *b*, position of optic thalami; *c*, optic lobes; *d*, cerebellum; *e*, medulla oblongata; *A*, upper end of spinal cord.

* It is not necessary to remove the dura mater.

ponding groups of muscles will be seen if the narcosis is not too deep. Movements of the head, neck, and eyelids may also be called forth by stimulating the motor areas for these regions. Stimulation in front of the crucial sulcus may also cause great dilatation of the pupil, the iris almost disappearing. The dilatation takes place most promptly, and is greatest on the opposite side, but the pupil on the same side is also widened. Even after section of both vago-sympathetic nerves in the neck, a slow and slight dilatation, greatest perhaps on the same side, may be caused by cortical stimulation. Repeat the whole experiment on the opposite side of the brain. In the course of his observations the student will perhaps have the opportunity of seeing general epileptiform convulsions set up by a localized excitation. They begin in the group of muscles represented in the portion of the cortex directly stimulated. After the convulsions have been sufficiently studied, they should be again induced, and the stimulated motor area rapidly excised during their course. In some cases this will be followed by immediate cessation of the spasms.

7. **Removal of the Motor Areas on One Side in the Dog.**—Proceed as in 6, but use antiseptic precautions, and instead of stimulating, destroy with the actual cautery or remove with the knife all the grey matter around the crucial sulcus on one side. Stop bleeding by iodoform gauze wrung out of hot normal saline solution. Sew up the muscles by one set of sutures, the skin by another, and cover the wound with collodion. When the dog has recovered from the operation, study the deficiency of motor and sensory power on the opposite side (p. 747). (Fig. 265, p. 743.)

CHAPTER XIII.

THE SENSES.

HITHERTO we have been considering from a purely objective standpoint the organs that compose the body, and their work. The student has been assumed to be in the little world—'the microcosm'—of organization which he has been studying, but not of it. He has listened to the sounds of the heart, seen its contraction, felt it hardening under his fingers; but we have not inquired as to the meaning or the mechanism of this hearing, seeing, and feeling. We have now to recognise that all our knowledge of external things comes to us by the channels of the senses, and, like the light that falls through coloured windows on the floor of a church, is tinged, and perhaps distorted, in the act of reaching us.

The Senses in General.—The old and orthodox enumeration of 'the five senses' of sight, hearing, touch, taste and smell must be augmented by at least two more, the senses of pressure and temperature. The power of appreciating the amount of a muscular effort; the power of localizing the various portions of the body in space; the sensations of pain, tickling, itching, hunger, and thirst; the sensations accompanying the generative act, etc., have also been looked upon by some as separate senses subserved by special nerves and connected with definite centres. In the development of a simple sensation we may distinguish three stages: the stimulation of a peripheral end-organ, the propagation of the impulses thus set up along an afferent nerve, and their reception and elaboration in a central organ.

We do not know in what manner a series of transverse vibrations in the ether when it falls upon the eye, or a series of longitudinal vibrations in the air when it strikes the ear, excites a sensation of light or sound. We can trace the ray of light through the refractive

media of the eyeball, see it focussed on the retina, lead off the current of action set up in that membrane, which, doubtless, gives token of the passage of nervous impulses into and up the optic nerve. We can even follow the nervous impulses to a definite portion of the cortex of the occipital lobe, and determine that if this is removed no sensation of sight will result from any excitation of retina or optic nerve. And it is fair to conclude that in some manner this part of the cerebral cortex is essential to the production of visual sensations. But in what way the chemical or physical processes in the axis cylinders or nerve-cells are related to the psychical change, the interruption of the smooth and unregarded flow of consciousness which we call a sensation of light, we do not know. To our reasoning, and even to our imagination, there is a great gulf fixed between the physical stimulus and its psychical consequence; they seem incommensurable quantities; the transition from light to sensation of light is certain, but unthinkable.

Each kind of peripheral end-organ is peculiarly suited to respond to a certain kind of stimulus. The law of 'adequate' or 'homologous' stimuli is an expression of this fact. The 'adequate' stimuli of the organs of special sense may be divided into: (1) vibrations set up at a distance without the actual contact of the object, *e.g.*, light, sound, radiant heat; (2) changes produced by the contact of the object, *e.g.*, in the production of sensations of taste, touch, pressure, alteration of temperature (by conduction). Midway between (1) and (2) lies the adequate stimulus of the olfactory end-organs, which are excited by material particles given off from the odoriferous body and borne by the air into the upper part of the nostrils.

The end-organs of the special senses all agree in consisting essentially of modified epiblastic cells, but they occupy areas by no means proportioned to their importance and to the amount of information we acquire through them. The extent of surface which can be affected by light in a man is not more than 20 sq. cm.; the endings of both nerves of hearing taken together do not at most expand to more than 5 sq. cm.; the olfactory portion of the mucous membrane of the nose has an area of not more than 10 sq. cm.; the sensations of taste are ministered to by an area of less than 50 sq. cm.; the end-organs of the senses of pressure, touch, and temperature are distributed over a surface reckoned by square metres. As the physiological status of the sensory end-organs rises, their anatomical distribution tends to shrink. The organs of comparatively coarse and common sensations are widely spread, intermingled with each other, and seated in tissues whose primary function may not be sensory at all. Even the nerve-endings of the sense of taste are not confined to one definite and circumscribed

patch, but scattered over the tongue and palate; and both tongue and palate are at least as much concerned in mastication and deglutition as in taste. The olfactory portion of the nasal mucous membrane, although a continuous area with fairly distinct boundaries, is still a part of the general lining of the nostril. The epithelial surfaces which minister to the supreme sensations of sight and hearing—the retina and the sensitive structures of the cochlea—are the most sequestered of all the sensory areas, as the organs of which they form a part are, of all the organs of sense, the most highly specialized in function, and anatomically the most limited. But although hidden in protected hollows, they are endowed, either in virtue of their own movements or of those of the head, with the power of receiving impressions from every side, and their actual size is thus indefinitely multiplied.

VISION.

Physical Introduction.—Physically a ray of light is a series of disturbances or vibrations in the luminiferous ether, which radiates out from a luminous body in what is practically a straight line. The ether is supposed to fill all space, including the interstices between the molecules of matter and the atoms of which those molecules are composed. Suppose a bar of iron to be gradually heated in a dark room. In the cold iron the molecules are moving on the average at a relatively slow rate, and the waves set up in the ether by their vibrations are comparatively long. Now, the long ethereal vibrations do not excite the retina, because it is only fitted to respond to the impact of the shorter waves; and, indeed, the long waves are largely absorbed by the watery media of the eye. As the temperature of the iron bar is increased, the molecules begin to move more quickly, and waves of smaller and smaller length, of greater and greater frequency, are set up, until at last some of them are just able to stimulate the retina, and the iron begins to glow a dull red. As the heating goes on the molecules move more quickly still, and, in addition to waves which cause the sensation of red, shorter waves that give the sensation of yellow appear. Finally, when a high temperature has been reached, the very shortest vibrations which can affect the eye at all mingle with the medium and long waves, and the sensation is one of intense white light.

We have said that a ray of light travels in a straight line, and the direction of the straight line does not change so long as the medium is homogeneous. But when a ray reaches the boundary of the medium through which it is passing, a part of it is in general turned back or reflected. If the second medium is transparent (water or glass, *e.g.*), the greater part of the ray passes on through it, a smaller portion is reflected. If the second medium is opaque, the ray does not penetrate it for any great distance; if it is a piece of polished metal, *e.g.*, nearly the whole of the light is reflected; if it is a layer of lampblack, very little of the light is reflected, most of it is absorbed.

Reflection.—The first law of reflection is that *the reflected ray, the*

ray which falls upon the reflecting surface (*incident ray*), *and the normal to the surface, are in one plane.* The second law is that *the reflected ray makes, with the perpendicular* (*normal*) *to the reflecting surface, the same angle as the incident ray.* A corollary to this is that a ray perpendicular to the surface is reflected along its own path.

Reflection from a Plane Mirror.—Let a ray of light coming from the point P meet the surface DE at B, making an angle PBA with the normal to the surface. The reflected ray BC will make an equal angle ABC with the normal; and the eye at C will see the image of P as if it were placed at P′, the point where the prolongation of BC cuts the straight line drawn from P perpendicular to DE. This is the position of an ordinary looking-glass image.

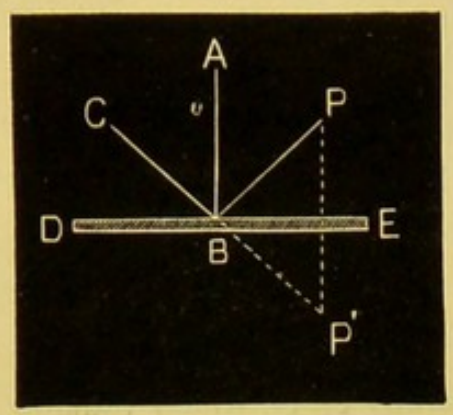

FIG. 274.—REFLECTION FROM A PLANE MIRROR.

Reflection from a Concave Spherical Mirror.—A spherical surface may be supposed to be made up of an infinite number of infinitely small plane surfaces. The normal to each of these plane surfaces is the radius of the sphere, and the reflected ray makes with the radius at the point of incidence the same angle as the incident ray. Let D (Fig. 275) be the middle point of the mirror, and C its centre of curvature, *i.e.*, the centre of the sphere of which it is a

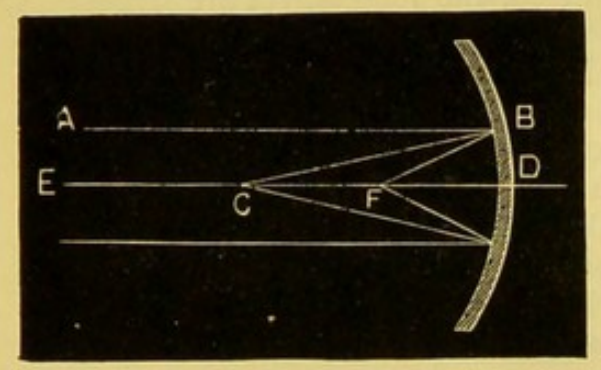

FIG. 275.—REFLECTION FROM A CONCAVE SPHERICAL MIRROR.

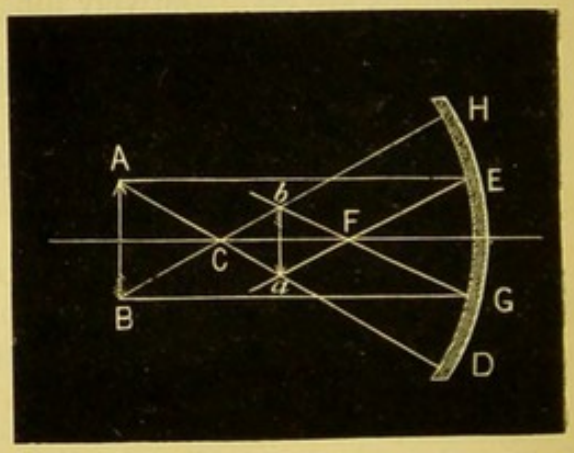

FIG. 276.—FORMATION OF REAL INVERTED IMAGE BY A CONCAVE SPHERICAL MIRROR.

segment. Then CD is the principal axis, and any other line through C which cuts the mirror is a secondary axis. When the mirror is a small portion of a sphere, rays parallel to the principal axis are focussed at the principal focus F midway between C and D; rays parallel to any secondary axis are focussed in a point lying on that axis; and rays diverging from a point on any axis are focussed in a point on the same axis.

These facts afford a simple construction for finding the position of the image of an object formed by a concave mirror. Let AB be the

object (Fig. 276). Then the image of A is the point in which all rays proceeding from A and falling on the mirror, including rays parallel to the principal axis, are focussed. But the ray AE, parallel to the principal axis, passes after reflection through the principal focus F, therefore the image of A must lie on the straight line EF. If any secondary axis ACD be drawn, the image of A must lie on ACD. It must therefore be the point of intersection, *a*, of EF and ACD. Similarly, the image of B must be the point of intersection, *b*, of GF and BCH. The image *ab* of an object AB farther from the mirror than the principal focus is real and inverted. The Purkinje-Sanson image reflected from the concave anterior surface of the vitreous humour (Fig. 292) is an example.

After *reflection from a convex mirror*, rays of light always diverge, and only erect, virtual images are formed, *i.e.*, images which do not really exist in space, but which, from the direction of the rays of light, we judge to exist. The position of the image of an object AB (Fig. 277) may be found by a construction similar to that for reflection from a concave mirror. The image of a flame reflected from the anterior surface of the cornea or lens is erect and virtual. It diminishes in size with increase in the curvature or convexity of the reflecting surface (Fig. 292).

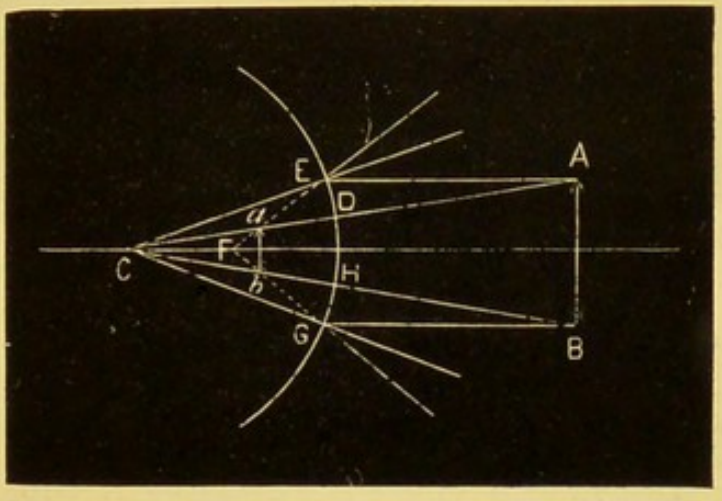

FIG. 277.—FORMATION OF IMAGE BY A CONVEX MIRROR.

Refraction.—A ray of light passing from one medium into another has its velocity, and consequently its direction, altered. It is said to be refracted. The first law of refraction is that *the refracted ray is in the same plane as the incident ray and the normal to the surface.* The second law is that the *sine of the angle of incidence has a constant ratio* (for any given pair of media) *to the sine of the angle of refraction.* The angle of incidence is the angle which the ray makes with the normal to the surface, separating the two media; the angle of refraction is the angle made with the normal in the second medium. This ratio is called the index of refraction between the two media. For purposes of comparison, the refractive index of a substance is usually taken as the ratio of the sine of the angle of incidence to the sine of the angle of refraction of a ray passing from *air* into the substance.

When a ray strikes a surface at right angles, it passes through without suffering refraction. When a ray passes from a less dense to a denser medium (*e.g.*, from air to water), it is bent towards the perpendicular. When it passes from a more dense to a less dense medium (as from water to air), it is bent away from the perpendicular.

When a ray passes across a medium bounded by parallel planes, it issues parallel to itself; in other words, it undergoes no refraction (Fig. 279).

Refraction and Dispersion by a Prism.—The beam of light is bent towards the normal N as it passes across BA and away from the

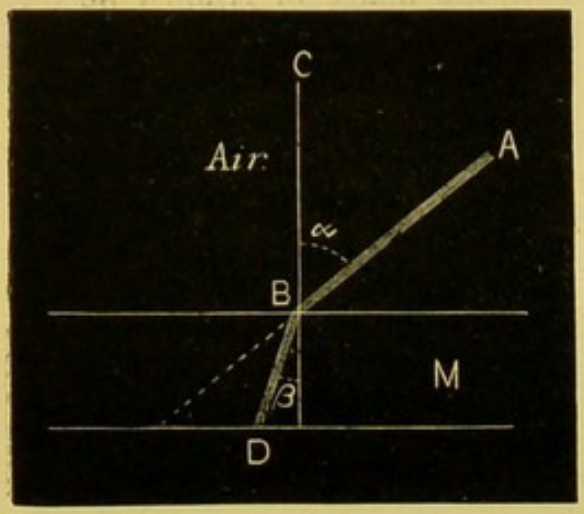

FIG. 278.—REFRACTION AT A PLANE SURFACE.

AB is the incident; BD, the refracted ray; CB, the normal to the surface. When the ray passes from air into another medium, the refractive index of the latter is the fraction $\frac{\sin \alpha}{\sin \beta}$.

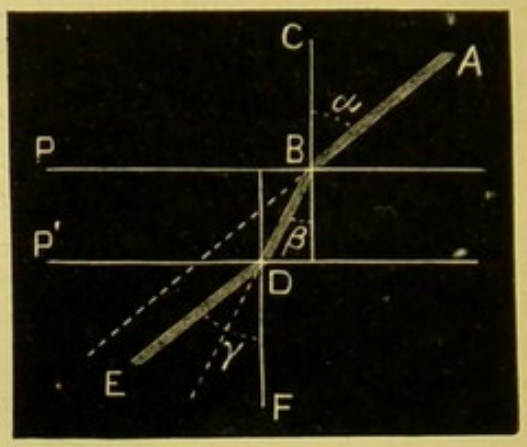

FIG. 279.—REFRACTION BY A MEDIUM BOUNDED BY PARALLEL PLANES, P AND P'.

The ray ABDE issues parallel to its original direction; CB, FD, normals to P and P'; α, angle of incidence; β, γ, angles of refraction.

normal N' as it passes across BC (Fig. 280); at both surfaces it is bent towards the base of the prism AC. At the same time the light suffers dispersion; that is, the rays of shorter wave-length are more refracted than those of greater wave-length. The **deviation** of any

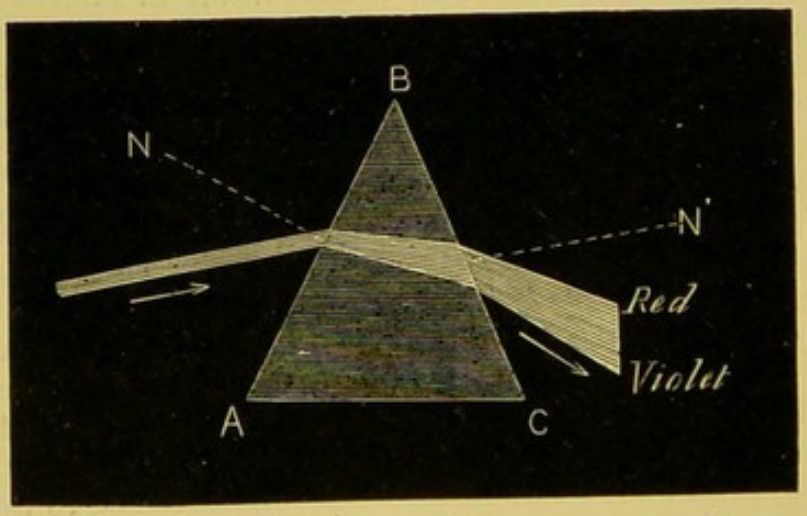

FIG. 280.—REFRACTION AND DISPERSION BY A PRISM.

given ray is measured by the angle which the refracted ray makes with its original direction. The amount of dispersion produced by a prism is measured by the difference in the deviation of the extreme rays of the spectrum. The dispersion produced by any given sub-

stance is proportional to the difference of its refractive indices for the extreme rays.

Refraction by a Biconvex Lens.—A straight line ACB passing through the centres of curvature of the two surfaces of the lens is called the principal axis. A point C lying on the *principal axis* between the two centres of curvature, and possessing the property that rays passing through it do not suffer refraction, is called the *optical centre* of the lens. Any straight line, DCE, passing through the optical centre is a *secondary axis*. Rays of light proceeding from a point in the principal axis are focussed in a point on that axis. When the rays proceed from an infinitely distant point in the principal axis, *i.e.*, when they are parallel to it, they are focussed in F, the *principal focus*. Similarly, rays parallel to, or proceeding from, a point in a secondary axis are focussed in a point on that axis; but if the focus is to be sharp, the angle between the secondary and the principal axis must not be so large as is indicated in Fig. 281.

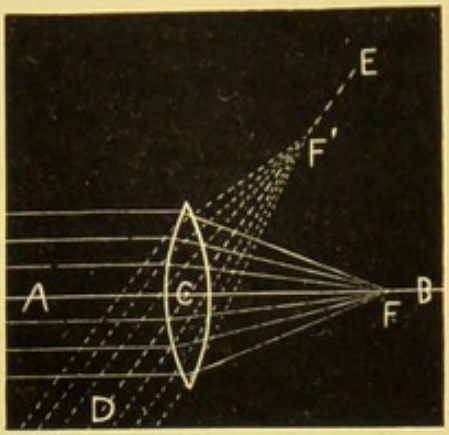

FIG. 281.—REFRACTION BY A BICONVEX LENS.

Formation of Image by Biconvex Lens (Fig. 282).—Let AB be the object; then if AHD be the path of a ray from A parallel to the principal axis, the image of A will be the intersection of the straight line DF and the secondary axis passing through A. Similarly, the image of B will be the intersection of GF and the secondary axis BC. Where AB is farther from the lens than the principal focus, the image *ab* is real and inverted. This is the case with the image of an external object formed on the retina. When the object is nearer than the principal focus, the image is virtual and erect. The image formed by the objective of a microscope when the object is in focus is real and inverted; the ocular forms a virtual erect image of this real image.

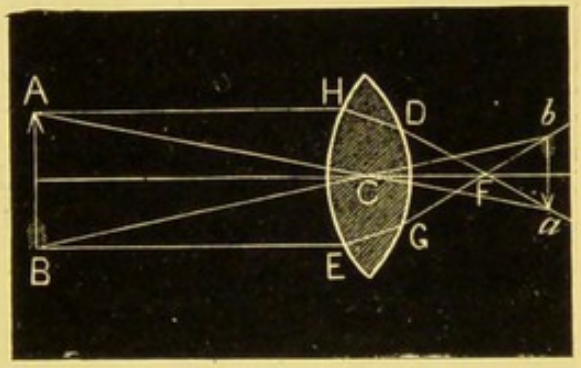

FIG. 282.—FORMATION OF IMAGE BY BICONVEX LENS.

Refraction by a Biconcave Lens (Fig. 283).—Parallel rays are rendered divergent by the lens; there is no real focus; but if the rays are prolonged backwards they meet in the virtual focus F, from which they appear to come when received by the eye through the lens.

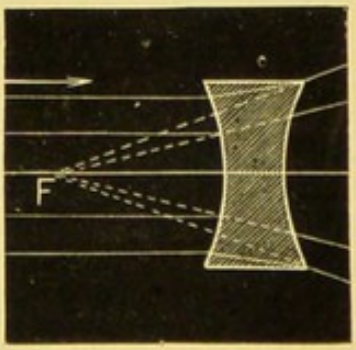

FIG. 283.—REFRACTION BY A BICONCAVE LENS.

Formation of Image by Biconcave Lens (Fig. 284).—Let AB be the object. Let AHDI be the path of a ray from any point A of the object parallel to the principal axis. Produce DI backwards (dotted line); it will pass through the principal focus F. Through A draw the secondary axis AC. The image of A must lie both on AC and on IDF; *i.e.*, it must be the intersection, *a*, of these straight lines. Similarly, the image of B is *b*, the intersection of KGF and BC. The image is virtual and erect.

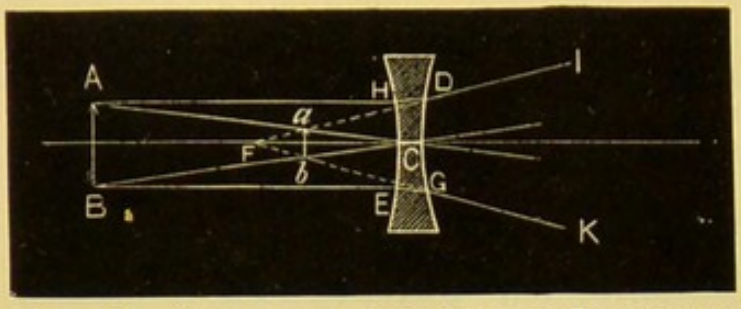

FIG. 284.—FORMATION OF IMAGE BY BICONCAVE LENS.

Absorption.—No substance is perfectly transparent; in addition to what is reflected, some light is always absorbed. In other words, in passing through a body some of the light is transformed into heat, a portion of the energy of the short, luminous waves going to increase the vibrations of the molecules of the medium, just as a wave passing under a row of barges or fishing-boats sets them swinging and pitching, and so imparts to them a certain amount of energy, which is ultimately changed into heat by friction against the water, and against each other, and by the straining and rubbing of the chains at their points of attachment. Some bodies absorb all the rays in the proportion in which they occur in white light; whether looked at or looked through, they appear colourless or white. Other substances absorb certain rays by preference, and the amount of absorption is proportional to the thickness of the layer. The colours of most natural bodies are due to this *selective absorption*. Even when looked at in reflected light, they are seen by rays that have penetrated a certain way into the substance and have then been reflected; and, of course, a smaller number of the rays which the body specially absorbs are reflected than of the rays which it readily transmits, for more of the latter than of the former reach any given depth. This is called '*body colour*'; and such substances have the same colour when seen by reflected and by transmitted light. The colour of hæmoglobin is due to the absorption of the violet and many of the yellow and green rays, as is shown by the position of the *absorption bands* in its spectrum (p. 48). In Fig. 285 the violet rays are repre-

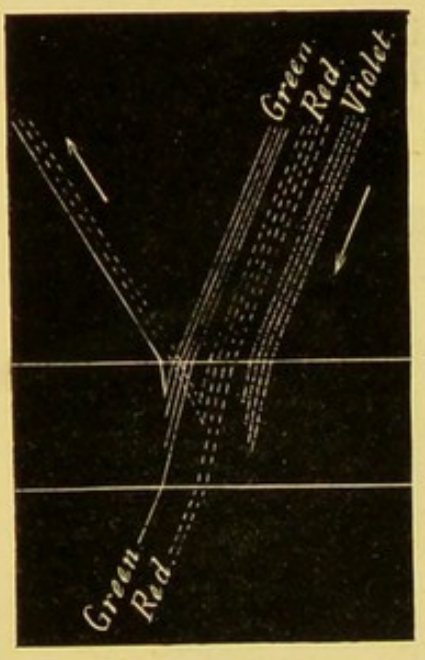

FIG. 285.—DIAGRAM TO SHOW CONNECTION OF BODY COLOUR WITH SELECTIVE ABSORPTION.

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sented as being totally absorbed before passing through the substance. Some of the green rays are reflected, some transmitted, some absorbed. The red rays are supposed to be mostly reflected and transmitted, only to a slight extent absorbed. The colour of such a substance, both when looked at and when looked through, would therefore be that due to a mixture of red light with a smaller quantity of green. Then there is another class of substances which owe their colour to *selective reflection*. Certain rays only are reflected from their surface, and the light transmitted through a thin layer is complementary to the reflected light; that is, the reflected and transmitted rays together would make up white light. These bodies have

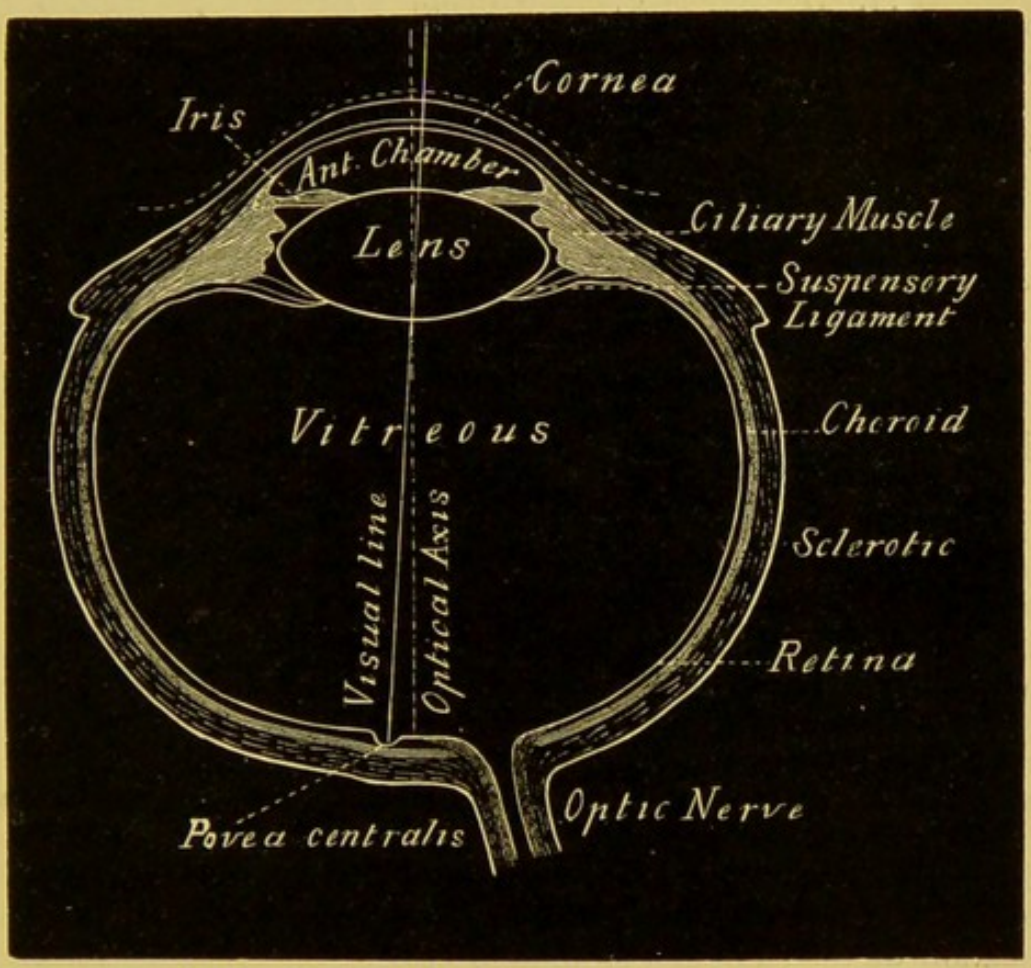


FIG. 286.—DIAGRAMMATIC HORIZONTAL SECTION OF THE LEFT EYE.

what is called '*surface colour*,' and include metals, various aniline dyes, and other substances.

Comparative.—Many invertebrate animals possess rudimentary sense-organs, by means of which they may receive certain luminous impressions. It is true that the mere sensation of light is not in itself sufficient for the exact appreciation of the form and situation of surrounding objects. But even the closure of the eyelids does not prevent a person of normal eyesight from distinguishing differences in the intensity of illumination. And it is possible that many of the humbler animals may, through the pigment spots which are often called eyes, or perhaps, as in the earthworm, by means of end-

organs more generally diffused in the skin, attain to some such dim consciousness of light and shadow as will enable them to avoid an obstacle or an enemy, to seek the sunny side of a boulder or the obscurity of an overhanging ledge of rock. But the indispensable condition of distinct vision is that an image of each part of an object should be formed upon a separate portion of the receiving or sensitive surface. This condition is, to a certain extent, fulfilled by the compound eyes of some of the higher invertebrates (insects, *e.g.*). Here rays from one point of the object pass through one of the funnel-shaped elements of the compound eye, and rays from another point through another. Rays striking obliquely on the facets are stopped by the opaque partitions between them. In the Cephalopods we find that this compound type of eye has already been abandoned; the single system of curved refracting surfaces so characteristic of the vertebrate eye has made its appearance; and the formation of a clean-cut image of the object on the retina, with the excitation of a sharply-bounded area of that membrane, follows as a geometrical consequence from the theory of lenses.

We have to consider (1) the mechanism by which an image is formed on the retina, and (2) the events that follow the formation of such an image and their relations to the stimulus that calls them forth.

Structure of the Eye.—The eye may be described with sufficient accuracy as a spherical shell, transparent in front, but opaque over the posterior five-sixths of its surface, and filled up with a series of transparent liquids and solids. The shell consists of three layers concentrically arranged, like the coats of an onion: (1) An external tough, fibrous coat, *the sclerotic*, the anterior portion of which appears as the white of the eye. In front this external layer is completed by the transparent *cornea*. (2) A vascular and pigmented layer, *the choroid*, which, in the restricted sense of the term, ends in front in a series of folds or plaits, the ciliary processes. These abut on the outer boundary of the iris, which may be looked upon as an anterior continuation of the choroidal or middle coat of the eyeball. Between the corneo-sclerotic junction and the anterior portion of the choroid is interposed a ring of unstriped muscular fibres, the ciliary muscle. (3) The inner or sensitive coat, termed the *retina* (Figs. 287, 288). This covers the choroid as a delicate membrane, extending to the ciliary processes, where it ends in a toothed margin, the ora serrata. The *optic nerve* forms a kind of stalk to which the eyeball is attached. Its point of entrance at the *optic disc* is a little nearer the median line than the antero-posterior axis, which nearly passes through the centre of a small depression, the fovea centralis, situated in the middle of the macula lutea, or yellow spot. From the optic disc (sometimes called the optic papilla) the optic nerve spreads over the retina as a layer of non-medullated fibres, separated from the interior of the eyeball only by the internal limiting membrane. This so-called

membrane is formed by the expanded feet of the fibres of Müller, which run like a scaffolding or framework through nearly the whole thickness of the retina, terminating at the outer limiting membrane. External to the layer of nerve-fibres is the stratum of large ganglion cells, whose axons they are; next to this the inner molecular layer, made up largely of the branching dendrites of these cells. The fifth layer is the inner granular or nuclear layer, containing many fusiform

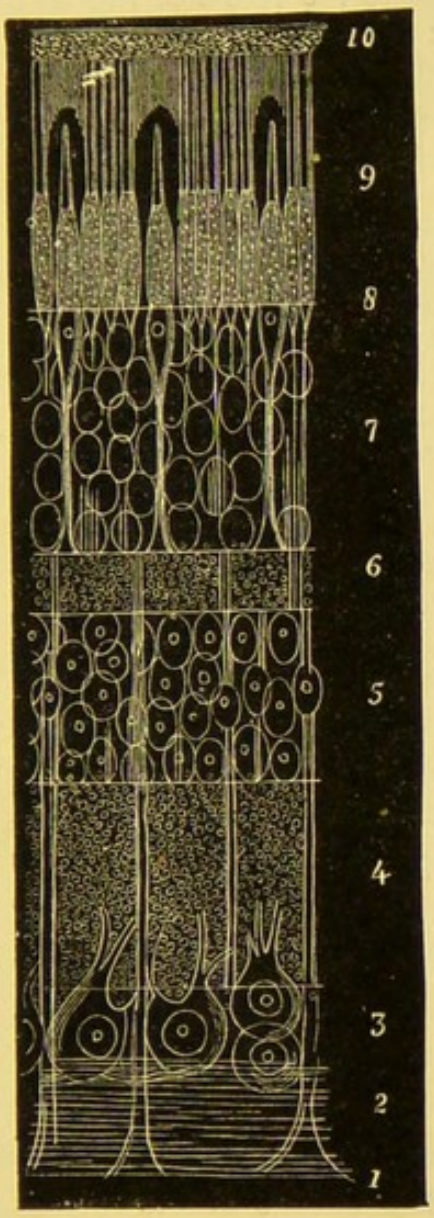


FIG. 287.—THE RETINA.

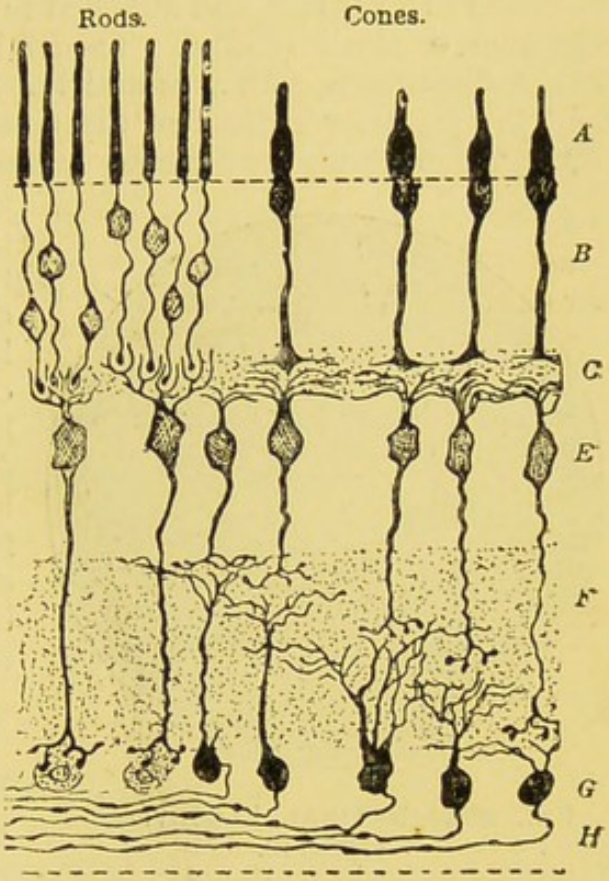


FIG. 288.—DIAGRAM OF STRUCTURE OF RETINA (BOWDITCH, AFTER CAJAL).

Figs. 287, 288.—1, internal limiting membrane; 2, *H*, layer of nerve-fibres; 3, *G*, layer of ganglion cells; 4, *F*, internal molecular layer; 5, *E*, internal nuclear layer; 6, *C*, external molecular layer; 7, *B*, external nuclear layer; 8, external limiting membrane; 9, *A*, layer of rods and cones; 10, pigmented epithelium.

'granule' cells which send out axons into the fourth, and dendrites into the sixth, or outer molecular layer, and are thus connected with the ganglion cells of the third layer on the one hand, and with the seventh or outer nuclear layer on the other. The seventh stratum receives its name from the large number of nuclei which it contains. These are connected with the rods and cones of the ninth layer, which is divided from the seventh by the external limiting membrane. At the *fovea centralis* the rods are entirely absent, and the

other layers of the retina greatly thinned; over the optic disc neither rods nor cones are present. The disc is pierced by the retinal blood-vessels (Fig. 289).

External to the rods and cones is a sheet of pigmented epithelial cells of hexagonal shape, belonging to the choroid, but remaining attached to the retina when the latter is separated, and therefore often reckoned as its most external layer.

A little behind the cornea and anterior to the retina is the *lens*, enclosed in a capsule, and attached to the choroid by the suspensory ligament, or *zonule of Zinn*. The *iris* hangs down in front of the lens like a diaphragm, with a central hole, the pupil. Between the iris and the posterior surface of the cornea is the *anterior chamber* of the eye, filled with the aqueous humour. Between the iris and the anterior surface of the lens lies the *posterior chamber*, which is rather a potential than an actual cavity. The space between the lens and the retina is accurately occupied by an almost structureless semi-fluid mass, the *vitreous humour*, enclosed by the delicate hyaloid membrane, which in front is reflected over the folds of the ciliary processes, and blends with the suspensory ligament of the lens.

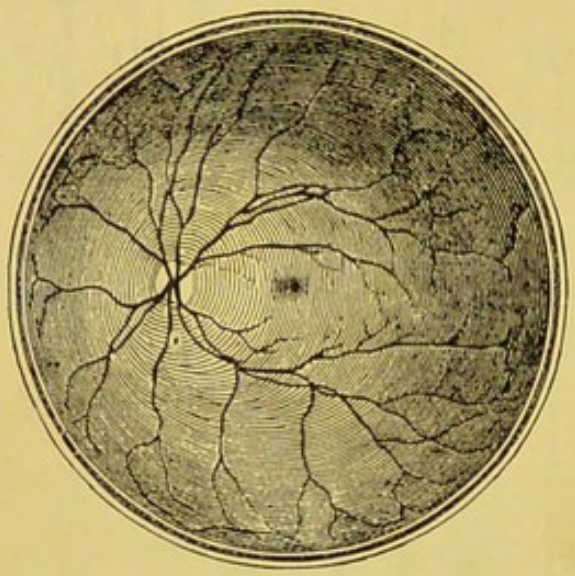


FIG. 289.—RETINAL BLOODVESSELS (HENLE).

The arteria centralis is seen issuing from the optic disc and branching over the retina. The shaded area in the middle of the figure representing the yellow spot with the fovea centralis in its centre.

Refraction in the Eye—Formation of the Retinal Image.—The amount of refraction which a ray of light undergoes at a curved surface depends upon two factors, the radius of curvature of the surface, and the difference between the refractive indices of the media from which the ray comes and into which it passes. The smaller the radius of curvature, and the greater the difference of refractive index, the more is the ray bent from its original direction. A ray of light passing into the eye meets first the approximately spherical anterior surface of the cornea, covered with a thin layer of tears. Since the refractive index of the tears and of the cornea is greater than that of air, refraction must occur here. At the parallel posterior surface of the cornea, however, the ray is but slightly bent, for the refractive indices

of aqueous humour and corneal substance are nearly equal. At the anterior and posterior surface of the lens the ray is again refracted, since the refractive index of the aqueous and vitreous humour is less than that of the lens. The following tables show the radii of curvature of the refracting surfaces and the refractive indices of the dioptric media, as well as some other data which are of use in studying the problems of refraction in the eye :

		In accommodation for Far Vision.	In accommodation for Near Vision.
Radius of curvature of	Cornea	7·8 mm.	7·8 mm.
	Anterior surface of lens	10·0 „	6·0 „
	Posterior surface of lens	6·0 „	5·5 „
Distance between	Anterior surface of cornea and anterior surface of lens	3·6 „	3·2 „
	Anterior surface of cornea and posterior surface of lens	7·6 „	7·6 „
	Anterior and posterior surface of lens	4·0 „	4·4 „
	Posterior surface of lens and retina	14·6 „	14·6 „
Antero-posterior diameter of eye along the axis		22·2 „	22·2 „

Refractive Indices—

Air	1·000
Cornea	1·377
Aqueous humour	1·3365
Vitreous humour	1·3365
Lens (mean for all its layers)	1·437
Water	1·335

It will be seen that the refractive indices of the cornea and the aqueous and vitreous humours are all nearly the same as that of water. That of the lens differs for its various layers, the central core having a higher refractive index than the more superficial portions; but a mean may be struck, and, although such calculations are open to error, it has been computed that the lens acts as a homogeneous lens of the same curvatures, and with a refractive index of 1·437, would do.

The optical problems connected with the formation of the retinal image are complicated by the existence in the eye of several media, with different refractive indices, bounded by surfaces of different and, in certain cases, of variable curvature. For many purposes, however, the matter can be greatly simplified, and a close enough approximation yet

arrived at, by considering a single homogeneous medium, of definite refractive index, and bounded in front by a spherical surface of definite curvature, to replace the transparent solids and liquids of the eye. The principal focus being supposed to lie on the retina, the position of the nodal point (*i.e.*, the point through which rays pass without refraction) of such a 'reduced' or 'schematic' or 'simplified' eye, and other constants, are shown in the following table. The single refracting surface would be situated behind the cornea and in front of the lens, at a rather smaller distance from the anterior surface of the latter than from the anterior surface of the former. The nodal point would be less than half a millimetre in front of the posterior surface of the lens (Fig. 290, p. 785). The refractive index of the single transparent medium would be a little greater than that of water.

Reduced Eye—

Radius of curvature of the single refracting surface	5·1	mm.
Index of refraction of the single refracting medium	1·35*	,,
Antero-posterior diameter of reduced eye (distance of principal focus from the single refracting surface)	20.0	,,
Distance of the single refracting surface behind the anterior surface of the cornea	2·2	,,
Distance of the nodal point of the reduced eye from its anterior surface	5·0	,,
Distance of the nodal point from the principal focus (retina)	15·0	,,

Knowing the position of the centre of curvature of the single ideal refracting surface, *i.e.*, the nodal point of the reduced eye, all that is necessary in order to determine the position of the image of an object on the retina is to draw straight lines from its circumference through the nodal point. Each of these lines cuts the refracting surface at right angles, and therefore passes through without any deviation. The retinal image is accordingly inverted, and its size is proportional to the solid angle contained between the lines drawn from the boundary of the object to the nodal point, or the equal angle contained by the prolonga-

* Or about the same as that of the aqueous humour.

tions of the same lines towards the retina. This angle is called the *visual angle*, and evidently varies directly as the size of the object, and inversely as its distance. Thus the visual angle under which the moon is seen is much larger than that under which we view any of the fixed stars, because the comparative nearness of the earth's satellite more than makes up for its relatively small size.

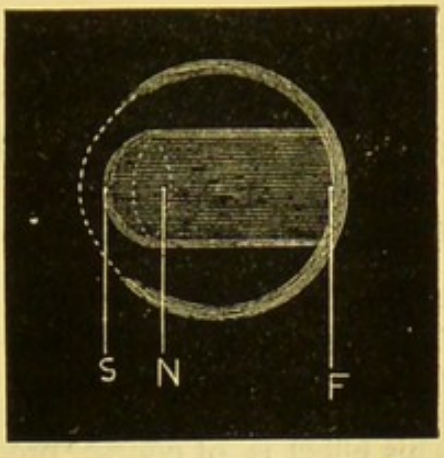


FIG. 290.—THE REDUCED EYE.

S, the single spherical refracting surface, 2·2 mm. behind the anterior surface of the cornea; N, the nodal point, 5 mm. behind S; F, the principal focus (on the retina), 20 mm. behind S. The cornea and lens are put in in dotted lines in the position which they occupy in the normal eye.

The dimensions of the retinal image of an object are easily calculated when the size of the object and its distance are known. For let AB in Fig. 291 represent one diameter of an object, A′B′ the image of this diameter, and let AB′, BA′, be straight lines passing through the nodal point. Then AB and A′B′ may be considered as parallel lines, and the triangles of which they form the bases, and the nodal point the common apex, as similar triangles.

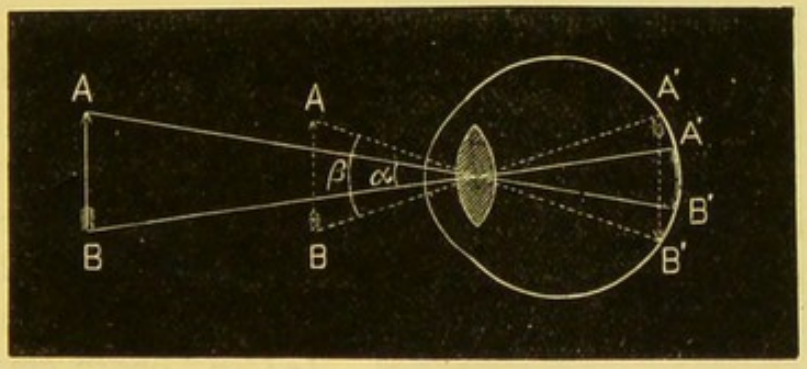


FIG. 291.—FIGURE TO SHOW HOW THE VISUAL ANGLE AND SIZE OF RETINAL IMAGE VARIES WITH THE DISTANCE OF AN OBJECT OF GIVEN SIZE.

For the distant position of AB the visual angle is α, for the near position (dotted lines) β.

Accordingly, if D is the distance of the nodal point from A, and d its distance from B′, we have $\frac{AB}{D}=\frac{A'B'}{d}$. Now, d may approximately be taken as 15 mm. Suppose, then, that the size of the moon's image on the retina is required. Here D = 238,000 miles, and AB (the diameter of the moon) = 2,160 miles. Thus we get

$\frac{2,160}{238,000} = \frac{A'B'}{15}$, or (say) $\frac{1}{110} = \frac{A'B'}{15}$, from which A′B′ (the diameter of the retinal image) $= \frac{15}{110}$, or about $\frac{1}{7}$ mm.

A ship's mast 120 feet high, seen at a distance of 25 miles, will throw on the retina an image whose height is $\frac{120 \text{ feet}}{25 \text{ miles}} \times 15$ mm., *i.e.*, $\frac{120 \text{ feet}}{5,280 \times 25 \text{ feet}} \times 15$ mm., or $\frac{1}{1,100} \times 15$ mm., equal to ·013 mm., or 13 μ in size. This is not much larger than a red blood-corpuscle, and only four times the diameter of a cone in the fovea centralis, where the cones are most slender. In this calculation the effect of aberration (p. 794) in enlarging the image has been neglected. This effect is, of course, proportionately greater for small and distant than for large and near objects; and it is doubtful whether the smallest possible image can be confined to an area of the retina of the size of a single cone.

Accommodation.—A lens adjusted to focus upon a screen the rays coming from a luminous point at a given distance will not be in the proper position for focussing rays from a point which is nearer or more remote. Now, it is evident that a normal eye possesses a great range of vision. The image of a mountain at a distance of 30 miles, and of a printed page at a distance of 30 cm., can be focussed with equal sharpness upon the retina. In an opera-glass or a telescope accommodation is brought about by altering the relative position of the lenses; in a photographic camera and in the eyes of fishes and cephalopods (Beer), by altering the distance between lens and sensitive surface; in the

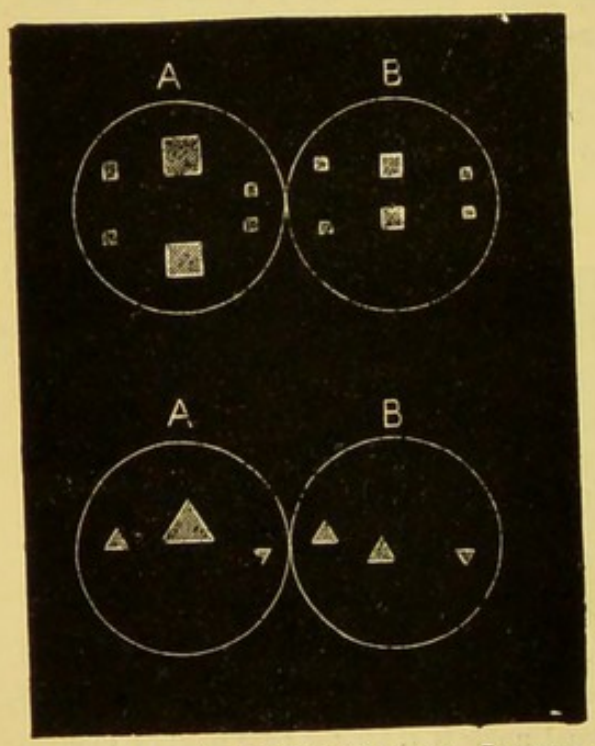


FIG. 292.—PURKINJE-SANSON IMAGES.

A, in the absence of accommodation; B, during accommodation for a near object. The upper pair of circles enclose the images as seen when the light falls on the eye through a double slit or a pair of prisms; the lower pair show the images seen when the slit is single and triangular in shape.

eye of man, by altering the curvature, and therefore the refractive power of the lens. That the cornea is not alone concerned in accommodation, as was at one time widely held, is shown by the fact that under water the power of accommodation is not wholly lost. Now, the refractive index of the cornea being practically the same as that of water, no changes of curvature in it could affect refraction under these circumstances. That the sole effective change is in the lens can be most easily and decisively shown by studying the behaviour of the mirror images of a luminous object reflected from the bounding surfaces of the various refractive media when the degree of accommodation of the eye is altered. Three images are clearly recognised: the brightest an erect virtual image, from the anterior (convex) surface of the cornea; an erect virtual image, larger, but less bright, from the anterior (convex) surface of the lens; and a small inverted real image from the (concave) posterior boundary of the lens (Purkinje-Sanson images). The second image is intermediate in position between the other two. It is possible with special care to make out a fourth image; but since it is reflected from the posterior surface of the cornea, at which only a slight change in the refractive index occurs, it is less brilliant than the first three. When the eye is accommodated for near vision, as in focussing the ivory point of the phakoscope (Fig. 330), the corneal image is entirely unchanged in size, brightness, and position. The middle image diminishes in size, comes forward, and moves nearer to the corneal image. This shows that the curvature of the anterior surface of the lens has been increased—that is to say, its radius of curvature diminished—for the size of the image of an object reflected from a convex mirror varies directly as the radius of curvature. A slight change takes place in the image from the posterior surface of the lens, indicating a small increase of its curvature too. By means of a method founded on the observation of the changes in these images, and a special instrument called an ophthalmometer which allows of their measurement, Helmholtz has calculated that, during maximum accommodation, the radius of curvature of the anterior surface of the lens is only 6 mm.,

as compared with 10 mm. when the eye is directed to a distant object and there is no accommodation. When the lens has been removed for cataract, fairly distinct vision may still be obtained by compensating for its loss by convex spectacles of suitable refractive power (10 diopters* for distant vision, and 15 diopters for the distance at which a book is usually held), but no power of accommodation remains. The person does indeed contract the pupil in regarding a near object, just as happens in the intact eye; the most divergent rays are thus cut off and the image made somewhat sharper, and there may *appear* to be some faculty of accommodation left. But the loss of the whole iris by operation does not affect accommodation in the least; the iris, therefore, takes no part in it. That no change in the antero-posterior diameter of the eyeball, caused by its deformation by the contraction of the extrinsic muscles, can have any share in accommodation, as has been suggested, is clearly proved by the fact that atropia, which does not affect the action of these muscles, paralyzes the mechanism of accommodation. To the consideration of that mechanism we now turn.

The Mechanism of Accommodation.—While everybody is agreed that the main factor in accommodation is the alteration in the curvature of the lens, there is by no means the same unanimity as to the manner in which this is brought about. Helmholtz's explanation, which has long been the most popular, is as follows: In the unaccommodated eye the suspensory ligament and the capsule of the lens are tense and taut, the anterior surface of the lens is flattened by their pressure, and parallel rays (or, what is the same thing, rays from a distant object) are focussed on the retina without any sense of effort. In accommodation for a near object, the meridional or antero-posterior fibres of the

* A diopter (1 D) is the unit of refractive power generally adopted in measuring the strength of lenses, and corresponds to a lens of 1 metre focal length. A lens of 2 diopters (2 D) has a focal length of ½ metre, a lens of 4 diopters (4 D) a focal length of ¼ metre, and so on. The diverging power of concave lenses is similarly expressed in diopters, with the negative sign prefixed. Thus, a concave lens of 1 metre focal length has a strength of −1 D and will just neutralize a convex lens of 1 D.

ciliary muscle by their contraction pull forward the choroid and relax the suspensory ligament. The elasticity of the lens at once causes it to bulge forwards till it is again checked by the tension of the capsule.

The explanation of Helmholtz, although widely adopted in the text-books, has not escaped question in the archives. Tscherning has put forward the view that when the ciliary muscle contracts, the suspensory ligament is pulled backwards and outwards. Its tension is thus increased, and the soft external layers of the lens are in consequence moulded upon the harder nucleus, so as to increase the curvature especially around the anterior pole. And Schoen, reviving a similar theory originated forty years ago by Mannhardt, believes that the ciliary muscle in contracting exerts pressure on the anterior portion of the lens, and so increases its curvature. He likens the process to the bulging of an indiarubber ball when it is held in both hands and compressed by the fingers a little behind one of the poles. It will be observed that in both of these theories the suspensory ligament is supposed to be stretched during accommodation, not relaxed as Helmholtz supposed. While they have certain advantages over the theory of Helmholtz, particularly in taking account of the presence of radial and circular as well as meridional fibres in the ciliary muscle, they do not agree so well with such experimental tests as have been applied, and therefore Helmholtz's explanation must still be regarded as the best.

Changes in the Pupil during Accommodation.—It has been already mentioned that along with the alteration in the curvature of the lens a change in the diameter of the pupil takes place in accommodation. When a distant object is looked at, the pupil becomes larger; when a near object is looked at, it becomes smaller. Narrowing of the pupil is thus associated with contraction of the ciliary muscle, and widening of the pupil with its relaxation.

This physiological correlation has its anatomical counterpart; for the third nerve supplies both the iris and the ciliary muscle. Stimulation of the nerve within the cranium causes contraction of the pupil, while stimulation of certain portions of its nucleus in the floor of the third ventricle and the Sylvian aqueduct or of the short ciliary nerves coming off from the ophthalmic ganglion (Fig. 293), which receives branches from the third nerve, or of the ganglion itself, is followed by that change in the anterior surface of the lens which constitutes accommodation (Hensen and Voelckers). This can be observed either through a window in the sclerotic in a dog or by following the movements of a needle thrust into the eyeball. By carefully localized stimulation near the junction of the aqueduct with the third ventricle, it is possible to bring about the forward bulging of the lens

without any change in the iris; but the normal and voluntary act of accommodation cannot be disjoined from the corresponding alterations in the size of the pupil. Inward rotation of the eyes accompanies contraction of the pupil in accommodation.

Changes in the Pupil produced by Light.—It is not only by accommodation that the size of the pupil may be affected. In the dark it dilates, at first rapidly, then gradually, and it maintains the width it has reached for several hours. This has been shown by taking photographs of the eye with the magnesium flashlight. In this way the width of the pupil is recorded before it has time to alter. Or a longer exposure

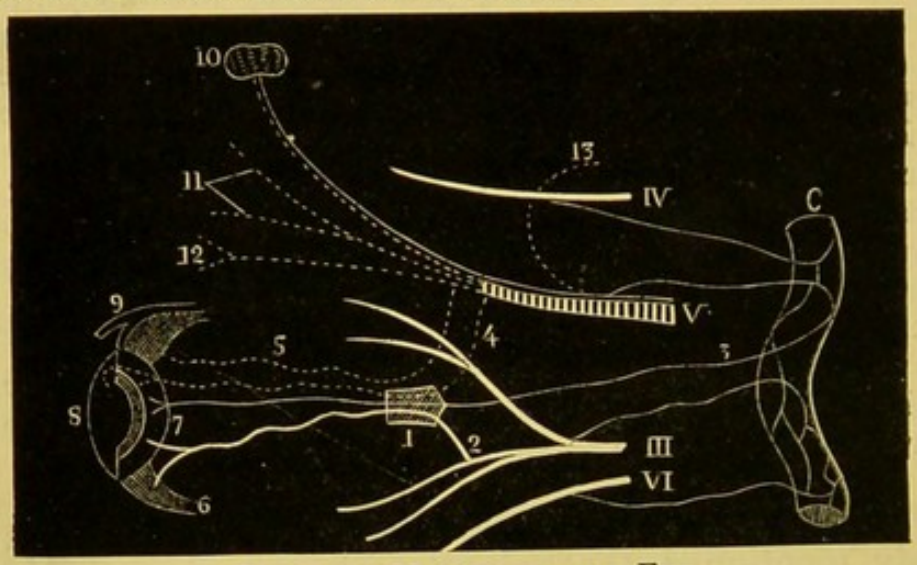


FIG. 293.—NERVES OF THE EYE.

III, third or oculo-motor nerve; IV, fourth or trochlear nerve; V, ophthalmic branch of fifth nerve; VI, sixth or abducens; C, carotid artery with its plexus of sympathetic fibres; 1, ophthalmic ganglion, with its motor root 2, its sympathetic root 3, and its sensory root 4; 5, direct ciliary filament; 6, ciliary muscle; 7, iris; 8, cornea; 9, conjunctiva; 10, lachrymal gland; 11, frontal nerve; 12, nasal nerve; 13, recurrent branch of ophthalmic division of fifth. The thick white lines represent the motor nerves; the thin continuous lines the sympathetic fibres; the dotted lines the sensory nerves.

to ultra-violet light, which affects the pupil but little, may be employed. When ordinary light falls upon the retina the pupil contracts, and the amount of contraction is roughly proportional to the intensity of the light. Contraction of the pupil to light is brought about by a reflex mechanism, of which the optic nerve forms the afferent and the oculo-motor the efferent path, while the centre is situated in the floor of the aqueduct of Sylvius. The relation of this centre to that which controls the changes in the pupil during accommodation has not as yet been sufficiently elucidated; but this we do know, that one of the paths may be interrupted by disease, while the other is intact. For in loco-

motor ataxia the light-reflex sometimes disappears, while the constriction of the pupil in accommodation still takes place (Argyll-Robertson pupil). Artificial stimulation of the optic nerve has the same effect on the pupil as the 'adequate' stimulus of light; and in many animals (including man), though not in those whose optic nerves completely decussate, both pupils contract when one retina or optic nerve is excited. This should be remembered in using the pupil-reaction as a test of the condition of the retina. For although the absence of contraction may show that the retina of the eye on which the light is allowed to fall is insensible (unless there is some physical hindrance to its passage, such as opacity of the lens or cataract), the occurrence of contraction does not exclude insensibility of the retina unless the other eye has been protected from the light.

But not only is the iris under the control of constrictor nerve-fibres, it is also governed by dilator nerves; and the size of the pupil at any given moment depends on the play of two nicely-balanced forces.

The dilator fibres pass out by the anterior roots of the first three thoracic nerves (dog, cat, rabbit), accompanied apparently by vaso-constrictor fibres for the iris. Reaching the sympathetic chain through the corresponding rami communicantes, they traverse the first thoracic ganglion, the annulus of Vieussens, the inferior cervical ganglion and the cervical sympathetic. They end by arborizing around some of the cells of the superior cervical ganglion, whose axons eventually arrive at the Gasserian ganglion, and running along the ophthalmic division of the trigeminal to the eye, reach the iris by its ciliary branches.

Stimulation of the cervical sympathetic causes marked dilatation of the pupil (Practical Exercises, p. 861), even when the third nerve is excited at the same time. All the evidence at our command goes to show that the pupillo-dilator fibres do not act by constricting the bloodvessels of the iris. For dilatation of the pupil can be caused in a bloodless animal by stimulating the sympathetic. And even when the circulation is going on, a short stimulation of the sympathetic causes dilatation of the pupil without vaso-constriction, while with longer excitation the dilatation of the pupil begins before the narrowing of the bloodvessels. Nor does it seem possible to accept the view that the sympathetic fibres are inhibitory for the sphincter muscle of the

iris. In all probability they act directly upon dilator muscular fibres. It has, indeed, long been known that in the iris of the otter and of birds a radial dilator muscle exists; and it has been shown by Langley and Anderson that in the iris of the rabbit, cat, and dog, the presence of radially arranged contractile substance, different it may be in some respects from ordinary smooth muscle, must be assumed. Reflex dilatation of the pupil through the sympathetic fibres is caused in man by painful stimulation of the skin, by dyspnœa, by muscular exertion, and in some individuals even by tickling of the palms. In animals the stimulation of naked sensory nerves has the same effect. The 'starting of the eyeballs from their sockets,' which the records of torture so often note, is due to a similar reflex excitation of the sympathetic fibres supplying the smooth muscle of the orbits and eyelids.

The statement has been made that in addition to the sympathetic dilators of the pupil, dilating fibres pass out directly from the bulb along the fifth nerve; and after section of the cervical sympathetic or excision of the superior cervical ganglion, reflex dilatation can still be caused. Stimulation of certain areas on the cortex of the frontal lobe of the cerebrum (p. 742) causes slight dilatation even after the sympathetic has been divided. But it is not known whether this is due to inhibition of the pupillo-constrictor fibres in the third nerve or to excitation of cerebral pupillo-dilator fibres. The reflex centre for dilatation of the pupil is in the medulla oblongata. The lower cervical and upper thoracic portion of the spinal cord has received the name of the cilio-spinal region from its relation to the pupillo-dilator fibres. It must not be looked upon as a centre in any proper sense of the term, but rather as the pathway by which these fibres pass down from the bulb, and where they may accordingly be tapped by stimulation.

That, in addition to the cerebral centre for the constrictor and the bulbar centre for the dilator fibres, there exists within the eye some local mechanism which controls the muscles of the iris and regulates the size of the pupil is rendered certain by many facts. The excised eye of a frog or an eel constricts its pupil on exposure to light, and dilates it in the dark. It is said that even the isolated iris of the eel contracts to light; and it is known, although here the explanation is less difficult, that the iris both of cold- and warm-blooded animals contracts in warm, and dilates in cold normal saline solution. The local application of *atropia*

causes temporary paralysis of accommodation and dilatation of the pupil. When the third nerve is divided, the pupil dilates; it dilates still more when atropia is administered after the operation. Dropped into one eye in small quantity, atropia only produces a local effect; the pupil of the other eye remains of normal size, or somewhat constricted on account of the greater reflex stimulation of its third nerve by the greater quantity of light now entering the widely-dilated pupil of the atropinized eye. Even in the excised eye the effect of the drug is the same. Introduced into the blood, atropia causes both pupils to dilate. Other **mydriatic**, or pupil-dilating drugs, are *cocaine*, *daturine*, and *hyoscyamine*. *Eserine*, *pilocarpine*, and *morphia* are the chief **myotics**, or pupil-constricting substances. They also cause spasm of the ciliary muscle, and inability to accommodate for distant objects. The work of the mydriatics can be undone by the myotics. Thus the dilatation produced by atropia is removed by pilocarpine. The explanation of the action of these drugs is that the mydriatics paralyze the third nerve, and stimulate the dilator nerve-fibres of the iris, while the myotics paralyze the dilators and stimulate the third. Nicotine, which ultimately causes constriction of the pupil, does so by paralyzing the cells on the course of the dilating fibres in the superior cervical ganglion.

Inward rotation of the eyes is associated with contraction of the pupil, and the contraction that occurs during sleep is thus explained, for in sleep the eyes converge to some extent. When the pressure in the anterior chamber is diminished, as by tapping the aqueous humour through the cornea, contraction of the pupil occurs; and stimulation of the sympathetic has now a far smaller dilating effect than usual. Removal of the cornea narrows the pupil, partly by occasioning direct stimulation of the sphincter pupillæ, partly by abolishing the pressure of the aqueous humour. The attached (ciliary) border of the iris then bulges forward, and the pupil becomes smaller. On the other hand, an increased pressure in the anterior chamber forces back the ciliary border of the iris, and causes mechanical dilatation of the pupil.

Functions of the Iris.—In vision, the iris performs two chief functions: (1) It regulates the quantity of light allowed to fall upon the retina. The larger the aperture of a lens, the greater is its collecting power, the more light does it gather in its focus. In the eye, the area of the pupil determines the breadth of the pencil of light that falls upon

the lens. If this area was invariable, the retina would either be 'dark from excess of light' in bright sunshine, or dark from defect of light in dull weather or at dusk. In order that the iris may act as an efficient diaphragm it must be pigmented, and it is the pigment in it which gives the colour to the normal eye. The vision of albinos, in whose eyes this pigment is wanting, is often, though not invariably, deficient in sharpness. There is always intolerance of bright light; and the same is true in the condition known as irideremia, or congenital absence or defect of the iris.

(2) Another, and perhaps equally important, function of the iris is to cut off the more divergent rays of a pencil of light falling upon the eye, and thus to increase the sharpness of the image. This leads us to the consideration of certain defects in the dioptric arrangements of the eye.

Defects of the Eye as an Optical Instrument. (1) **Spherical Aberration.**—It is a property of a spherical refracting surface that rays of light passing through the peripheral portions are more strongly refracted than rays passing near the principal axis. Hence a luminous point is not focussed accurately in a single point by a spherical lens; the image is surrounded by circles of diffusion. In the eye this spherical aberration is partly corrected by the interposition of the iris, which cuts off the more peripheral rays, especially in accommodation for a near object, when they are most divergent. In addition, the anterior surfaces of the cornea and lens are not segments of spheres, but of ellipsoids, so that the curvature diminishes somewhat with the distance from the optic axis, and, therefore, the refracting power as we pass away from the axis does not increase so rapidly as it would do if the surfaces were truly spherical. Further, the refractive index of the peripheral parts of the lens is less than that of its central portions.

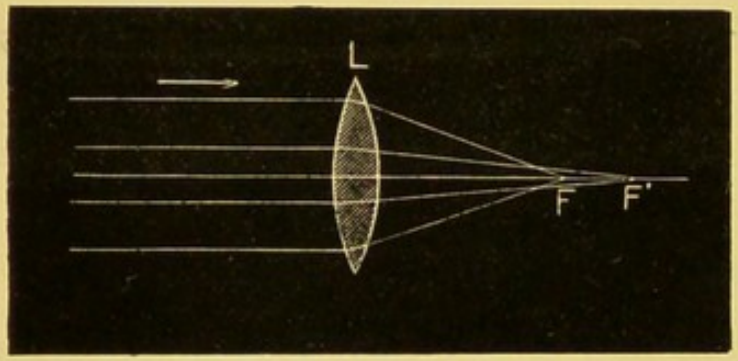


FIG. 294.—SPHERICAL ABERRATION.

Rays passing through the more peripheral parts of a biconvex lens L are brought to a focus F nearer the lens than F', the focus of rays passing through the central portions of the lens.

(2) **Chromatic Aberration.**—All the rays of the spectrum do not travel with the same velocity through a lens, and are, therefore, unequally refracted by it, the short violet rays being focussed nearer

the lens than the long red rays. It was at one time supposed that this chromatic aberration, as it is called, is compensated in the eye; and it is said that this mistake gave the first hint that Newton's dictum as to the proportionality between deviation and dispersion was erroneous, and led to the discovery of achromatic lenses. But in reality the eye is not an achromatic combination; and the violet rays are focussed about $\frac{1}{2}$ mm. in front of the red. Thus, in Fig. 295 the white light passing through the lens is broken up into its constituents: the violet focus is at V, and the red at R, behind it. A screen placed at R would show not a point image, but a central point surrounded by concentric circles of the spectral colours, with violet outside. If the screen was placed at V, the centre would be violet and the red would be external. For this reason it is impossible

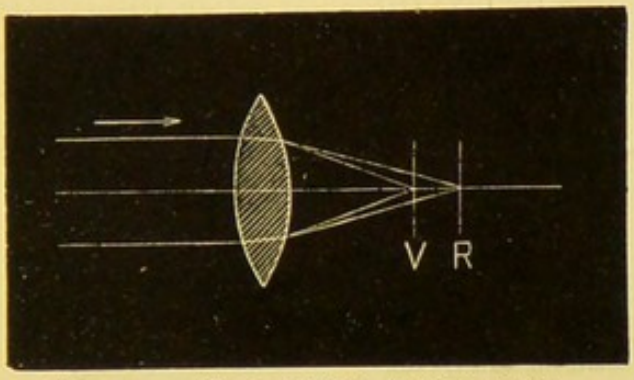


FIG. 295.—CHROMATIC ABERRATION.

The violet rays are brought to a focus V nearer the lens than R, the focus of the red rays.

FIG. 296.—TO SHOW DISPERSION IN EYE.

View the figure from a distance too small for accommodation. Approach the eye towards it; the white rings appear bluish owing to circles of dispersion falling on them. A little closer, and the black rings become white or yellowish-white.

to focus at the same time and with perfect sharpness objects of different colours: a red light on a railway track appears nearer than a blue light, partly perhaps for the reason that it is necessary to accommodate more strongly for the red than for the blue, and we associate stronger accommodation with shorter distance of the object, although other data are also involved in such a visual judgment. When we look at a white gas-flame through a cobalt glass, which allows only red and violet to pass, we see either a red flame surrounded by a violet ring, or a violet flame surrounded by a red ring, according as we focus for the red or for the violet rays. The dispersive power of the eye, however, is so small, and the capacity of rapidly altering its accommodation so great, that no practical inconvenience results from the lack of achromatism, which, however, may be easily demonstrated by looking at a pattern such as that in Fig. 296 at a distance too small for exact accommodation.

It is also reckoned among the optical imperfections of the eye (3) that the curved surfaces of the cornea and lens do not form a 'centred' system—that is to say, their apices and their centres of curvature do not all lie in the same straight line; (4) that the pupil is eccentric, being situated not exactly opposite the middle of the lens and cornea, but nearer the nasal side, and that in consequence

the *optic axis*, or straight line joining the centre of curvature of the lens and cornea, does not coincide with the *visual axis*, or straight line joining the fovea centralis with the centre of the pupil, which is also the straight line joining the centre of the pupil and any point to which the eye is directed in vision. The angle between the optic and visual axis is about 5° (Fig. 286). (5) Muscæ volitantes, the curious bead-like or fibrillar forms that so often flit in the visual field when one is looking through a microscope, are the token that the refractive media of the eye are not perfectly transparent at all parts; they seem to be due to floating opacities in the vitreous humour, probably the remains of the embryonic cells from which the vitreous body was developed. (6) Lastly, it may be mentioned that slight irregularities in the curvature of the lens exist in all eyes, so that a point of light, like a star or a distant street-lamp, is not seen as a point, but as a point surrounded by rays (irregular astigmatism). In bringing this review of the imperfections of the dioptric media of the normal eye to a close, it may be well to explain that what are defects

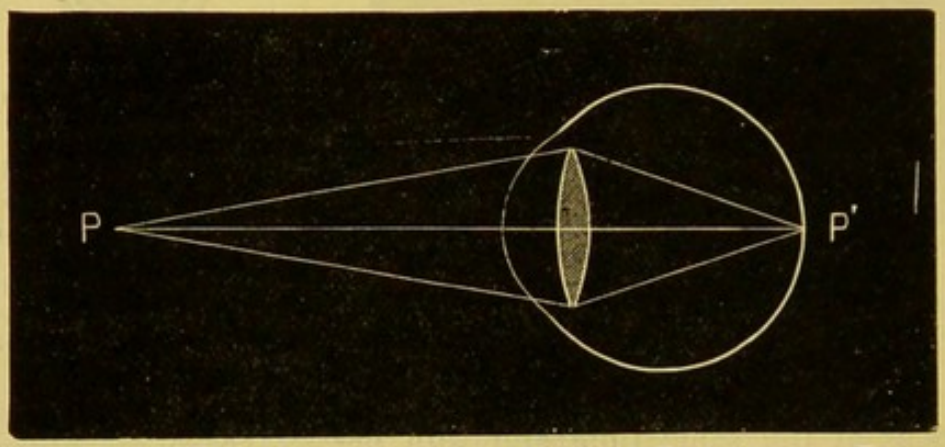


FIG. 297.—REFRACTION IN THE (NORMAL) EMMETROPIC EYE.
The image P' of a distant point P falls on the retina when the eye is not accommodated. To save space, P is placed much too near the eye in Figs. 297—299.

from the point of view of the student of pure optics are not necessarily defects from the freer standpoint of the physiologist, who surveys the mechanism of vision as a whole, the relations of its various parts to one another and to the needs of the organism it has to serve, the long series of developmental changes through which it has come to be what it is, and the possibilities, so far as we can limit them, that were open to evolution in the making of an eye. The optician may perhaps assert, and with justice, that he could easily have made a better lens than Nature has furnished, but the physiologist will not readily admit that he could have made as good an eye.

While the defects hitherto mentioned are shared in greater or less degree by every normal eye, there are certain other defects which either occur in such a comparatively small number of eyes, or lead to such grave disturbances of vision when they do occur, that they must be reckoned

as abnormal conditions. In the normal or **emmetropic eye**, parallel rays—and for this purpose all rays coming from an object at a distance greater than 65 metres may be considered parallel—are brought to a focus on the retina without any effort of accommodation. The distance at which objects can be distinctly seen is only limited by their size, the clearness of the atmosphere, and the curvature of the earth; in other words, the *punctum remotum*, or far point of vision, the most distant point at which it is possible to see with distinctness, is practically at an infinite distance. When accommodation is paralyzed by atropia, only remote objects can be clearly seen. On the other hand, the normal eye, or, to be more precise, the normal eye of

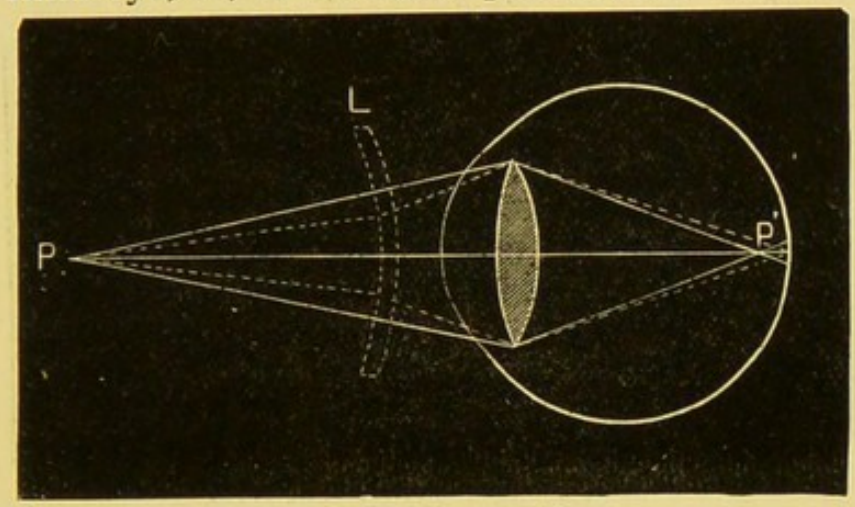


FIG. 298.—MYOPIC EYE.

The image P' of a distant point P falls in front of the retina even without accommodation. By means of a concave lens L the image may be made to fall on the retina (dotted lines).

a middle-aged adult, can be adjusted for an object at a distance of not more than 12 cm. (or 5 inches). Nearer than this it is not possible to see distinctly; this point is accordingly called the *punctum proximum*, or near point. The range of accommodation for distinct vision in the emmetropic eye is from 12 cm. to infinity.

Myopia, or short-sightedness, is generally due to the excessive length of the antero-posterior diameter of the eyeball in relation to the converging power of the cornea and the lens. Even in the absence of accommodation, parallel rays are not focussed on the retina, but in front of it; and in order that a sharp image may be formed on the retina

the object must be so near that the rays proceeding from it to the eye are sensibly divergent—that is to say, it must be at least nearer than 65 metres; but as a rule an object at a distance of more than 2 to 3 metres cannot be distinctly seen. With the strongest accommodation the near point may be as little as 5 cm. from the eye. The range of vision in the myopic eye is therefore very small. The defect may be corrected by concave glasses, which render the rays more divergent. It is to be noted that many cases of internal squint in children are connected with myopia, the eyes necessarily rotating inwards as they are made to fix an abnormally near object. The treatment both of the squint and the myopia in these cases is the use of concave spec-

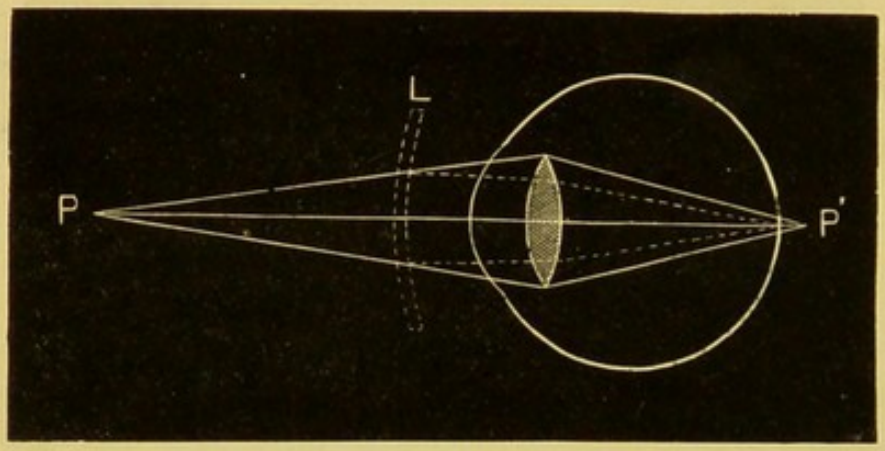


FIG. 299.—HYPERMETROPIC EYE.

The image P' of a point P falls behind the retina in the unaccommodated eye. By means of a convex lens it may be focussed on the retina without accommodation (dotted lines).

tacles (Fig. 298). Myopia, although a condition that shows a distinct hereditary tendency, is rarely present at birth: the elongation of the antero-posterior diameter of the eye-ball develops gradually as the child grows.

In **hypermetropia**, or long-sightedness, the eye is, as a rule, too short in relation to its converging power; and with the lens in the position of rest, parallel rays would be focussed behind the retina. Accordingly the hypermetropic eye must accommodate even for distant objects, while even with maximum accommodation an object cannot be distinctly seen unless it is farther away than the near point of the emmetropic eye. The far point of distinct vision is at the same distance as in the emmetropic eye, viz., at infinity;

the near point is farther from the eye. The defect is corrected by convex glasses (Fig. 299). Hypermetropia, unlike myopia, is present at birth.

Presbyopia, or the long-sightedness of old age, is not to be confounded with hypermetropia. It is essentially due to failure in the power of accommodation, chiefly through weakness of the ciliary muscle, but partly owing to increased rigidity and loss of elasticity of the lens. Images of distant objects are still formed on the retina of the unaccommodated eye with perfect sharpness; *i.e.*, the far point of vision is not affected. But the eye is unable to accommodate sufficiently for the rays diverging from an object at the ordinary near point; in other words, the near point is farther away than normal. Convex glasses are again the remedy.

The near point of distinct vision can be fixed in various ways—among others, by means of Scheiner's experiment (Practical Exercises, p. 858). Two pin-holes are pricked in a card at a distance less than the diameter of the pupil. A needle viewed through the holes appears single when it is accommodated for, double if it is out of focus. The near point of vision is the nearest point at which the needle can still, by the strongest effort of accommodation, be seen single.

Astigmatism.—It has been mentioned that slight differences of curvature along different meridians of the refracting surfaces exist in all eyes. But in some cases the difference in two meridians at right angles to each other is so great as to amount to a serious defect of vision. To this condition the name of 'astigmatism' or 'regular astigmatism' has been given. It is usually due to an excess of curvature in the vertical meridians of the cornea, less frequently in the horizontal meridians; occasionally the defect is in the lens. Rays proceeding from a point are not focussed in a point, but along two lines, a horizontal and a vertical, the horizontal linear focus being in front of the other when the vertical curvature is too great, behind it when the horizontal curvature is excessive. The two limbs of a cross or the two hands of a clock when they are at right angles to each other cannot be seen distinctly at the same time, although they

can be successively focussed. The condition may be corrected by glasses which are segments of cylinders cut parallel to the axis.

The Ophthalmoscope.—The pupil of the normal eye is dark, and the interior of the eye invisible, without special means of illuminating it. But this is not because all the light that falls upon the fundus is absorbed by the pigment of the choroid, for even the pupil of an albino appears dark when the eye is covered by a piece of black cloth with a hole in front of the pupil. The explanation is as follows:

Let the rays from a luminous point P be focussed by the lens L at P′ (Fig. 300). It is plain that rays proceeding from P′ will exactly retrace the path of those from P and be focussed at P. Now, the eye receives rays from all directions, and, when it is sufficiently well illuminated, sends rays out in all directions. The moment, however, that the observing eye is placed in front of the observed eye, the latter ceases to receive light from the part of the field occupied by the pupil of the former, and therefore ceases to reflect light into it.

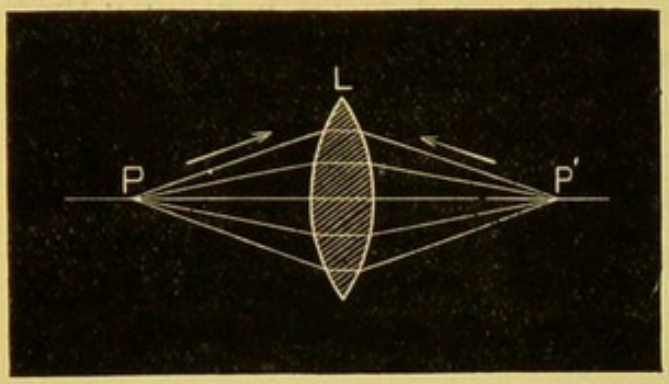


FIG. 300.

This difficulty is avoided by the use of an ophthalmoscopic mirror. The original and theoretically the most perfect form of such a mirror is a plate, or several superposed plates, of glass, from which a beam of light from a laterally placed candle or lamp is reflected into the observed eye, and through which the eye of the observer looks (Fig. 301). But the illumination thus obtained is comparatively faint; and a concave mirror is now generally used. In the centre is a small hole or a small unsilvered portion of the mirror for the observer's eye. In the direct method of examination (Fig. 302), the mirror is held close to the observed eye, and an erect virtual image of the fundus is seen. When the eye of the observer and of the patient are both emmetropic, and both eyes are unaccommodated, the rays of light proceeding

from a point of the retina of the observed eye are rendered parallel by its dioptric media, and are again brought to a focus on the observer's retina.

If the observed eye is myopic, the rays of light coming from a point of the retina leave the eye, even when it is

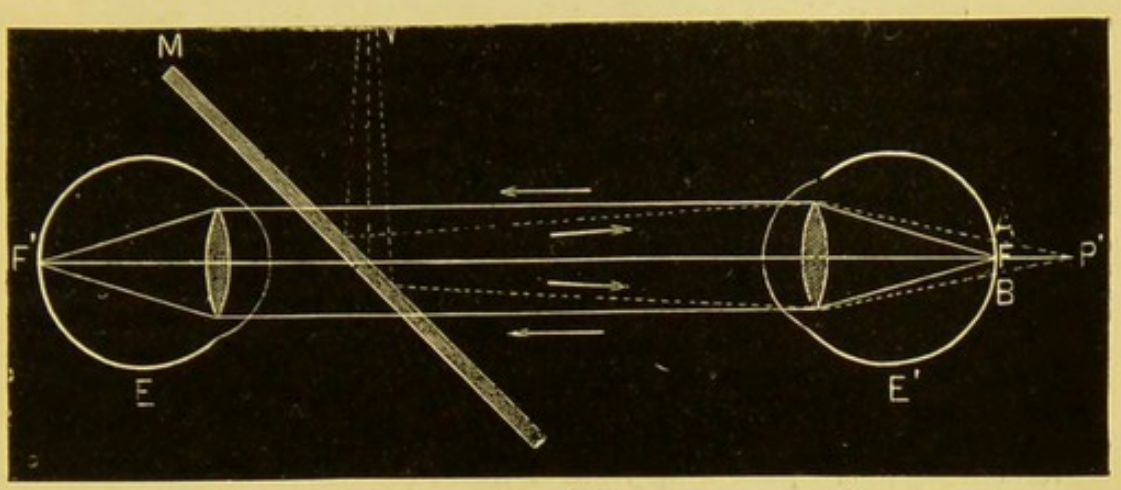


FIG. 301.—FIGURE TO ILLUSTRATE THE PRINCIPLE OF THE OPHTHALMOSCOPE.

Rays of light from a point P are reflected by a glass plate M (several plates together in Helmholtz's original form) into the observed eye E'. Their focus would fall, as shown in the figure, at P', a little behind the retina of E'. The portion of the retina AB is therefore illuminated by diffusion circles; and the rays from a point of it F will, if E' is emmetropic and unaccommodated, issue parallel from E' and be brought to a focus at F' on the retina of the (emmetropic and unaccommodated) observing eye E.

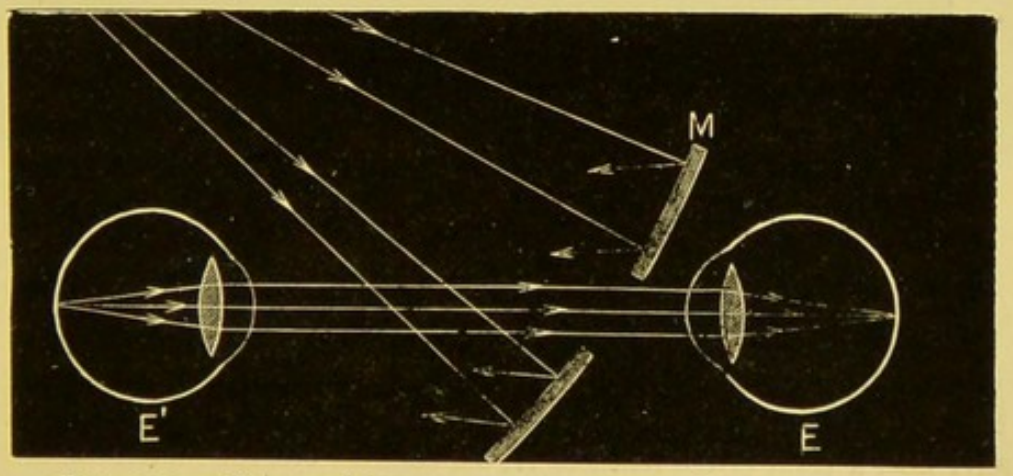


FIG. 302.—DIRECT METHOD OF USING THE OPHTHALMOSCOPE.

Light falling on the perforated concave mirror M passes into the observed eye E'; and, both E' and the observing eye E being supposed emmetropic and unaccommodated, an erect virtual image of the illuminated retina of E' is seen by E.

unaccommodated, as a convergent pencil; and the emmetropic non-accommodated eye of the observer must have a concave lens placed before it in order that the fundus may be distinctly seen.

When the observed eye is hypermetropic, the rays emerg-

ing from the unaccommodated eye are divergent, and a convex lens, the strength of which is proportional to the amount of hypermetropia, must be placed before the observer's unaccommodated eye if he is to see the fundus distinctly. By accommodating, the observer can see the fundus clearly without a convex lens.

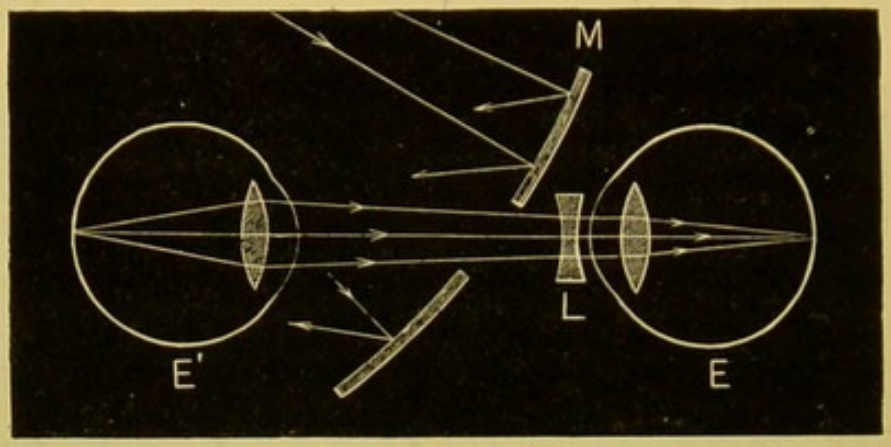


FIG. 303.—USE OF THE OPHTHALMOSCOPE (DIRECT METHOD) FOR TESTING ERRORS OF REFRACTION IN MYOPIC EYE.

Rays issuing from a point of the retina of E', the observed (myopic and unaccommodated) eye, pass out, not parallel, but convergent. They will therefore be focussed in front of the retina of the observing (unaccommodated) eye E if the latter is emmetropic. By introducing a concave lens L of suitable strength, however, a clear view of the retina of E' will be obtained, and the strength of this lens is the measure of the amount of myopia.

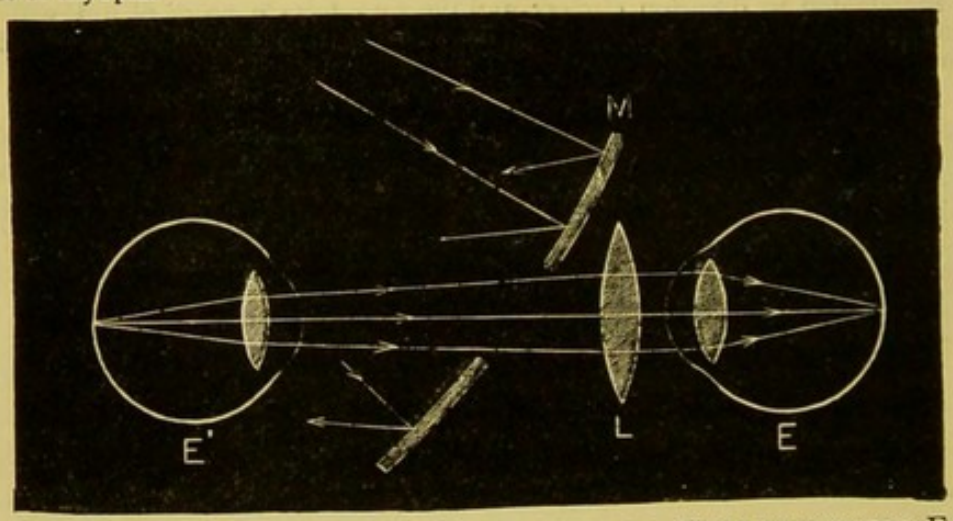


FIG. 304.—TESTING ERRORS OF REFRACTION IN HYPERMETROPIC EYE.

Rays from a point of the retina of E', the observed eye, issue divergent, and are focussed behind the retina of the observing (unaccommodated and emmetropic) eye E. The strength of the convex lens L, which must be introduced in front of E to give clear vision of the retina of E', measures the degree of hypermetropia.

By this method errors of refraction in the eye may be detected and measured.* The observer must always keep

* To a great extent the opthalmoscopic method of measuring errors of refraction has been replaced by the more modern method of skiascopy (shadow test), which, however, it would be out of place to describe here.

his eye unaccommodated, and if it is not emmetropic, he must know the amount of his short- or long-sightedness, *i.e.*, the strength and sign of the lens needed to correct his defect of refraction, and must allow for this in calculating the defect of his patient. Non-accommodation of the eye of the latter can always be secured by the use of atropia.

By the direct method of ophthalmoscopic examination, only a small portion of the retina can be seen at a time, and this is highly magnified. A larger, though less magnified,

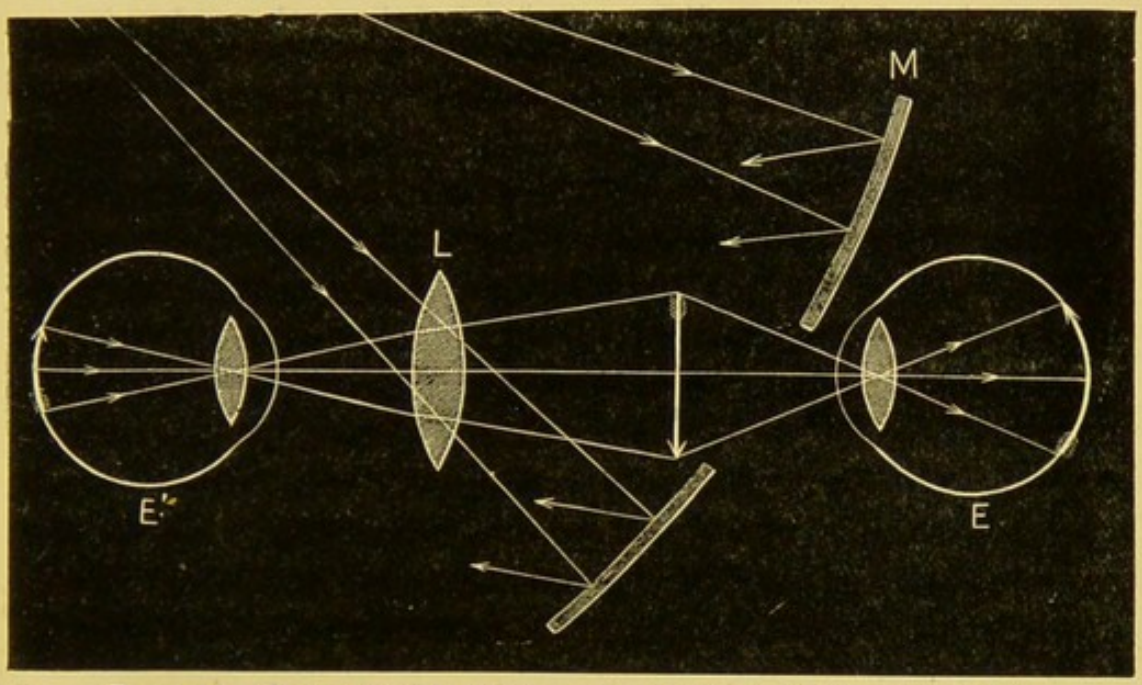


FIG. 305.—INDIRECT METHOD OF USING THE OPHTHALMOSCOPE.

The rays of light issuing from E', the observed eye, are focussed by the biconvex lens L, and a real inverted image of a portion of the retina of E', magnified four or five times, is formed in the air between the lens and the observing eye E. This image is viewed by E at the ordinary distance of distinct vision (10 or 12 inches). (The exaggeration of the size of the mirror makes it appear as if some of the rays from the lamp passed through the lens before being reflected from the mirror. This would not be the case in an actual observation.)

view can be got by the indirect method. The observed eye is illuminated as before, but the mirror and the observer's eye are at a greater distance (Fig. 305). Here the rays from a considerable portion of the retina are brought to a focus by a convex lens held near the eye of the patient, so as to form a real and inverted aerial image of the retina. This image is viewed by the observer at his ordinary visual distance. It is not necessary in this method that the observed eye should be non-accommodated, although it is convenient

as in the direct method to cause dilatation of the pupil by atropia, which also relaxes the accommodation. (Practical Exercises, p. 861.)

A method of photographing the retina in the living eye which has recently been employed with success by Dogiel bids fair to become an important supplementary means of investigating the fundus.

Single Vision with Both Eyes—Diplopia.—Scheiner's experiment shows that it is possible to have double vision, or diplopia, with a single eye when two separate images of the same object fall upon different parts of the retina. In vision with both eyes, or binocular vision, an image of every object looked at is, of course, formed on each retina, and we have to inquire how it is that as a rule these images are blended in consciousness so as to produce the perception of a single object; and how it is that under certain conditions this blending does not take place, and diplopia results. Two chief theories have been invoked in the attempt to answer these questions: (1) the theory of identical points, (2) the theory of projection.

In regard to the second theory, we shall merely say that it assumes that in some way or other the retina, or, rather, the retino-cerebral apparatus, has the power of appreciating not only the shape and size of an image, but also the direction of the rays of light which form it, and that the position of the object is arrived at by a process of mental projection of the image into space along these directive lines. The first theory we shall examine in some detail.

The Theory of Identical Points.—This theory assumes that every point of one retina 'corresponds' to a definite point of the other retina, and that in virtue of this correspondence, either by an inborn necessity or from experience, the mind refers simultaneous impressions upon two corresponding or identical points to a single point in external space. If we imagine the two retinæ in the position which the eyes occupy when fixing an infinitely distant object (that is, with the visual axes parallel) to be superposed, with fovea over fovea, every point of the one retina will be covered by the corresponding point of the other retina, so that identical

points could be pricked through with a needle. But since the actual centre of the retina does not correspond with the fovea centralis (Fig. 286), but lies nearer the nasal side, the nasal edge of the left retina will overlap the temporal edge of the right, and the nasal edge of the right will overlap the temporal edge of the left; so that a part of each retina has no corresponding points in the other.

The adherents of this theory claim, and with justice, that a small object so situated that its image must be formed on corresponding points of the two retinæ does, as a rule, appear single, and, what is even more striking, that a phosphene, or luminous circle produced by pressing the blunt end of a pencil or the finger-nail on a point of the globe of one eye, is not doubled by pressure over the corresponding point of the other eye, although two circles are seen when pressure is made upon points which do not correspond. If in rotating the eyes one eye is prevented by pressure with the finger from following the movement of the other, there is double vision. When squinting is produced by paralysis of the third (p. 720) or the sixth cranial nerve (p. 722), it is accompanied by diplopia, until in course of time the mind learns to disregard one of the images. Here it is obvious that the two images of an object cannot fall on corresponding points.

But too much weight must not be allowed to such evidence, for it is also a fact that images situated on corresponding points may not, and that images not situated on corresponding points may, give rise to a single impression. For example, if one of the closed eyes be held slightly out of its ordinary position by the finger, pressure on identical points of the two eyes gives rise to two separate phosphenes. And some of the phenomena of stereoscopic vision (p. 806) show clearly that images falling on non-corresponding points may give a single impression; while we do not habitually see double, although it is certain that the images of multitudes of objects are constantly falling on points of the retinæ not anatomically identical.*

The question therefore arises, How is it that we do not see these double images? This is one of the difficulties of the theory of

* In every fixed position of the eyes, the objects whose images fall on corresponding points will be arranged on certain definite lines or surfaces, which vary with the direction of the visual axis, and to which the name of horopter, or point-horopter, has been given. For most eyes when directed to the horizon, that is, with the visual axes parallel, the horopter is practically the horizontal plane of the ground, so that all objects within the field of vision, and resting on the ground, fall upon corresponding points, and are seen single. When the eyes are directed to a point at such a distance that the lines of vision are sensibly convergent, the horopter consists (1) of a straight line drawn through the fixing-point and at right angles to the plane passing through the fixing-point and the two visual lines (visual plane); (2) of a circle passing through the fixing-point and the nodal points of the two eyes (the famous horopteric circle of Müller).

identical points. The following is a partial explanation: (1) The images of objects in the portion of the field most distinctly seen, that is, the portion in the immediate neighbourhood of the intersection of the visual lines, or the part to which the gaze is directed, are formed on identical points; and by rapid movements the eyes fix successively different parts of the field of view. (2) Vision grows less distinct as we pass out from the centre of the retina, and we are accustomed to neglect the blurred peripheral images in comparison with those formed on the fovea. (3) When the images of an object do not fall on identical points, one of the points on which they do fall may be occupied with the images of other objects, some of which may be so boldly marked as to enter into conflict with the extra image and to suppress it. (4) And, lastly, the physiological 'identical point' is not a geometrical point, but an area which increases in size in the more peripheral zones of the retina, so that images which lie wholly or in chief part within two corresponding areas practically coincide.

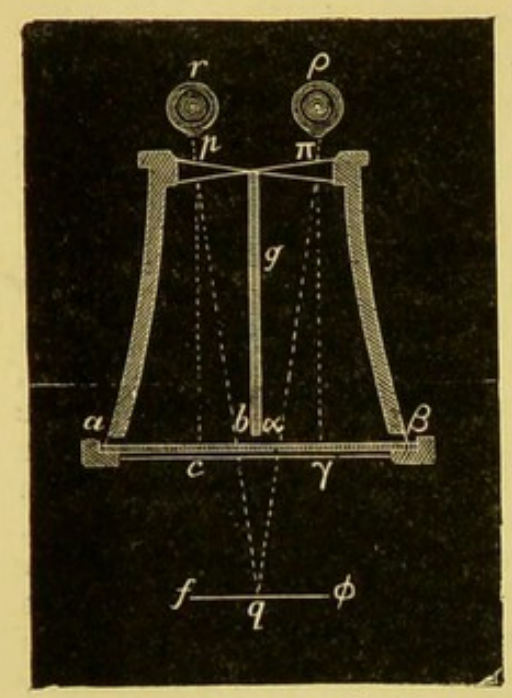


FIG. 306.—BREWSTER'S STEREOSCOPE.

π and π are prisms, with their refracting angles turned towards each other. The prisms refract the rays coming from the points *c*, γ of the pictures *ab* and αβ so that they appear to come from a single point *q*. Similarly, the points *a* and α appear to be situated at *f*, and the points *b* and β at Φ.

Stereoscopic Vision.—Although the retinal image is a projection of external objects on a surface, we perceive not only the length and breadth, but also the depth or solidity of the things we look at. When we look directly at the front of a building, the impression as to its form is the same whether one or both eyes be used, although with a single eye its distance cannot be judged so accurately. But when we view the building from such a position that one of the corners is visible, we obtain a more correct impression of its depth with the two eyes. This is partly due to the fact that to fix points at different distances from the eyes the visual lines must be made to converge more or less, and of the amount of this convergence we are conscious through the contraction of the muscles which regulate it. But there is another element involved. When the two eyes look at a uniformly-coloured plane surface, the retinal image is precisely the same in both. But when the two eyes are directed to a solid object, say a book lying on a table, the picture formed on the left retina differs slightly from that formed on the right, for the left eye sees more of the left side of the book, and the right eye more of the right side.

That there is a close connection between uniformity of retinal

images and impression of a plane surface on the one hand, and difference of retinal images and impression of solidity on the other, is proved by the facts of stereoscopy. It is evident that if an exact picture of the solid object as it is seen by each eye can be thrown on the retina, the impression produced will be the same, whether these images are really formed by the object or not. Now, two such pictures can be produced with a near approach to accuracy by photographing the object from the point of view of each eye. It only remains to cast the image of each picture on the corresponding retina, while the eyes are converged to the same extent as would be the case if they were viewing the actual object. This is accomplished by means of a stereoscope (Fig. 306).

It is found that the resultant impression is that of the solid object. It is impossible to reconcile this with the doctrine of strictly identical points. A pair of identical pictures gives with the stereoscope not the impression of a solid, but of a plane surface. If the relative position of any two points differs in the two pictures, the blended picture has a corresponding point in relief. So great is the delicacy of this test that a good and a bad banknote will not blend under the stereoscope to a flat surface, and the method may be actually used for the detection of forgery.

When the pictures are interchanged in the stereoscope so that the image which ought to be formed on the right retina falls on the left, and that which is intended for the left eye falls on the right, what were projections before become hollows, and what were hollows stand out in relief. The pseudoscope of Wheatstone is an arrangement by which each eye sees an object by reflection, so that the images which would be formed on the two retinæ, if the object were looked at directly, are interchanged, with the same reversal of our judgments of relief.

Visual Judgments.—We say *judgments* of relief; for what we call seeing is essentially an act that involves intellectual processes. As the retina is anatomically and developmentally a projection of the brain pushed out to catch the waves of light which beat in upon the organism from every side, so physiologically retina, optic nerve and visual nervous centre are bound together in an indissoluble chain. We cannot say that the retina sees, we cannot say that the optic nerve sees—the optic nerve in itself is blind—we cannot say that the visual centre sees. The ethereal waves falling on the retina set up impulses in it which ascend the optic nerve; certain portions of the brain are stirred to action, and the resulting sensations of light springing up, we know not where, are elaborated, we know not how (by processes of which we have not the faintest guess), into the perception of what we call external objects—trees, houses, men, parts of our own bodies, and into judgments of the relations of these things among themselves, of their distance and movements.

A child learns to see, as it learns to speak, by a process, often unconscious or subconscious, of 'putting two and two together.' The musical sounds united and terminated by noises which make up the spoken word 'apple' are gradually associated in its mind with the

visual sensation of a red or green object, the tactile sensation of a smooth and round object, and the gustatory and olfactory sensations which we call the taste or flavour of an apple. And as it is by experience that the child learns to label this bundle of sensations with a spoken, and afterwards with a written name, so it is by experience

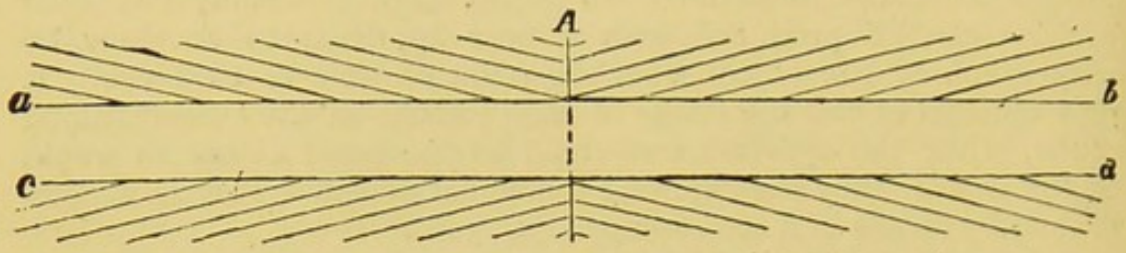


FIG. 307.—ILLUSION OF PARALLEL LINES (HERING)

that it learns to group the single sensations together, and to make the induction that if the hand be stretched out to a certain distance and in a certain direction (*i.e.*, if various muscular movements, also associated with sensations, be made), the tactile sensation of grasping a smooth round body will be felt, and that if the further muscular movements involved in conveying it to the mouth be carried out, a sensation agreeable to the youthful palate will follow. At length the child comes to believe, and, unless he happens to be specially instructed, carries his belief with him to his grave, that when he looks at an apple he sees a round, smooth, tolerably hard body, of definite size and colour; while in reality all that the sense of sight can inform him of is the difference in the intensity and colour of the light falling on his retina when he turns his head in a particular direction.

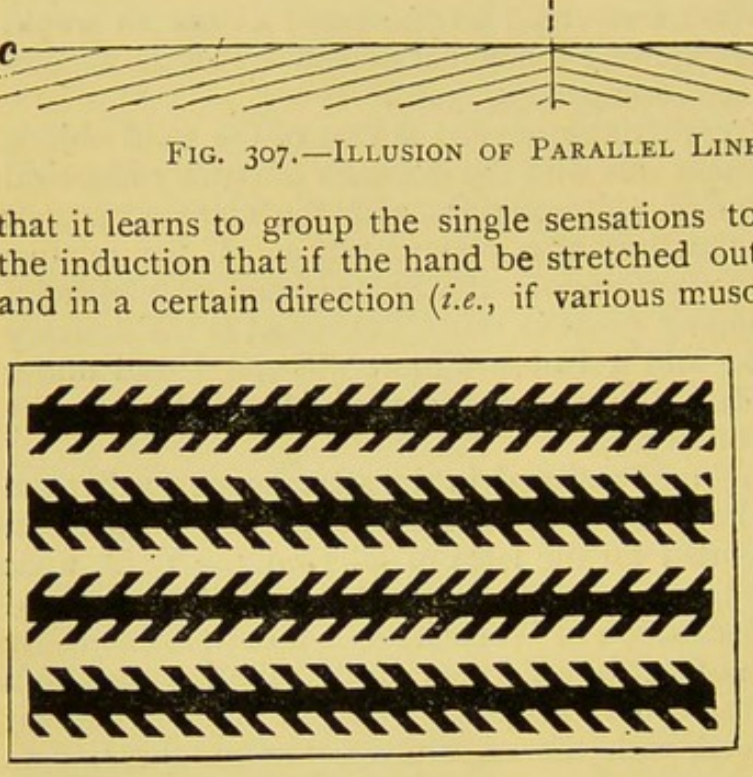


FIG. 308.—ILLUSION OF PARALLEL LINES (ZÖLLNER).

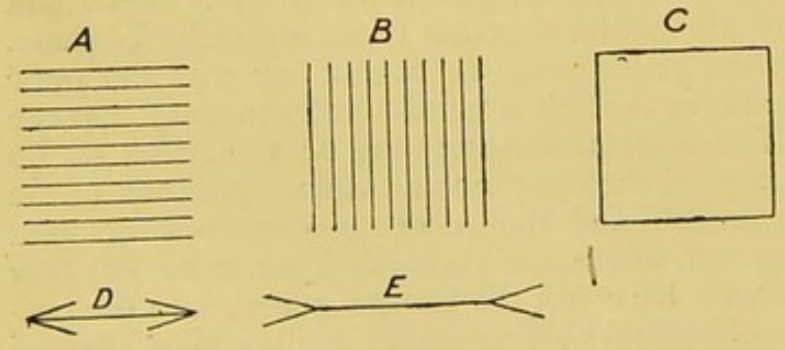


FIG. 309.—ILLUSIONS OF SPACE-PERCEPTION.

An interesting illustration of the rôle of experience in shaping our visual judgments is found in the sensations of persons born blind and relieved in after-life by operation. A boy between thirteen and fourteen years of age, operated on by Cheselden, thought all the objects he looked at touched his eyes. 'He forgot which was the dog and

which the cat, but catching the cat (which he knew by feeling), he looked at her steadfastly and said, "So, Puss, I shall know you another time." Pictures seemed to him only parti-coloured planes; but all at once, two months after the operation, he discovered they represented solids.' Nunnely, perhaps remembering the dictum of Diderot, true as it is in the main, though tinged with the exaggeration of the *Encyclopédie*, that 'to prepare and interrogate a person born blind would not have been an occupation unworthy of the united talents of Newton, Des Cartes, Locke and Leibnitz,' made an elaborate investigation in the case of a boy nine years old, on whom he operated for congenital cataract of both eyes, and, what is of special importance, instituted a set of careful experiments and interrogations *before* the operation, so as to gain data for comparison. Objects (cubes and spheres) which before the operation he could easily recognise by touch were shown him afterwards, but although 'he could at once perceive a difference in their shapes, he could not in the least say which was the cube and which the sphere.' It took several days, and the objects had to be placed many times in his hands before he could tell them by the eye. 'He said everything touched his eyes, and walked most carefully about, with his hands held out before him to prevent things hurting his eyes by touching them.'

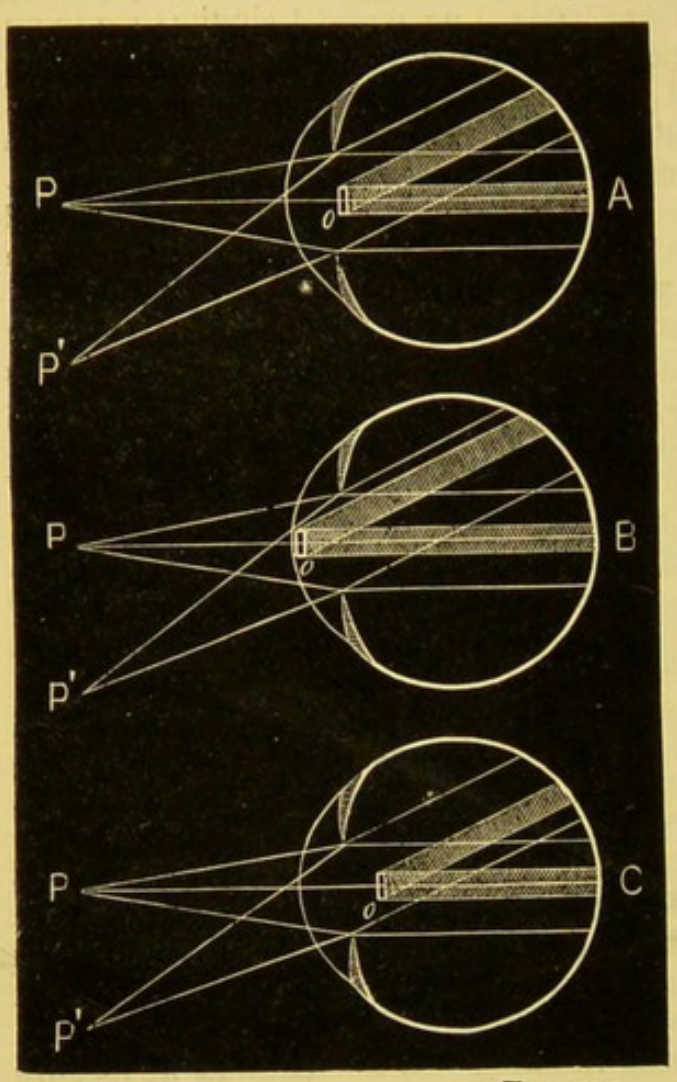
Many other illustrations might be given of the fact that 'seeing' is largely an act of reasoning from data which may sometimes mislead.

Thus in Figs. 307 and 308 the long horizontal lines are really parallel, but do not appear so owing to the confusion of judgment produced by the short sloping lines.

In Fig. 309 the spaces covered by A, B, and C are equal squares, but A appears taller than B, and C smaller than either A or B. In the same figure the lines D and E are of the same length, but E seems considerably longer than D.

The **apparent size and form** of an object is intimately related to the size, form, and sharpness of its image on the retina. We are, therefore, able to discriminate with great precision the unstimulated from the excited portions of that membrane, especially in the fovea centralis, and also the degree of excitation of neighbouring excited parts. But instead of localizing the image on the retina as we localize on the skin the pressure of an object in contact with it, we project the retinal image into space, and see everything outside the eye. In vision, in fact, we have no conception of the existence of either retina or retinal image; and even the shadows of objects within the eye are referred to points outside it. Thus, for instance, an opacity or a foreign body in any of the refractive media—and no eye is entirely free from relatively opaque spots—can be detected, and its position determined by the shadow which it casts on the retina when the eye is examined by a pencil of light proceeding from a very small point. Let a diaphragm with a small hole in it be placed in front of the eye at such a distance that a pencil diverging from the hole will pass through the vitreous humour as a parallel beam, equal in cross-section to the pupil (Fig. 310), and let the aperture be illuminated by focussing on it the light of a lamp placed behind a screen. The

proper position of the hole will obviously be that of the anterior principal focus of the eye, *i.e.*, the point at which parallel rays passing from the vitreous into the lens and then out of the eye would be focussed. This method of examination of the eye is, therefore, called *focal illumination*. Opaque bodies in the vitreous humour will cast shadows on the retina equal in area to themselves. The shadows of opacities in the lens and in front of it will be somewhat larger than the bodies themselves, since the latter intercept rays which are still diverging;



In A the opaque body *o* is in the plane of the pupil. The position of the shadow relatively to the bright field is not altered when the illuminating pencil is focussed at P′ instead of P. In B the opaque body is in front of the plane of the pupil. When P is lowered to P′, the shadow moves towards the upper edge of the bright field, and *appears* to move downwards in the visual field. When P is raised, the shadow moves towards the lower edge of the bright field, and appears to move upwards. In C the opaque body is behind the plane of the pupil. When P is moved downwards to P′, the shadow moves towards the lower edge of the bright field, and appears to the person under observation to move upwards, and *vice-versâ* when P is moved upwards. The farther the opaque body is from the pupil, the greater is the apparent movement, or parallax, of its shadow for a given movement of the source of light.

FIG. 310.

but since the greater part of the refraction of the eye occurs at the anterior surface of the cornea, it is only the shadows of objects on the front of the cornea, such as drops of mucus, which will be much magnified. Fig. 310 shows diagrammatically how the shadows shift their position within the bright field when the direction of the illuminating beam is altered. Generally opacities in the vitreous humour are movable, in the lens not.

Purkinje's Figures.—As was first pointed out by Purkinje, the shadows of the bloodvessels in the retina itself, and even of the corpuscles circulating in them, although neglected in ordinary vision, may be recognised under suitable conditions, a conclusive proof that the sensitive layer must lie behind the vessels (p. 812).

If a beam of sunlight is concentrated on the sclerotic as far as possible from the margin of the cornea, and the eye directed to a

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dark ground, the network of retinal bloodvessels will stand out on it. Another method is to look at a dark ground while a lighted candle, held at one side of the eye at a distance from the visual line, is moved slightly to and fro. In the first method, a point of the sclerotic behind the lens is illuminated, and rays passing from it across the interior of the eyeball in every direction cast shadows of the vessels of the retina on its sensitive layer. In the second method, the image of the flame formed on the retina by rays falling obliquely through the pupil becomes in the general darkness itself a source of light, by interrupting the rays from which the retinal vessels form shadows. The distance of the sensitive from the vascular layer may be approximately calculated by measuring the amount by which the shadows change their position, when the position of the illuminated point of the sclerotic is altered. The nearer a vessel lies to the sensitive layer, the smaller must be the angle through which the apparent position of its shadow moves for a given movement of the spot of light. In this way it has been calculated that the sensitive layer is about 0·2 to 0·3 mm. behind the stratum which contains the bloodvessels. This corresponds sufficiently well with the position of the layer of rods and cones, which all other evidence shows to be the portion of the retina actually stimulated by light. The shadows

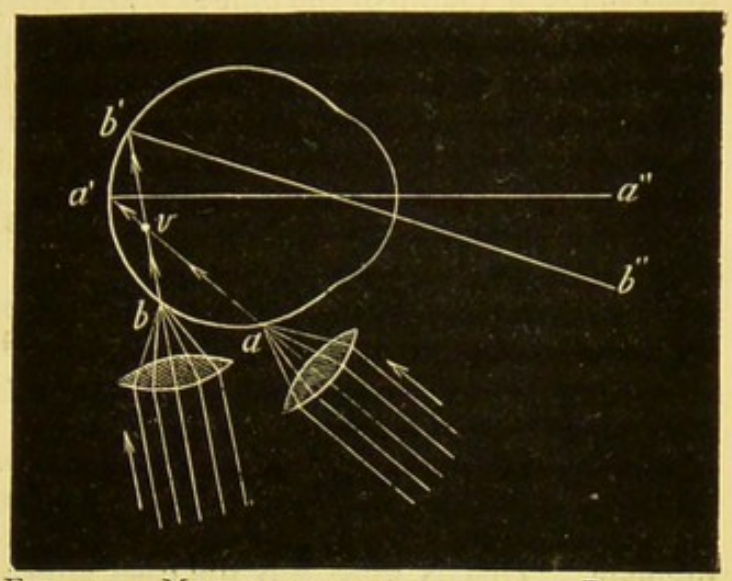

FIG. 311.—METHOD OF RENDERING THE RETINAL BLOODVESSELS VISIBLE BY CONCENTRATING A BEAM OF LIGHT ON THE SCLEROTIC.

From the brightly illuminated point of the sclerotic, a, rays issue, and a shadow of a vessel, v, is cast at a'. It is referred to an external point a'' in the direction of the straight line joining a' with the nodal point. When the light is shifted so as to be focussed at b, the shadow cast at b' is referred to b'', *i.e.*, it appears to move in the same direction as the illuminated point of the sclerotic.

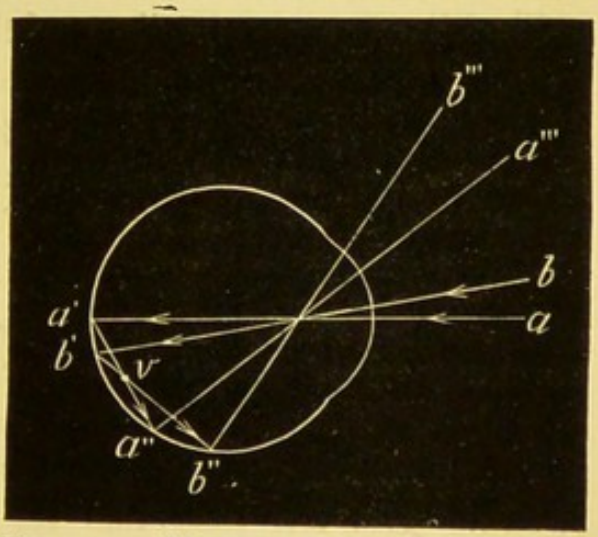

FIG. 312.—METHOD OF RENDERING THE BLOODVESSELS OF THE RETINA VISIBLE BY OBLIQUE ILLUMINATION THROUGH THE CORNEA.

Light from a candle at a illuminates a', and rays proceeding from a' cast a shadow of the bloodvessel v at a'', which is referred to a'''. When a is moved to b, the shadow on the retina moves to b'', and the shadow in the visual field of the illuminated eye to b'''.

of the blood-corpuscles in the retinal vessels may be rendered visible by looking at a bright and uniformly illuminated ground, like the milk glass shade of a lamp or the blue sky, and moving the slightly separated fingers or a perforated card rapidly before the eye. From the rate of their apparent movement, Vierordt calculated the velocity of the blood in the retinal capillaries at 0·5 to 0·9 mm. per second. One reason why the shadows of these intra-retinal structures do not appear in ordinary vision seems to be their small size. The retinal vessels are in reality only vascular threads; the thickest branch of the central vein is not $\frac{1}{25}$ mm. in diameter. The apex of the cone of complete shadow (umbra) cast by a disc of this size, at a distance of 20 mm. from a pupil 4 mm. wide, would lie only $\frac{1}{5}$ mm. behind the disc—that is to say, the umbra of the retinal vessels would not reach the layer of the rods and cones at all, and only the penumbra, or region of relative darkness, would fall upon it.

When the eyes, after being closed for some time, are suddenly opened, the branches of the retinal vessels may be seen for a moment. This is especially the case after sleep; and a good view of the phenomenon may be obtained by looking at a white pillow or the ceiling immediately on awaking. If the eyes are kept open for a few seconds, the branching pattern fades away; if they are only allowed to remain open for an instant, it may be seen many times in succession. The main vessels appear to radiate out from a central point. But their actual junction there is not seen, since it lies in the optic disc or blind spot.

The Blind Spot.—The fibres of the optic nerve are insensible to light; light only stimulates them through their end-organs. This can be proved by directing by means of an ophthalmoscope a beam of light upon the optic disc, where the true retinal layers do not exist. The person experimented on has no sensation of light when the beam falls entirely upon the disc; when its direction is shifted so that it impinges upon any other portion of the retina, a sensation of light is at once experienced. The blind spot is not recognised in ordinary vision, for (1) the two optic discs do not correspond. The left disc has its corresponding points on a sensitive part of the right retina, and the right disc on a sensitive part of the left retina; and the consequence is that in binocular vision the objects whose images are formed on the corresponding points fill up the blind spots. (2) The optic disc does not lie in the line of direct, and therefore distinct, vision. The eye is constantly moving so as to bring the surrounding objects successively on the fovea centralis; and the gap which the blind spot makes in the visual field

of a single eye is thus more easily neglected. In any case we ought not to see it as a dark spot, for darkness is only associated with the absence of excitation in parts of the retina capable of being excited by light. There is no more reason why the optic discs should appear dark than there is for our having a sensation of darkness behind us when we are looking straight in front. And since the experience of our other senses, the sense of touch, for example, tells us that the objects we look at do not in general have a gap in the position corresponding to the part of the image that falls on the blind spot, we see, so to speak, across the spot.

By **Mariotte's experiment**, however, the existence of the blind spot can not only be demonstrated, but its size determined and its boundaries mapped out. Let the left eye be closed, and fix with the right the small cross; then, if the eye be moved towards or away from the paper, keeping the cross fixed all the time, a position will

FIG. 313.—MARIOTTE'S EXPERIMENT.

be found in which the white disc disappears altogether. In this position its image falls on the blind spot. (See Practical Exercises, Figs. 332, 333.)

Relation of the Rods and Cones to Vision.—We have more than once referred to the rods and cones as the sensitive layer of the retina. It is now necessary to develop a little more the evidence in favour of this statement. And at the outset, since the sensitive layer has been shown to lie behind the plane of the retinal bloodvessels, the only competitors of the rods and cones are the external nuclear layer and the pigmented epithelium. The nuclear layer may be at once excluded, because in the fovea centralis, where vision is most distinct, it becomes very thin and inconspicuous.

The layer of pigmented hexagonal cells, or at least their pigment, cannot be essential to vision, for albino rats,

rabbits and men, in whose eyes pigment is absent, can see. In man and most mammals there are cones, but no rods in the yellow spot and fovea centralis; the relative proportion of rods increases as we pass out from the fovea towards the ora serrata. But this does not enable us to analyze the bacillary layer into sensitive cones and non-sensitive rods, for on the rim of the retina, which is still sensitive to light, there are only rods; in the bat and mole there are no cones even in the yellow spot, in the rabbit very few. Reptiles possess only cones over the whole retinal surface, and birds, true to their reptilian affinities, have everywhere more cones than rods, as have also fishes.

One of the most serious difficulties in the way of understanding how a ray of light can set up an excitation in a rod or cone is the transparency of these structures. An absolutely transparent substance—that is, a substance which would allow light to traverse it without the least absorption—would, after the passage of a ray, remain in precisely the same state as before; its condition could not be altered by the passage of the light unless some of the energy of the ethereal vibrations was transferred to it. But an absolutely transparent body does not exist in Nature; and it is not necessary to suppose that all the energy required to stimulate the end-organs of the optic nerve comes from the luminous vibrations. These may, and probably do, act by setting free energy stored up in the retina, just as the touch of a child's hand could be made to fire a mine, or launch a ship, or flood a province. Some have looked upon the transverse lamellæ into which the outer members of the rods and cones can be made to split as an arrangement for reflecting back the light to the inner members, and have compared them to a pile of plates of glass, which, transparent as it is, is a most efficient reflector. It is even possible, although here we are already treading the thin air of pure speculation, that the light may be polarized in the process of reflection, and that the rods and cones may be less transparent to light polarized in certain planes than to unpolarized light.

As to the nature of the transformation undergone by the ethereal vibrations in the rods and cones, various theories

have been formed. Some have supposed that the absorbed light-waves are transformed into long heat-waves, and that the endings of the optic nerve are thus excited by thermal stimuli. This hypothesis has so little evidence in its favour that it is perhaps an unjustifiable waste of time even to mention it. It is ruled out of court by the mere fact that the long radiations of the ultra red, filtered from luminous rays by being passed through a solution of iodine, and focussed on the eye by a lens of rock-salt, produce not the slightest sensation of light, although they are by no means all absorbed in their passage through the dioptric media. Again, it has been suggested that the energy of the waves of light is first transformed into electrical energy, and that the visual stimulus is really electrical. In support of this view it has been urged that light undoubtedly causes (p. 647) an electrical change in the retina and optic nerve. But, as has more than once been pointed out, an electrical change is the token and accompaniment of the activity of the excitable tissues in general; and all that the currents of action of the retina show is that light excites the retina—a proposition which nobody who can see requires an objective proof of, and which does not carry us very far towards the solution of the problem how that excitation is brought about. Then there is the photo-mechanical theory, according to which the pigmented epithelial cells of the retina, altering their shape and volume under the stimulus of light, press upon the rods and cones, and thus mechanically stimulate them. Lastly, there is the photo-chemical theory, which supposes that some chemical change produced in the rods and cones under the influence of light sets up impulses in them which ascend the optic nerve. This is the most probable of all the theories, notwithstanding the fact that the discovery by Boll of the famous visual purple or rhodopsin, which at first seemed likely to place it upon a sure foundation, has, since the elaborate investigations of Kühne, lost much of its significance in this regard. But although the visual purple has thus disappointed the hopes excited in sanguine minds, and has not explained, or even lessened, the mystery of vision, its discovery is in itself so interesting and so sugges-

tive as a basis for future work, that a short account of the properties of the substance cannot be omitted here.

FIG. 314.—OPTOGRAM.

Part of retina of rabbit, the eye of which had been directed to an illuminated plate of glass covered with strips of black paper.

Visual Purple.—If the eye of a frog or rabbit, which has been kept in the dark, be cut out in a dimly-lighted chamber or in a chamber illuminated only by red light, and the retina removed, it is seen, when viewed in ordinary light, to be of a beautiful red or purple colour. Exposed to bright light, the colour soon fades, passing through red and orange to yellow, and then disappearing altogether. The yellow colour is due to the formation of another pigment, visual yellow; the preceding stages are due to the intermixture of this visual yellow with the unchanged visual purple in different proportions. With the microscope it may be seen that the pigment is entirely confined to the outer segment of the rods, where it exists in most vertebrate animals. It may be extracted by a watery solution of bile-salts, and the properties of the pigment in solution are very much the same as its properties *in situ;* light bleaches the solution as it does the retina. Examined with the spectroscope, the solution shows no definite bands, but only a general absorption, which is very slight in the red, and reaches its maximum in the yellowish-green. In accordance with this, it is found that of all kinds of monochromatic light the yellowish-green rays bleach the purple most rapidly, the red rays most slowly.

If a portion of the retina is kept dark while the rest is exposed to light, only the latter portion is bleached. And when the image of an object possessing well-marked contrasts of light and shadow (*e.g.*, a glass plate with strips of black paper pasted on it at intervals, or a window with dark bars) is allowed to fall on an eye otherwise protected from light, the pattern of the object is picked out on the retina in purple and white A veritable photograph or 'optogram' may thus be formed even on the retina of a living rabbit; and if the eye be rapidly excised, the picture may be 'fixed' by a solution of alum, and thus rendered permanent.

These facts certainly suggest that light falling on the retina may cause in some sensitive substance or substances chemical changes, the products of which stimulate the endings of the optic nerve, and set up the impulses that result in visual sensations.

The visual purple cannot itself be such a substance, for it is absent from the cones of all animals and the rods of some.

Frogs and rabbits can undoubtedly see at a time when, by continued exposure to bright sunlight, the purple must have been completely bleached. And although the absence of the pigment in the eye of the bat might seem to afford a ready explanation of the proverbial 'blindness' of that animal, such a hasty deduction would be at once corrected by the fact that birds with as sharp vision as the pigeon are equally devoid of visual purple. The pigmented retinal epithelium is undoubtedly sensitive to light, and has important relations to the formation of the visual purple. When the eye is exposed to light, the pigmented cells push down processes between the rods. In the dark they draw them back again, so that while it is easy to separate the retina without the pigmented layer from the eye of an animal kept in the dark, the hexagonal epithelium always adheres to a retina which has shortly before death been acted upon by light. The precise meaning of these changes of form in the pigmented cells is unknown. Some have supposed that they alone contain the essential visual substance, and that, by mechanical pressure on the rods and cones caused by alterations in their form or bulk under the stimulus of light, they set up impulses in the optic nerve. By others it has been plausibly urged that in bright light the processes that stretch in among the rods serve as insulators to confine the excitation, by preventing the lateral passage of scattered light from one element to another. But it may be that the movements are related rather to the formation of photo-chemical substances to act as stimuli to the end-organs of the optic nerve.

The pigmented epithelium is known to be concerned in the regeneration of the visual purple. When a frog is curarized, œdema occurs between the retina and the choroid, so that the former membrane is separated from the hexagonal epithelium. If the frog is now exposed to sunlight till the visual purple is bleached, and the retina then taken out and placed in the dark, no regeneration of the pigment takes place. When the same experiment is repeated on a non-curarized frog, the visual purple is restored in the dark, and may be seen under the microscope in the rods. The only difference in the two experiments is that in the latter the pigmented epithelium adheres to the retina, and it must therefore have a hand in the regeneration of the pigment. Even the visual purple of a retina from

which the epithelium has been detached will, after being bleached, be restored if the retina is simply laid again on the epithelial surface. And it does not seem to be the black pigment of the hexagonal cells which is the agent in this restoration, for it takes place in the pigment-free retinæ of albino rabbits or rats. Even a retina isolated from the pigmented epithelium, and then bleached, may, to a certain extent, develop new visual purple in the dark. This is even true when it has been kept in the dark in a saturated solution of sodium chloride, and is then, after washing with normal saline, bleached by light. Here the regeneration of the pigment cannot be the result of vital processes, but must be due to chemical changes in products formed from the original pigment by the action of light. No such regeneration takes place in a retina which, after having been bleached *in situ*, is removed without the pigmented epithelium and placed in the dark; and the only probable explanation of the difference is that in this case the photo-chemical substances from which visual purple can be formed have been absorbed into the circulation, and have so escaped.

The inner segments of the cones of certain animals (birds, reptiles, amphibia, and some fishes) contain globules of various colours, ranging over almost the whole spectrum, and including, besides, the non-spectral colour, purple. The globules are composed chiefly of fat with the pigments (chromophanes, as they have been called) dissolved in it. The function of these globules is unknown. They cannot be concerned in colour vision, or, at least, they cannot be essential to it, for in the human retina they do not exist.

The yellow pigment of the macula lutea does not belong to the layer of rods and cones; it only exists in the external molecular layer and the layers in front of it; in the fovea centralis it is absent.

Time necessary for Excitation of the Retina by Light—Fusion of Stimuli.—Whatever the exact nature of retinal excitation may be, it is called forth by exceedingly slight stimuli. A lightning flash, although it may last only $\frac{1}{1,000,000}$th of a second, lasts long enough to be seen. A beam of light thrown from a rotating mirror on the eye stimulates when it only acts for $\frac{1}{8,000,000}$th of a second. The minimum stimulus in the form of green light corresponds, as we have already seen (p. 593), to a quantity of work equivalent to no more than $\frac{1}{10^8}$ erg, that is, about $\frac{1}{10^{10}}$ gramme-millimetre, or $\frac{1}{10^7}$ milligramme-millimetre, which is the work done by $\frac{1}{10,000,000}$th of a milligramme in falling through a millimetre; and it cannot be doubted that a portion even of this Lilliputian bombardment is wasted as heat. So quickly, too, is the stimulus followed by the response that no latent period has as yet ever been measured. It is certain, however, that there is a latent period, as surely as there is a latent period in the excitation of a naked nerve-trunk, although this also has never been experimentally detected. The analogies, in fact, between a muscular contraction and a retinal excitation are numerous

and close. Like the muscle, the retina seems to possess a store of explosive material which the stimulus serves only to fire off. The retina, like the muscle, is exhausted by its activity, and recovers during rest. Like the muscle curve, the curve of retinal excitation rises not abruptly, but with a measurable slowness to its height, and when stimulation is stopped, takes a sensible time to fall again, the retinal impression outlasting the luminous stimulus by about one-eighth of a second. With comparatively slow intermittent stimuli the retinal, like the muscle curve, flickers up and down. When the rate of stimulation is increased, the steady contraction of the tetanized muscle is analogous to the fusion of the individual stimuli by the tetanized retina (or retino-cerebral apparatus) into a continuous sensation of light, such, *e.g.*, as the bright 'trail' of a falling star, or the fiery circle traced in the air when a firebrand is rapidly whirled round. But the maximum retinal excitation which a stimulus of given strength can call forth depends much more closely upon the time during which the stimulus acts than the maximum contraction does upon the length of the muscular stimulus.

As the strength of the light increases in geometrical progression, the time during which it must act in order to produce its maximum effect decreases approximately in arithmetical progression (Exner). For light of moderate intensity this time is about $\frac{1}{4}$ second. Since for complete fusion the stimuli must follow each other at a much more rapid rate than four in the second, the intensity of the resultant sensation is always less when a succession of similar stimuli are fused than when one of the stimuli is allowed to produce its maximum effect.

If the time of each stimulus is equal to the interval during which there is no stimulation, the sensation, when complete fusion has been reached, is the same as would be produced by a constant light of half the strength employed. And, in general, if m be the proportion of the time during which the eye is stimulated by a light of intensity I, and n the proportion of the time during which it is not stimulated, the resultant impression is the same as that which would be produced by an uninterrupted light of intensity $\left(\frac{m}{m+n}\right)I$. This is **Talbot's law**, which may be expressed without the aid of symbols thus: *When a light of given intensity is allowed to act on the eye at intervals so short that the impressions are completely fused, the resultant sensation is independent of the absolute length of each flash, and is proportional only to the fraction of the whole time which is occupied by flashes and to the intensity of the light.* Talbot's law may be readily demonstrated by means of a rotating disc with alternate white and black sectors (Fig. 315), so arranged that the same proportion of the circumference of each of the three concentric zones is black.

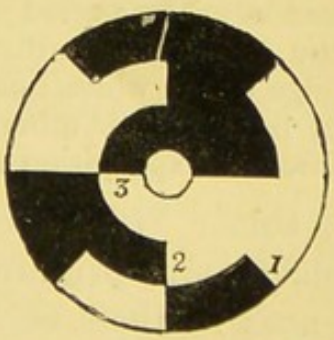

FIG. 315.—DISC FOR DEMONSTRATING TALBOT'S LAW.

When the rotation is sufficiently rapid to give complete fusion (say 20 to 30 times a second), the whole disc

appears equally bright. However much the rate of rotation is now increased, no further change occurs. It has been shown that even for stimuli as short as the $\frac{1}{8000000}$th of a second, repeated at interval of $\frac{1}{170}$th second, Talbot's law holds good. So that not only does a flash so inconceivably brief affect the retina, but it sets up changes which last for a measurable time. For intense stimuli Talbot's law ceases to be true: the field appears brighter than it should be (Grünbaum).

Two chief theories have been proposed to account for the fusion of intermittent retinal stimuli: (1) The *persistence* theory, according to which the excitatory process in the retina remains for a short time at the maximum reached when the light ceases to act. Steady fusion is supposed to be obtained when the interval between successive stimuli does not exceed this time. (2) The theory of Fick, who maintains that as soon as the light is withdrawn the retinal excitation begins to sink, at first rapidly, then more gradually. As the rate of stimulation is increased the time allowed for the decline of the excitation is, of course, correspondingly shortened, and ultimately the oscillations become so small that a continuous smooth sensation results. Fick's theory appears to explain the phenomena best.

The experiments of Charpentier have shown that the retina when stimulated has a natural tendency to enter into oscillations at the rate of about 36 in the second, so that the effect of a flash of light when it falls on a retinal area is not a single excitation which rises smoothly to its maximum and then declines smoothly to zero, but a series of swings which die away like the vibrations of an elastic body. This may be demonstrated by slowly rotating a well-illuminated disc, one quadrant of which is white and the rest black, while the eye is kept fixed on the centre. A black band, or rather sector, running but from centre to circumference, will be seen in the white quadrant a little behind the border of it which first passes the eye. This band may be succeeded by one or more fainter black bands placed at regular intervals in the white portion of the disc. The explanation is this. At the moment when the image of the advancing edge of the white quadrant falls upon the retina it is excited, and we get the sensation of white. Then comes a swing in the opposite direction which gives rise to the first black band, and succeeding swings cause the other bands. The period of the oscillatory process can be calculated from the speed of the disc, and the distance of the first band from the edge of the white quadrant. The well-known fact that a single flash of lightning, or other intense stimulus, may appear as two flashes, finds its explanation in these retinal oscillations.

Colour Vision.—Besides differences in the distance, size, shape, and brightness of objects, the eye recognises differences in their colour; and we have now to consider the physical and physiological differences on which these depend.

Colours may differ from each other—(1) In *tone or hue*, *e.g.*, red, yellow, green. (2) In degree of *saturation or fulness or purity*, *i.e.*,

in the degree in which they are free from admixture with white light; *e.g.*, a 'pale' or 'light' blue is a blue mixed with much white light, a 'deep' or 'full' blue with little or none. (3) In *brightness or intensity*, *i.e.*, in the amount of the light coming from unit area of the coloured object. Thus, a 'dark' red cloth sends comparatively little light to the eye, a 'bright' red cloth sends a great deal.

When a beam of sunlight falls into the eye, a sensation of 'white light' results. When a prism is placed before the eye, the sensation is entirely different; we see a spectrum running up from red through green to violet, with a multitude of intermediate shades, the eye being able to distinguish in the solar spectrum at least one thousand different hues (Aubert). What, then, has happened? Physically, nothing more has taken place than a rearrangement of the rays in the beam of white light. A few of them may have been lost by reflection, but upon the whole the beam is made up of exactly the same constituents as before; only the rays are now arranged in the precise order of their refrangibility, the more refrangible, which are also those of shortest wave-length, being displaced more towards the base of the prism than the longer and less refrangible rays. Instead of the long and short rays falling together on the same elements of the retina, as they did in the absence of the prism, they now fall, if proper precautions have been taken to secure a pure spectrum, in regular order from one side to the other of the portion of retina on which the image is formed. The physical condition, then, of our sensations of the prismatic colours is, that rays of approximately the same wave-length should fall unmixed with other rays upon the retinal elements. Rays of a wave-length of $760_{\frac{\mu}{1000}}$ to $650_{\frac{\mu}{1000}}$ give the sensation of red; from $650_{\frac{\mu}{1000}}$ to $590_{\frac{\mu}{1000}}$, the sensation of orange; from $430_{\frac{\mu}{1000}}$ to $400_{\frac{\mu}{1000}}$, the sensation of violet, and so on. When rays of all these wave-lengths fall together, in the proportions in which they are present in sunlight, upon the same part of the retina, the resultant physiological effect is very different; we are no longer able to distinguish red, blue, green, etc.; we receive the single sensation of white light. The sensation is a simple one; in consciousness we have no hint that it has a multiple physical cause.

But we find further that it is not necessary for the sensation of white light that waves of every length present in the solar spectrum should be mixed. If rays of wave-length $675\frac{\mu}{1000}$ (which acting alone produce the sensation of red) be mixed in certain proportions, *i.e.*, be allowed to fall on the same part of the retina, with rays of wave-length $496\frac{\mu}{1000}$ which give the sensation of bluish-green), the resultant sensation is also that of white light. And an indefinite number of sets can be combined, two and two, so as to give the same sensation of white. Such colours are called complementary. The following are pairs of complementary colours :

Red and bluish-green.	Yellow and ultramarine-blue.
Orange and cyan-blue.*	Greenish-yellow and violet.

The green of the spectrum has no simple complementary colour ; purple, a mixture of red and violet, may be considered complementary to it. Suppose now that one of a pair of complementary colours is added to the other in greater intensity than is required to give white, the resultant sensation is a colour which has a certain amount of resemblance both to white and to the colour present in excess. Thus, if the two colours are orange and blue, and the blue is present in greater intensity than is necessary to give white, the resultant colour is a whitish or pale blue, or, to use the technical phrase, an unsaturated blue. The more nearly the intensity of the blue rays in the mixed light approaches the proportion necessary to give white, the less saturated is the resultant colour ; the greater the excess of blue, the more nearly does the resultant sensation approach that of the saturated blue of the spectrum. But any non-saturated spectral colour produced by the mixture of two complementary colours may be equally well produced by the mixture of the corresponding spectral colour with a certain quantity of ordinary white light. And it is found that when two spectral colours which are not complementary are mixed together the resultant is not white, but a colour which may be matched by some spectral colour lying between the two, either without addition or plus a larger or smaller quantity

* Cyan-blue is a greenish-blue.

of ordinary white light. From all this it follows that the retina may be excited by an infinite number of different physical stimuli, and yet the resultant sensation may be the same. This leads straight to the conclusion that somewhere or other in the retino-cerebral apparatus simplification, or synthesis, of impressions must take place; and we have to inquire what the simplest assumptions are which will explain all the phenomena. Now, it is not possible, from two spectral colours alone, to produce a sensation corresponding to all the others. By mixing three standard spectral colours, however, in various proportions, we can produce not only

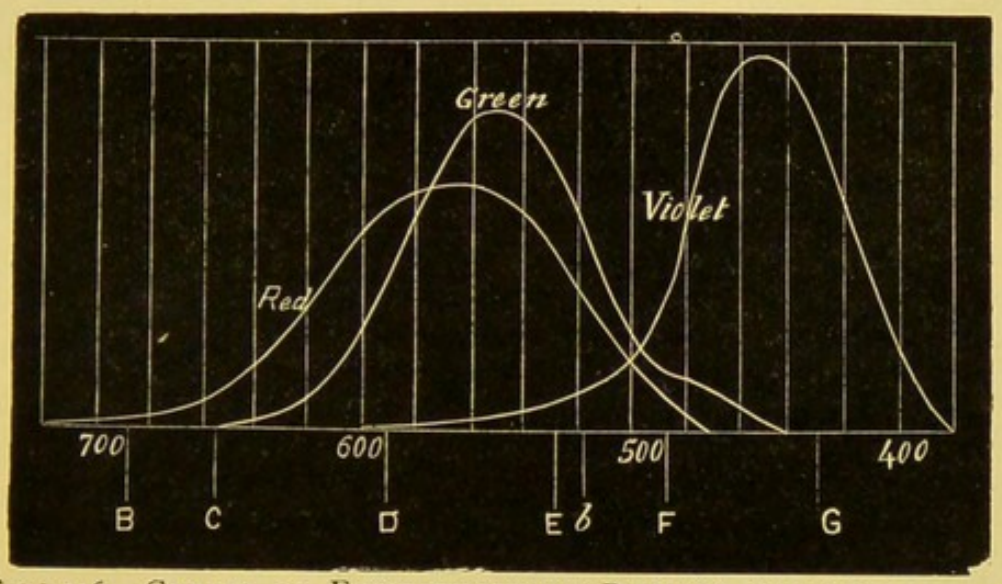

FIG. 316.—CURVES OF EXCITABILITY OF PRIMARY SENSATIONS FROM OBSERVATIONS ON COLOUR MIXTURES (KÖNIG).

The numbers give wave-lengths of the spectrum in millionths of a millimetre.

the sensation of white light, but that of every colour of the spectrum.

Primary Colours.—The simplest assumption we can make, then, is that there are three standard sensations, and that either the retina itself can respond by no more than three distinct modes of excitation to the multiplex stimuli of the luminous vibrations, or that complex impulses set up in the retina are reduced to simplicity because the central apparatus is capable of responding by only three distinct kinds of sensation. Which three sensations we select as fundamental or primary is, to a certain extent, arbitrary. Fick chooses red, green, and blue; most commonly red, green, and violet are accepted as the primary colours. Red, yellow,

and blue, although so long considered the primary colours, from data yielded by the mixture of pigments, will not do; for no possible combination of them will produce either a pure green or white light.

The Young-Helmholtz Theory. — The theory which best explains the facts, and has been most widely accepted, is that of Young, generally called, on account of its adoption and extension by Helmholtz, the **Young-Helmholtz theory.** It assumes that in the retina, or in the retino-cerebral apparatus, there are three kinds of elements *— (1) 'red fibres,' which are chiefly excited by light of comparatively long wave-length (red), to a less extent by light of medium wave-length (green), and to a still less extent by the shortest visible waves (violet); (2) 'green fibres,' mainly excited by medium, but also to a certain extent by long and short waves; (3) 'violet fibres,' chiefly affected by the short vibrations, less by the medium, and still less by the long waves. The curves in Fig. 316 illustrate these relations. It must be carefully remembered that here the word 'fibre' is merely a convenient term to avoid some such cumbrous phrase as 'physiological unit.' There is no ground for believing that an anatomical distinction of three 'fibre' groups can be made in retina, optic nerve, or brain.

This assumption explains the phenomena of colour-mixture to which we have referred above. When all the rays of the spectrum act upon the retina together, the three groups of fibres are about equally excited, and this equal excitation may be supposed to be the condition of the sensation of white light. When the green of the spectrum alone falls on the retina, the green fibres are strongly excited, the other two groups only slightly; this is the relation between the amount of excitation in the three groups which is associated with a sensation of spectral green. When two complementary colours, such as red and bluish-green, fall together on the same portion of the retina, the three fibre groups are excited in the relative proportions associated with the sensation of white light.

* Or, it may be, three kinds of visual substance capable of being acted on by light.

'When the retina is stimulated by a succession of short flashes of white light, that are not completely fused (as when the image of a flame is looked at in a small revolving mirror, or the flame directly viewed through a slit in a revolving disc), the proportion between the amount of excitation in the three hypothetical groups of fibres is not constant, and the resultant sensation is not that of white light. For any given intensity of light, violet preponderates with a certain duration of each stimulus ; with a shorter duration, green ; with a still shorter duration, red.' These phenomena are especially seen at the edges of the image, which is surrounded by coloured fringes. The explanation is that the sensation does not reach its maximum at the same time for different colours, the excitation in the red fibres increasing at first more rapidly than in the green, and in the green more rapidly than in the violet. When the flashes are completely fused, the colour phenomena disappear, and the resultant impression is white, because now the maximum excitation for the given intensity of light and duration of each stimulus is steadily maintained.

The **colour triangle** is a graphic method of representing various facts in colour-mixture, the most important of which are mentioned in the description of Fig. 317.

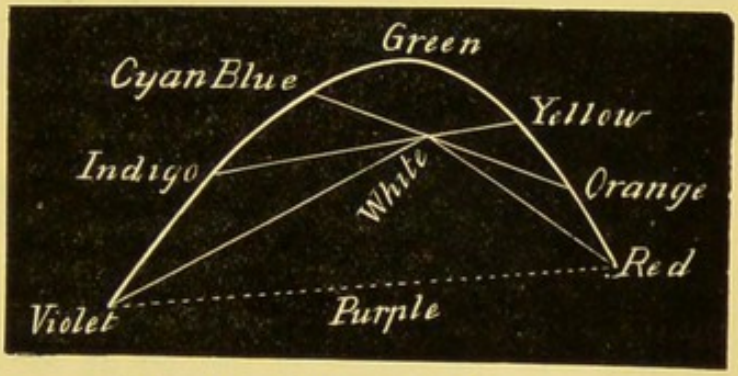

FIG. 317.—COLOUR TRIANGLE.
(In the description the point marked 'White' is referred to as W.)

The chief points to be noted are the following: (1) On the curve the spectral colours are arranged at such distances that the angle contained between straight lines drawn from the point W and intersecting the curve at the positions corresponding to any two colours is proportional to their difference in tone. (2) The distance of any point of the curve from W is proportional to the stimulation intensity of the colour corresponding to it. (If the stimulation intensities of all the colours be represented by proportional weights lying at the corresponding points on the curve, W will be the centre of gravity of the system.) (3) The position of a colour produced by the mixture of any pair of spectral colours is found by joining the corresponding points by a straight line. The mixed colour lies on this line at distances from the two points inversely proportional to the stimulation intensity of the two colours, *i.e.*, it lies in the centre of gravity of the weights representing the two colours. (4) It is a particular case of (3) that the complementary colours are situated at the points where straight lines drawn through W intersect the curve, since W is the centre of gravity corresponding to a pair of colours only when it lies on the straight line joining them. The non-spectral purple is represented by a broken line.

It is a point of great theoretical interest that on the Young-Helmholtz theory the pure spectral colours, although physically saturated (*i.e.*, due to ethereal vibrations of a definite wave-length for each colour), ought not to be physiologically saturated, since they all excite the three fibre groups, although in different degrees. In other words, the red, let us say, of the spectrum ought not to be the purest or fullest red which it is possible to perceive. Now, it is found that

this is really the case. If, for example, we look first at the bluish-green and then at the red of the spectrum, the sensation of red is fuller or more saturated than if we had looked at the red directly. Similarly, if we look first at a small bluish-green square on a black ground, and then at a red ground, we see a more fully saturated square in the middle of the latter. The explanation, on the Young-Helmholtz theory, is that the 'green' fibres being tired before the eye is turned upon the red, the latter colour no longer affects them, or affects them less than it would otherwise do, and therefore the excitation is almost entirely confined to the red fibres in the area fatigued for green. This brings us to the subject of retinal fatigue, and the related phenomena of after-images and contrast.

After-Images.—We have seen that the retinal excitation always takes time to die away after the stimulus is removed. If a white object is looked at, especially when the eye is fresh, for a time not long enough to cause fatigue, and the eye is then closed, an image of the object remains for a short time, diminishing in brightness at first rapidly, then more slowly. This is a positive after-image, and by careful observation it may, under certain conditions, be seen that the positive after-image of a white object, of a slit illuminated by sunlight, for example, undergoes changes of colour as it fades, passing through greenish-blue, indigo, violet, or rose, to dirty orange. On the Young-Helmholtz theory this is explained by the supposition that the excitation does not decline with the same rapidity in the three hypothetical fibre groups. If the object is looked at for a longer time, or if the eye is fatigued, a dark or negative image may be seen upon the faintly-illuminated ground of the closed eyes; but negative after-images may be more easily obtained when the eye, after being made to fix a small white object on a black ground, is suddenly turned upon a white or neutral tint surface.

Here the portion of the retina on which the image of the object is formed may be assumed to be more or less fatigued. And this fatigue will extend to all three kinds of fibres; so that white light of a given intensity will now cause less excitation in this part than in the rest of the retina. It is easy to understand that the negative after-image of a coloured object will be seen, upon a white ground, in the complementary colour, for the fibres chiefly excited by the latter will have been least fatigued. The negative after-images seen when the eye, after receiving the positive impression, is turned upon a coloured ground, vary with the colour of the object and ground in

a manner which can be readily explained as due to fatigue of one or other fibre group.

The phenomena of negative after-images are often included together as examples of successive contrast, the name implying mutual influence of the portions of the retina successively stimulated. We have now to consider simultaneous contrast, often spoken of simply as contrast.

Contrast.—A small white disc in a black field appears whiter, and a small black disc in a white field darker, than a large surface of exactly the same objective brightness. A disc with alternate sectors of white and black, so arranged that the proportion of white to black increases in each zone from centre to circumference, when set in rotation, ought, by Talbot's law, to show sharply marked and uniform rings, of which each is brighter than that internal to it. But each zone *appears* brightest at its inner edge, where it borders on a zone darker than itself, and darkest at its outer edge, where it borders on a brighter zone. The most natural explanation of this is that in the neighbourhood of an excited area of the retina, as well as within the area itself, the excitability is diminished; and the same explanation holds for the contrast phenomena of coloured objects. A small piece of grey paper, *e.g.*, is placed on a green sheet, and the whole covered with translucent tracing-paper. The grey patch appears in the complementary colour of the ground, viz., rose-red (Meyer). Here we may suppose that the fatigue of the group of fibres chiefly excited by the ground colour spreads into the portion of the retina occupied by the image of the grey paper; the white light coming from the latter, therefore, excites mainly the fibres which give the sensation of the complementary colour.

The curious phenomenon of coloured shadows is also an illustration of contrast. They may be produced in various ways. For example, when a lamp is lit in a room in the twilight, before it has yet grown too dark, the shadows cast by opaque objects on a white window-blind are coloured blue. The yellow light of the lamp overpowers the feeble daylight which passes through the blind, and the general ground is yellowish: but wherever a shadow is thrown it appears of a bluish tint in contrast to the yellow ground. Here the only illumination the eye receives from the region occupied by the shadow is the feeble daylight. Falling upon an area in which the fibres chiefly excited by yellow rays are more or less fatigued, it causes a sensation of the complementary colour. As darkness comes on, the shadows become black, for now practically no light at all comes from them.

Helmholtz looked upon simultaneous contrast as a result of false judgment, and not of a change of excitability in parts of the retina bordering on the actually excited parts. For the sake of perspective, it will be worth while to apply this theory by way of illustrating it, to the explanation of the case of contrast we have just been considering, from the other point of view in Meyer's experiment. Helmholtz's explanation of this experiment is as follows: When a coloured surface is covered with translucent paper, the latter appears as a

coloured covering spread over the field. The mind does not recognise that at the grey patch there is any breach of continuity in this covering; it is therefore assumed that the greenish veil extends over this spot too. Now, the grey seen through the translucent white paper is objectively white — *i.e.*, sends to the eye the vibrations which together would give the sensation of white light. But with a green veil in front of it, this could only happen if the really grey patch was of the colour complementary to green — that is, rose-red. The mind, therefore, judges falsely that the patch is red. Hering has severely criticised this theory of Helmholtz as to false judgments; and the weight of evidence certainly seems to be in favour of the view that simultaneous, like successive, contrast is due to the influence of one portion of the retina, or retino-cerebral apparatus, on another.

Hering's Theory of Colour Vision.—The Young-Helmholtz theory of colour vision has not met with universal acceptance. The best-known rival theory is that of Hering, who takes his stand upon the fact that certain sensations of light (red, yellow, green, blue, white, black) do appear to us to be fundamentally distinct from each other, while all the rest are obviously mixtures of these. Accepting these six as primary sensations, he assumes the existence in the visual nervous apparatus of substances of three different kinds, which may be called the black-white, the green-red, and the blue-yellow. Like all other constituents of the body, these substances are broken down and built up again—in other words, undergo disassimilation and assimilation, destructive and constructive metabolism. The sensations of black, of green, and of blue he supposes to be associated with the constructive, and the sensations of white, of red, and of yellow with the destructive, processes in the three substances. The black-white substance is used up under the influence of all the rays of the spectrum, but in different degrees; the smaller the quantity of light falling on the retina, the more rapidly is it restored, and the more intense is the sensation of black. The green-red substance is built up by green rays, broken down by red. The blue-yellow substance is destroyed by yellow rays, restored by blue. When any of the visual substances are consumed at one part of the retina, they are supposed to be more rapidly built up in the surrounding parts, and in this way many of the phenomena of contrast receive an easy and natural explanation.

Sensibility of Different Parts of the Retina.—The perception of colours, like the perception of white light, is not equally distinct over the whole retina. We have repeatedly had occasion to refer to the fovea centralis as the region of most distinct vision; but it would be a mistake to suppose that it is therefore necessarily more sensitive than the rest of the retina. As a matter of fact, when the minimum intensity of white light which will cause an impression at all is determined for each portion of the retina, it is found that the fovea centralis requires a somewhat stronger stimulus than the zone immediately surrounding it. Objects only a little brighter than the general ground on which they lie, *e.g.*, very faint stars, are best seen when the eye is directed a little to one side. This has been attributed to the absence of visual purple from the fovea, the visual purple being supposed to act as a mechanism which 'adapts' the retina for the perception of light of varying intensity. But, with this exception, the sensibility of the retina diminishes steadily from centre to periphery, both for white and for coloured light. König has, indeed, upheld the paradoxical view that the fovea is absolutely blind for blue rays, supporting this assertion by two main experiments: (*a*) that when a number of feebly illuminated blue points are looked at, those that fall on the fovea disappear; (*b*) that when the moon is examined through a blue glass, her image is blotted out as soon as it falls on the fovea. But, as Gad has pointed out, the moon's image is of such dimensions that it would lie well within the fovea, and there ought, therefore, to be no difficulty in getting it to disappear if König's theory were true. Yet König himself admits that his second experiment is difficult, and succeeds only under special conditions. Hering, too, seems to have shattered König's first argument by showing that the disappearance of the weakly illuminated blue points is only an illustration of the phenomenon known as Maxwell's spot, a dark-blue or almost black blot, seen in the visual field when the eye, after being kept closed for a short time, is directed to a surface illuminated by a weak blue light. It is due to the absorption of blue light by the pigment of the yellow spot, and stands out as a rose-coloured disc when a source of white light is looked at through a solution of chrome alum, since all the light which the greenish solution permits to pass is absorbed by the macula lutea, except the red rays. Hering, indeed, asserts that the fovea is the most sensitive part of the retina for colours, in opposition to Charpentier, who finds it slightly less sensitive for blue than the zone immediately external to it. When the eye is fixed and the visual field (that is, the whole space from which light can reach the retina in the given position, or, what comes to the same thing, the projection of the visual field on the retina by straight lines passing through the nodal point) explored by means of a perimeter (Figs. 318, 319), it is found that, under ordinary conditions, a white object is seen over a wider field than any coloured object, a blue object over a wider field than a red, and a red over a wider field than a green object. The exact shape, as well as size, of the visual field also differs somewhat for different colours. And although it has been

shown by Aubert and others that monochromatic light of considerable intensity can be perceived over the whole retina, yet it may be said that the retinal rim is even then relatively and, under ordinary conditions, absolutely colour-blind. This and other facts have given rise to the theory that the rods, which are alone present at the ora serrata, have for their function the mere perception of luminous impressions as such, without any distinction of quality or of colour. The cones are supposed on this theory to be more highly developed than the rods, their function being connected especially with the perception of colour. But although there are certain histological facts which favour the view that the cones are a more highly-developed form of the rods, it cannot be considered as proved that animals whose retinæ are devoid of cones are totally colour-blind. And, indeed, the observations of Hess and Hering on total colour-blindness in man show that the assumption of v. Kries and König, that in this condition the cones are either entirely insensitive or replaced by rods, is unfounded.

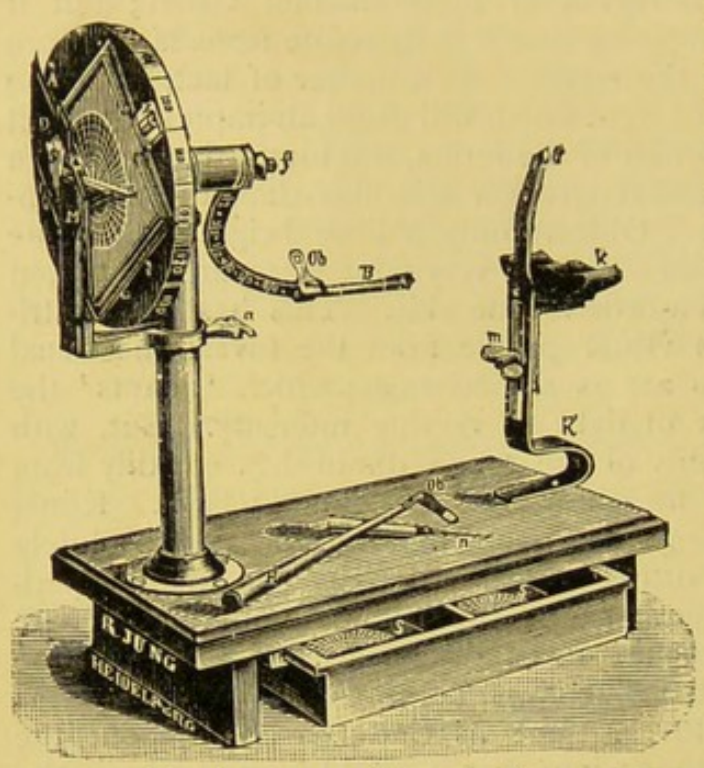

FIG. 318.—PRIESTLEY SMITH'S PERIMETER.

K, rest for chin; O, position of eye; Ob, object, white or coloured, which slides on the graduated arc B; f, point fixed by the eye.

This brings us to the subject of colour-blindness, a phenomenon of the greatest interest in its theoretical as well as in its practical bearings.

Colour-blindness. — A considerable number of persons (about 4 per cent. of all males, but only one-tenth of this proportion of females) are deficient in the power of distinguishing between certain colours. They are said to be colour-blind; but the term must not be taken to signify that they are absolutely devoid of colour-sensations. A very small minority of the colour-blind appear to have but one sensation of colour; a few confuse green with blue; the great majority are unable to distinguish between red and green. The condition will be most easily understood by considering some of the extraordinary mistakes which may

be made by the colour-blind without necessarily leading them to suspect that there is anything abnormal in their vision. Thus, to quote the words of a distinguished writer on this subject, himself a sufferer from the deficiency: 'A naval officer purchases red breeches to match his blue uniform; a tailor repairs a black article of dress with crimson cloth; a painter colours trees red, the sky pink, and human cheeks blue.' The shoemaker, Harris, the dis-

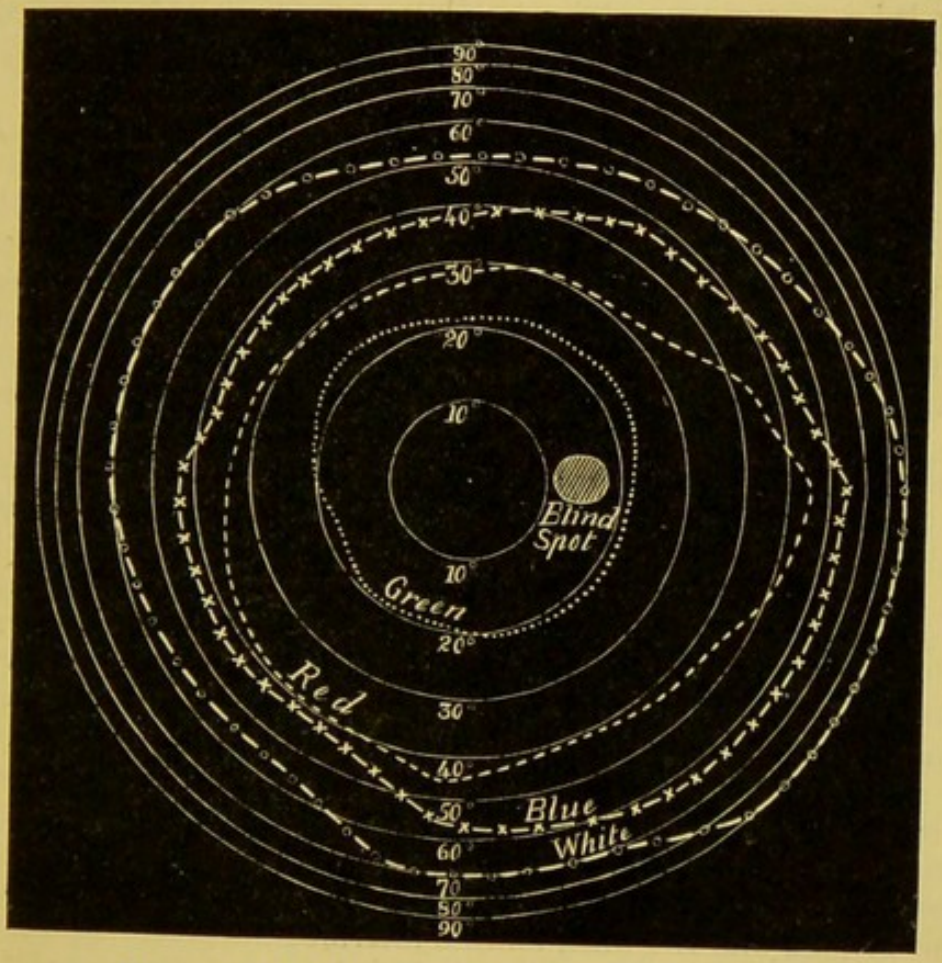

FIG. 319.—PERIMETRIC CHART OF RIGHT EYE.

Obtained with the perimeter shown in Fig. 318. The numbers represent degrees of the visual field measured on the graduated arc of the perimeter.

coverer of colour-blindness, picked up a stocking, and was surprised to hear other people describe it as a red stocking; it seemed to him only a stocking. The celebrated Dalton was twenty-six years of age before he knew that he was colour-blind. He matched samples of red, pink, orange, and brown silk with green of different shades; blue both with pink and with violet; lilac with grey.

When the condition of vision in the great majority of the colour-blind is tested by means of the spectrum, it is found that they fall into two classes: (1) A class (of green-blind) by whom the whole of the spectrum from red to yellow is described as yellow of different degrees of brightness (intensity); the green appears as a pale yellow with a grey or white band in its midst; while the violet end is seen as different shades of blue. (2) A class (of red-blind) whose whole spectrum, from red to green, is seen as green of different intensities, the extreme red being entirely invisible. The violet end is blue, as in (1), and there is a band of white or grey near the blue end of the green.

Sir John Herschell explained Dalton's peculiarity of vision on the hypothesis that he only possessed two, instead of three, primary sensations.

On the Young-Helmholtz theory, the missing sensation is supposed to be either red or green. At the intersection of the curves that represent the violet and green sensations (Fig. 316), the red-blind individual will see what he describes as white—viz., the sensation produced by the stimulation of the only two fibre-groups he possesses. Similarly, at the intersection of the red and violet curves, the green-blind person will see what is white to him.

On Hering's theory the colour-blind possess the blue-yellow, but lack the green-red, visual substance. So that on this theory there should be no difference between red-blindness and green-blindness. But v. Kries, in a study of twenty cases of congenital partial colour-blindness, brings forward strong evidence that the red-green blind can be divided, as regards the comparison of red (lithium) and orange (sodium) light, into two sharply-separated groups—a result which is emphatically in favour of the Young-Helmholtz theory, and against the theory of Hering. The observations of Burch on temporary colour-blindness produced by placing the eye behind a transparent coloured screen and focussing a beam of strong sunlight on it, lend additional support to the former theory. Thus, if a spectrum is looked at after green-blindness has been induced by exposure of the eye to green light, the red portion of the spectrum seems to pass into the blue, and no intermediate green band is seen. If the eye is exposed to yellow light it becomes temporarily blind not only for yellow, but also for red and green. This is in favour of the assumption of the Young-Helmholtz theory that the sensation of yellow is caused when the retinal elements concerned in the production of the sensations of red and green are simultaneously stimulated. It is, however, equally difficult to reconcile some of the phenomena of colour-blindness produced by disease (atrophy of the optic nerve) or by abuse of tobacco with the Young-Helmholtz theory, for in some of these cases the only colour seen in the spectrum is blue, the rest is white; and the theory does not provide for the production of the sensation of white by excitation of a single group of fibres with ordinary intensity of stimulation. Colour-blindness, in its true sense, is always congenital, often hereditary; the colour-blind are 'born, not made.' And although the con-

dition cannot be cured, it is of great importance that it should be recognised in the case of persons occupying positions such as those of engine-drivers, railway-guards, and sailors, in which coloured lights have to be distinguished. For, while it is true that the sensations which red and green lights give the colour-blind are far from being identical (Pole) under favourable conditions, it is precisely when the conditions are unfavourable, as in a fog or a snow-storm, that the capacity of distinguishing them becomes invaluable.

Irradiation was first described by Kepler, who gave as an example the appearance known as the 'new moon in the old moon's arms,' where the crescent of the new moon seems to overlap and embrace the unilluminated portion of the lunar disc. A white circle on a black ground (Fig. 320) appears, in a good light, to be larger than an exactly equal black circle on a white ground. The explanation seems to be as follows: Owing to the aberration of the refractive media of the eye (p. 794) all the rays proceeding from the luminous object are not brought accurately to a focus on the retina, and the image is surrounded by diffusion circles which encroach upon the unilluminated boundary. Physically these represent a weaker illumination than that of the image proper, and therefore the latter ought to stand out in its real size as a brighter area surrounded by weaker haloes. That this is not the case, and that the image is projected in its full brightness for a certain distance over its dark boundary, is due to the fact that the eye does not recognise very small differences of brightness. When the accommodation is not perfect, the diffusion circles are, of course, much wider, and irradiation is better marked when the object is a little out of focus.

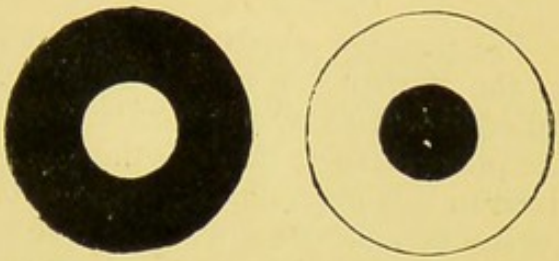

FIG. 320.

The Movements of the Eyes.—That the eyes may be efficient instruments of vision, it is necessary that they should have the power of moving independently of the head. An eye which could not move, though certainly better than an eye which could not see, would yet be as imperfect after its kind as a ship which could run before the wind, but could not tack. The mere fact that the angle between the visual axes must be adapted to the distance of the object looked at renders this obvious; and the beauty of the intrinsic mechanism of the eyeball has its fitting complement in the precision, delicacy, and range of movement conferred upon it by its extrinsic muscles.

Not only are movements of convergence and divergence

of the eyeballs necessary in accommodating for objects at different distances, but without compensatory movements of the eyes it would be impossible to avoid diplopia with every movement of the head; for the images of an object fixed in one position of the head would not continue to fall on corresponding points of the retinæ in another position.

All the complicated movements of the eyeball may be looked upon as rotations round axes passing through a single point, which to a near approximation always remains fixed, and is situated about 1·77 mm. behind the centre of the eye.

The position which the eyeballs take up when the gaze is directed to the horizon, or to any distant point at the level of the eyes, is called **the primary position.** Here the visual axes are parallel, and the plane passing through them horizontal. While the head remains fixed in this position, the eyeballs can rotate up or down around a horizontal axis, or from side to side around a vertical axis; or upwards and inwards, downwards and outwards, downwards and inwards, and upwards and outwards around oblique axes, which always lie in the same plane as the vertical and horizontal axes of rotation, *i.e.*, in the vertical plane passing through the fixed centre of rotation. These facts, spoken of collectively as **Listing's law,** and first deduced by him from theoretical considerations, were afterwards proved experimentally by Helmholtz and Donders. It necessarily follows from Listing's law (and this is, indeed, another way of stating it) that in moving from the primary position into any other, there is no rotation of the eyeball round the visual axis—no **wheel-movement,** as it is called.

A true rotation of the eye round the visual axis does, however, occur when the eyes are converged as in accommodation for a near object, each eyeball rotating towards the temporal side. This is especially the case when the eyes are at the same time converged and directed downwards; and the rotation may amount to as much as 5°. When the head is rolled from side to side, while the eyes are kept fixed on an object, a slight compensatory rotation of the eyeballs takes place against the direction of rotation of the head. The amount of rotation of the eyes is relatively greater for small than for large movements of the head (eye 5° for head 20°; eye 10° for head 80°—Küster).

The Extrinsic Muscles of the Eye.—The eyeball is acted upon by six muscles arranged in three pairs, which may be considered, roughly speaking, as antagonistic sets. These are the internal and external recti, the superior and inferior recti, and the superior and inferior obliqui.

Although the movements of the eye have been very fully studied, and are, upon the whole, well understood, our knowledge of the manner in which any given movement is brought about, and the exact action of the muscles which take part in it, is by no means as copious and precise. And from the nature of the case, the greater part of what we do know has been inferred from the anatomical relations of the muscles as revealed by dissection in the dead body rather than gained from actual observation of the living eye. A plane, called the *plane of traction*, is supposed to pass through the middle points of the origin and insertion of the muscle whose action is to be investigated, and through the centre

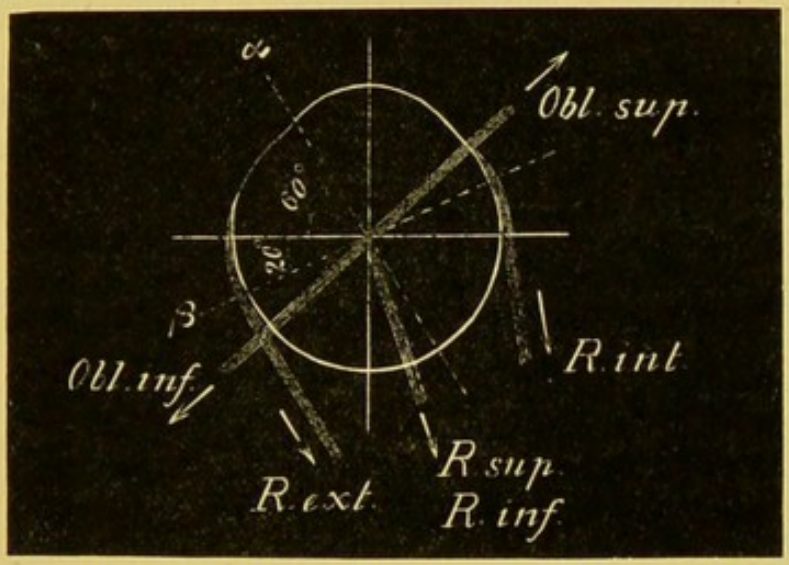

FIG. 321.—HORIZONTAL SECTION OF LEFT EYE.

Arrows show direction of pull of the muscles. The axis of rotation of the external and internal recti would pass through the intersection of α and β at right angles to the plane of the paper.

of rotation of the eyeball. A straight line drawn at right angles to this plane through the centre of rotation is evidently the axis round which the muscle when it contracts will cause the eye to rotate, provided that the fibres of the muscle are symmetrically distributed on each side of the plane of traction. The axes of rotation of the antagonistic pairs almost, but not completely, coincide with each other. The common axis of the external and internal recti practically coincides with the vertical axis of the eyeball (Fig. 321) in the primary position. The eye is turned towards the temple when the external rectus alone contracts, towards the nose when the internal rectus alone contracts. The common

axis of the superior and inferior recti, β, lies in the horizontal visual plane in the primary position, but makes an angle of about 20° with the transverse axis, its inner end being tilted forwards. The consequence is that contraction of the superior rectus turns the eye up, and contraction of the inferior rectus turns it down, but both movements are also combined with a slight inward rotation. The common axis of the oblique muscles, a, makes an angle of 60° with the transverse axis, the outer end of it being the most anterior. The direction of traction of the superior oblique is, of course, given not by the line joining its bony origin and its insertion, but by the direction of the portion reflected over the pulley. When the superior oblique contracts alone, the eyeball is rotated outwards and downwards; the inferior oblique causes an outward and upward rotation. None of the common axes of rotation of the pairs of muscles, except that of the external and internal recti, lies in Listing's plane. Now, as we have seen that every movement which the eye, supposed to be originally in the primary position, can execute may be considered as a rotation round an axis in this plane, it is clear that every movement, except truly transverse rotation, must be brought about by more than one pair of muscles. For vertical rotation, the inward pull of the superior rectus is antagonized by a simultaneous outward pull of the inferior oblique; for downward rotation, the inferior rectus and superior oblique act together. In oblique movements, a muscle of each of the three pairs is concerned. The effect on the eyeball of simultaneous contraction of certain pairs of muscles may be summarized thus:

External rectus (outward) + internal rectus (inward) = none.

Superior rectus (upward and inward) + inferior oblique (upward and outward) = upward.

Inferior rectus (downward and inward) + superior oblique (downward and outward) = downward.

HEARING.

The transverse vibrations of the ether fall upon all parts of the surface of the body, but only find nerve-endings capable of giving the sensation of light in the little discs which we call the retinæ. So the much longer and slower longitudinal waves of condensation and rarefaction which are being constantly originated in the air or imparted to it by solid or liquid bodies that have been themselves set vibrating fall upon all parts of the surface, but only produce the sensation of sound when they strike upon the tiny mechanism of the internal ear.

But just as the ethereal vibrations, and especially those of greater wave-length, are able to excite certain end-organs in the skin which have to do with the sensation of temperature, so the sound-waves, when sufficiently large, are also capable of stimulating certain cutaneous nerves and of giving rise to a sensation of intermittent pressure or thrill. This is readily perceived when the finger is immersed in a vessel of water into which dips a tube connected with a source of sound, or when a vibrating bell or tuning-fork is touched. So far as we know, what takes place in the ear is essentially similar — that is to say, a mechanical stimulation of the ends of the auditory nerve, but a stimulation which acts through, and is graduated and controlled by, a special intermediate mechanism.

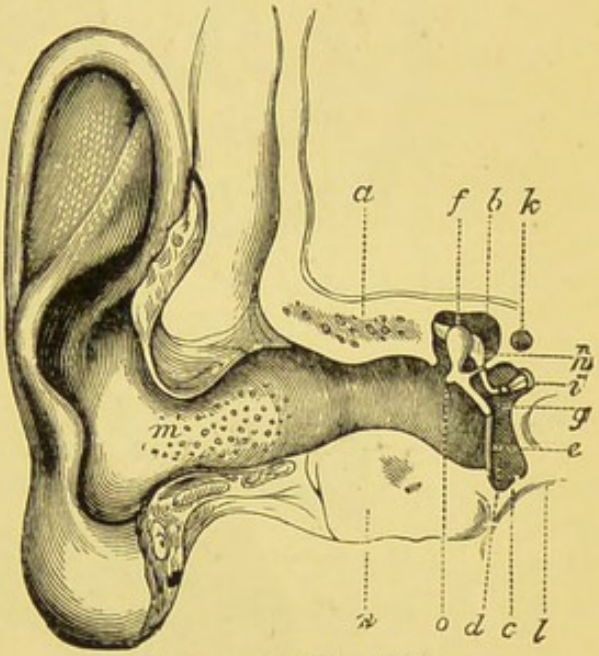

FIG. 322.—THE EAR.

m, external meatus; *f*, head of malleus; *o*, short process of malleus; *g*, handle of malleus; *h*, incus; *i*, foot of stapes in oval foramen; *e*, tympanic membrane.

As the visual apparatus consists of a sensitive surface, the retina, which contains the end-organs of the optic nerve and of dioptric arrangements which receive and focus the rays of light, the auditory apparatus consists of the sensitive end-organs of the eighth nerve and of a mechanism which receives the sound-waves and communicates them to these.

Physiological Anatomy of the Ear.—At the bottom of the external auditory meatus lies the membrana tympani, a nearly circular membrane set like a drum-skin in a ring of bone, and separating the meatus from the tympanum or middle ear. Its external surface looks

obliquely downwards, and at the same time somewhat forwards, so that if prolonged the membranes of the two ears would cut each other in front of, and also below, the horizontal line passing through the centre of each (Figs. 322, 323).

The tympanum contains a chain of little bones stretching right across it from outer to inner wall. Of these the malleus, or hammer, is the most external. Its manubrium, or handle, is inserted into the membrana tympani, which is not stretched taut within its bony ring, but bulges inwards at the centre, where the handle of the malleus is attached. The stapes, or stirrup, is the most internal of the chain of ossicles, and is inserted by its foot-plate into a small

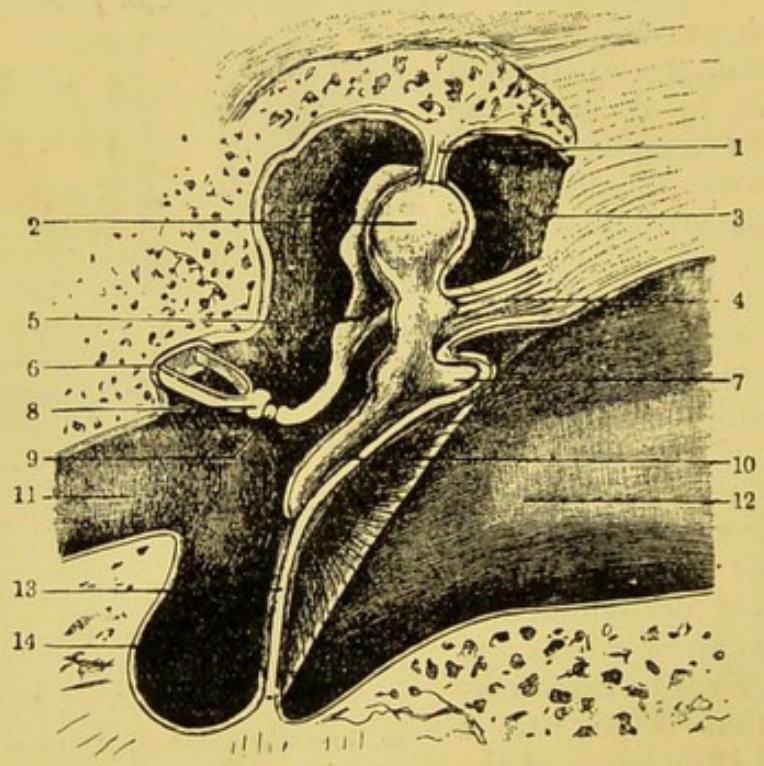

FIG. 323.—TYMPANUM OF LEFT EAR, SHOWING THE OSSICLES (MORRIS).

1, superior, and 4, external ligament of malleus; 2, head; 7, short process, and 10, manubrium or handle of malleus; 5, long process of incus, terminating in 9, the os orbiculare; 6, base, and 8, head of stapes; 11, Eustachian tube; 12, external auditory meatus; 13, membrana tympani; 3, upper, and 14, lower part of tympanum.

oval opening—the foramen ovale—on the inner wall of the tympanic cavity. A membranous ring—the orbicular membrane—surrounds the foot of the stapes, helping to fill up the foramen and attaching the bone to its edges. The incus, or anvil, forms a link between the malleus and the stapes. The auditory ossicles, as well as the whole cavity of the tympanum, are covered by pavement epithelium. The tympanum is not an absolutely closed chamber; it has one channel of communication with the external air—the Eustachian tube. By the action of the cilia which line this tube the scanty secretion of the middle ear is moved towards its pharyngeal opening. The loosely-jointed chain of ossicles is steadied and its movements directed by ligaments and by the tension of its terminal membranes. It forms

a kind of bent lever, by which the oscillations of the membrana tympani are transferred to the membrane covering the oval foramen, and at the same time reduced in size. Two slender muscles, the tensor tympani and stapedius, contained in the tympanic cavity are also connected with and may act upon the ossicles. The former lies

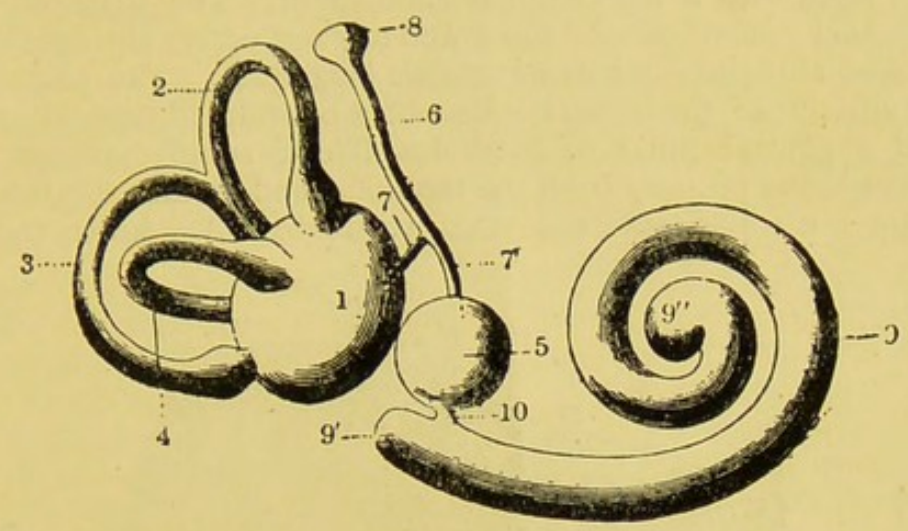

FIG. 324.—DIAGRAM OF RIGHT MEMBRANOUS LABYRINTH (SEWALL, AFTER TESTUT).

1, utricle ; 2, 3, 4, superior, posterior, and horizontal semicircular canals ; 5, saccule ; 6, ductus endolymphaticus arising by two branches, 7, 7′ ; 8, saccus endolymphaticus ; 9, canalis cochlearis (canal of the cochlea), ending at 9′, and 9″ ; 10, canalis reuniens.

in a groove above the Eustachian tube, and its tendon, passing round a kind of osseous pulley (processus cochleariformis), is inserted into the handle of the malleus ; the stapedius is lodged in a hollow of the inner bony wall of the tympanum. Its tendon is attached to the neck

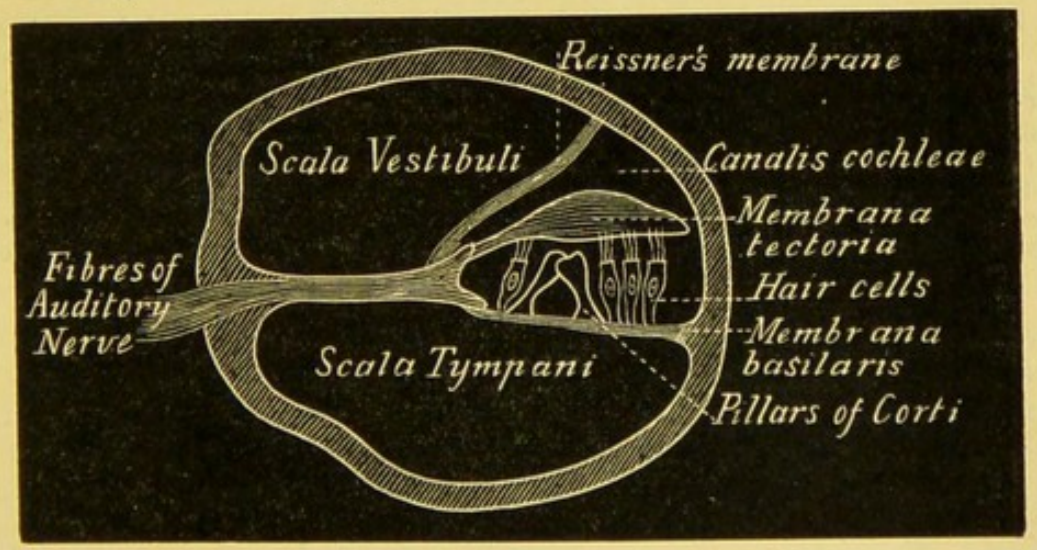

FIG. 325.—TRANSVERSE SECTION OF A TURN OF THE COCHLEA (DIAGRAMMATIC).

of the stapes near its articulation with the incus. This inner wall is pierced not only by the oval foramen, but also by a round opening, the fenestra rotunda, which is closed by a membrane to which the name of secondary membrana tympani is sometimes given.

The internal ear consists of the bony labyrinth, a series of curiously excavated and communicating spaces in the substance of the petrous portion of the temporal bone, filled with a liquid called the perilymph, in which, anchored by strands of connective tissue, floats a corresponding series of membranous canals (the membranous labyrinth), filled with a liquid called endolymph. The labyrinth of the internal ear is divided into three well-marked parts : the cochlea, the vestibule, and the semicircular canals (Fig. 324). The cochlea, the most anterior of the three, consists of a convoluted tube which coils round a central pillar or modiolus like a spiral staircase. The lamina spiralis projects from the modiolus and divides the tube into an upper compartment, the scala vestibuli, and a lower, the scala

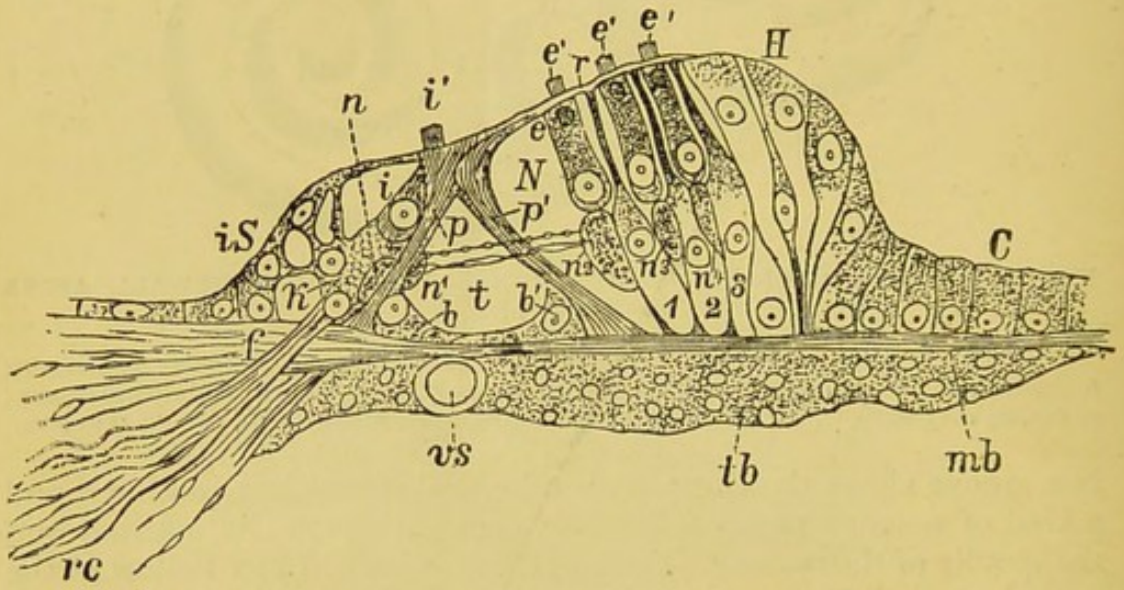

FIG. 326.—ORGAN OF CORTI (BARKER, AFTER RETZIUS).

mb, basilar membrane ; *tb*, its tympanal covering ; *vs*, blood-vessel (vas spirale) ; *rc*, medullated distal processes of bipolar nerve-cells in the ganglion spirale, passing in to arborize around the hair-cells ; *iS*, epithelial cells continuous with the epithelium of the sulcus spiralis internus ; *p*, inner pillar of Corti, with its basal cell *b* ; *p'*, outer pillar with its basal cell *b'* ; 1, 2, 3 supporting cells of Deiters, whose processes run up to be attached to the lamina reticularis, *r* ; H, Hensen's supporting cells ; C, cells of Claudius ; *i*, internal hair-cell with its hairs, *i'* (the upper part of the hair-cell is concealed by the head of the inner pillar of Corti) ; *e*, external hair-cell ; *e'*, hairs of three external hair-cells ; *n*, n^1 to n^4, cross-sections of the spiral strand of cochlear nerve-fibres.

tympani (Fig. 325). The part of the lamina next the modiolus is of bone, but it is completed at its outer edge by a membrane, the lamina spiralis membranacea. The scala tympani abuts on the fenestra rotunda, and its perilymph is only separated from the air of the tympanic cavity by the membrane which closes that opening. At the apex of the cochlea the lamina spiralis is incomplete, ending in a crescentic border, so that the scala tympani and the scala vestibuli here communicate by a small opening, the helicotrema. The scala vestibuli communicates with the vestibule, and the vestibule with the semicircular canals, so that the perilymph of the entire labyrinth forms a continuous sheet. separated from the cavity of the middle ear by the structures that fill up the round and oval foramina.

In the membranous labyrinth, and in it alone, are contained the end-organs of the auditory nerve. The membranous portion of the cochlea is a small canal of triangular section, cut off from the scala vestibuli by the membrane of Reissner, which stretches from near the edge of the bony spiral lamina to the outer wall (Fig. 325). It has received the name of the scala media, or canal of the cochlea. Below it ends blindly, but communicates by a side-channel with the portion of the membranous vestibule called the saccule, which in its turn communicates with the utricle by the Y-shaped origin of the ductus endolymphaticus. Into the utricle open the three semicircular canals, the endolymph of which has, therefore, free communication with that of the vestibule and cochlea. But although the semicircular canals and vestibule belong anatomically to the internal ear, and are supplied by branches of the auditory nerve, we have no positive proof that in the higher animals, at least, they are in any way concerned in hearing; and since experiment has assigned them, with a great degree of probability, a definite function of another kind (p. 732), we shall not consider them further in this connection. The scala media contains the organ of Corti, which (Fig. 326) consists of a series of modified epithelial cells planted upon the membranous spiral lamina or basilar membrane. The most conspicuous constituent of the latter is a layer of parallel transparent fibrils. The epithelial cells are of three kinds: (1) supporting epithelial cells; (2) the pillars or rods of Corti, sloped against each other like the rafters of a roof, and covering in a vault or tunnel which runs along the whole of the scala media from the base to the apex of the cochlea; (3) the hair-cells, around which the fibres of the auditory nerve arborize. These last are columnar epithelial cells, surmounted by hairs. They are arranged in several rows, one row lying just internal to the inner line of pillars, and several rows external to the outer line of pillars. A thin membrane, the membrana reticularis, covers the pillars and hair-cells of Corti, and is pierced by the hairs; while a thicker membrane, the membrana tectoria, springing from the edge of the osseous spiral lamina near the attachment of Reissner's membrane, forms a kind of canopy over both pillars and hair-cells. The fact that the hair-cells of Corti's organ are connected with the fibres of the cochlear division of the auditory nerve, and its elaborate structure, suggest that it must play a peculiar part in auditory sensation. Comparative anatomy shows us that the cochlea is the most highly-developed portion of the internal ear, the last to appear in its evolution, and the most specialized. It is absent in fishes, which possess only a vestibule and one to three semicircular canals. It first acquires importance in reptiles, but attains its highest development in mammals; and there is every reason to believe that it is the terminal apparatus of the sense of hearing.

Function of the Auditory Ossicles.—The anatomical arrangements of the middle ear suggest that the tympanic membrane and the chain of ossicles have the function of transmitting

the sound-waves to the liquids of the labyrinth; and observation and experiment fully confirm this idea. Tracings of the movements of the ossicles have been obtained by attaching very small levers to them, and their movements have been directly observed with the microscope. Even in man it may be shown, by viewing the membrane through a series of slits in a rapidly-revolving disc (stroboscope), that it vibrates when sound-waves fall on it.

When the handle of the malleus moves inwards, the joint between that bone and the incus is locked, on account of the shape of the articular surfaces, and the stapes is pressed into the oval foramen. When the tympanic membrane passes outwards, the handle of the malleus and foot of the stapes do the same. But the joint now unlocks, and excessive outward movement of the stapes, which might result in its being torn from its orbicular attachment, is prevented. The ossicles vibrate *en masse*. It is only to a trifling extent that sound can be conducted through them to the labyrinth as a molecular vibration; for when they are anchylosed, and the foot of the stapes fixed immovably in the foramen ovale, as sometimes occurs in disease, hearing is greatly impaired.

Of course, every vibration of the tympanic membrane must cause a corresponding condensation and rarefaction of the air in the middle ear; and this may act on the membrane closing the fenestra rotunda, and set up oscillations in the perilymph of the scala tympani. That this is a possible method of conduction of sound is shown by the fact that, even after closure of the oval foramen, a slight power of hearing may remain. But under ordinary conditions by far the most important part of the conduction takes place *viâ* the ossicles. And when it is remembered that the tympanic membrane is about thirty times larger than that which fills the oval foramen, it will be seen that the force acting on unit area of the foot of the stapes may be much greater than that acting on unit area of the membrana tympani, and that the mode of transmission by the ossicles is a very advantageous method of transforming the feeble but comparatively large excursion of the tympanic membrane into the smaller but

more powerful movements of the stapes. Even the so-called **cranial conduction of sound** when a tuning-fork is held between the teeth or put in contact with the head, which was at one time supposed to be due solely to direct transmission of the vibrations through the bones of the skull to the liquids of the labyrinth or the end-organs of the auditory nerve, has been shown to take place, in great part, through the membrana tympani and ossicles; the vibrations travel through the bones to the tympanic membrane, and set it oscillating. So that this test, when applied to distinguish deafness caused by disease of the middle ear from deafness due to disease of the labyrinth or the central nervous system may easily mislead, although it enables us to say whether the auditory meatus is blocked (by wax, *e.g.*) beyond the tympanic membrane.

When a tuning-fork is held between the teeth, a part of the sound passes out of the ear from the vibrating membrana tympani; if one ear is closed, the sound is heard better in this than in the open ear. If the tuning-fork is held between the teeth till, with both ears open, it becomes inaudible, it will be heard for a short time if one or both ears be stopped; and when in this position the sound again becomes inappreciable, it can still be caught if the handle be introduced into the auditory meatus.

A membrane like a drum-head has a note of its own, which it gives out when struck, and it vibrates more readily to this note than to any other. It would evidently be a serious disadvantage if the tympanic membrane, whose office it is to receive all kinds of vibrations, and respond to all, had a marked fundamental tone which would be continually obtruding itself among other notes. The difficulty is obviated by the damping action of the ossicles and the liquids of the labyrinth on the movements of the membrane, which in addition is not stretched, but lies slackly in its bony frame, so that when the handle of the malleus is detached from it, it retains its shape and position.

The **tensor tympani**, when it contracts, pulls inwards the handle of the malleus, and thus increases the tension of the tympanic membrane. The precise object of this is obscure. It has been suggested that damping of the movements of the auditory ossicles is thus secured. Another theory is that the increased tension of the membrane renders it more capable of responding to higher tones, and that the muscle thus acts as a kind of accommodating mechanism. But Hensen has observed that the tensor only contracts at the beginning of a sound, and relaxes again when the sound is continued; and this is difficult to reconcile with either of these hypotheses. The muscle is normally excited reflexly through the vibrations of the membrana tympani, but some individuals have the power of throwing it into voluntary contraction, which is accompanied by a feeling of pressure in the ear and a harsh sound. The function of the **stapedius**

is unknown. Its contraction would tend to press the posterior end of the foot-plate of the stapes deeper into the foramen ovale, and cause the anterior end to move in the opposite direction ; but it is not easy to see how this would affect the action of the auditory mechanism. It has been suggested that the rôle of the stapedius is to damp the oscillations of the stapes and orbicular ligament when very loud sounds are listened to, and thus prevent shocks of too great intensity from being transmitted to the labyrinth.

The tensor tympani is supplied by the fifth nerve through a branch from the otic ganglion ; the stapedius is supplied by the seventh. Paralysis of the fifth nerve may be accompanied with difficulty of hearing, especially for faint sounds. When the seventh nerve is paralyzed, increased sensitiveness to loud sounds has been observed.

The Perception of Pitch—Analysis of Complex Sounds.—As the eye, or, rather, the retina *plus* the brain, can perceive colour, so the labyrinth *plus* the brain can perceive pitch. The colour-sensation produced by ethereal waves of definite frequency depends on that frequency ; and upon the frequency of the aërial vibrations depends also the pitch of a musical note. But there is this difference between the eye and the ear : that while the sensation produced by a mixture of rays of light of different wave-length is always a simple sensation—that is, a sensation which we do not perceive to be built up of a number of sensations, which, in other words, we do not analyze—the ear can perceive at the same time, and distinguish from each other, the components of a complex sound. When a number of notes of different pitch are sounded together at the same distance from the ear, the disturbance which reaches the membrana tympani is the physical resultant of all the disturbances produced by the individual notes, and it strikes upon the membrane as a single wave. The ear or brain must, therefore, possess the power of resolving the complex vibrations into their constituents, else we should have a mixed or blended sensation, and not a sensation in which it is possible to distinguish the constituents of which it is made up. Two chief hypotheses have been proposed to explain this physiological analysis of sound : (1) the theory that the analysis takes place in the labyrinth ; (2) the theory that it takes place in the brain.

(1) Helmholtz attempted to explain the perception of pitch on the assumption that in the internal ear there exists a series of resonators, each of which is fitted to respond by

sympathetic vibration to a particular note, while the others are unaffected; just as when a note is sung before an open piano it is taken up by the string which is attuned to the same pitch and ignored by the rest. Let us suppose that a given fibre of the auditory nerve ends in an organ which is only set vibrating by waves impinging on it at the rate of 100 a second, and that the end-organ of another fibre is only influenced by waves with a frequency of 200 a second. Then, on the doctrine of 'specific energy' (according to which the sensation caused by stimulation of a nerve depends not on the particular kind of stimulus but on the anatomical connection of the nerve with certain nerve centres), in whatever way the first fibre is excited, a sensation corresponding to a note with a pitch of 100 a second will be perceived. Whenever the second fibre is excited, the sensation will be that of a note of 200 a second, or the octave of the first. If both fibres are excited at the same time the two notes will be heard together. Now, Hensen actually observed that in the auditory organs of some crustaceans the hair-like processes of certain epithelial cells can be set swinging by waves of sound, and, further, that they do not all vibrate to the same note unless the sound is very loud. In the lobster there are between four and five hundred of these hairs, varying in length from 14 μ tc 740 μ; and in some insects, such as the locust, similai hairs, also graduated in length, exist.

To gain an anatomical basis for his theory, Helmholtz supposed first of all that the pillars of Corti were the vibrating structures, and that, directly or through the hair-cells, their mechanical vibrations were translated into impulses in the auditory nerve-fibres. But apart from the fact that their number is too small (about 3,000) to allow us to assign one rod to each perceptible difference of pitch, and their dimensions too similar to permit of the requisite range of vibration frequency, it was pointed out that birds do not possess pillars of Corti—a fact which was decisive against the assumption of Helmholtz, since nobody denies to singing birds the power of appreciating pitch. Helmholtz accordingly, choosing between the remaining possibilities,

gave up the pillars of Corti, and, adopting a suggestion of Hensen, substituted the radial fibres of the basilar membrane as his hypothetical resonators. But while it is true that these are much more adequate to the task imposed on them, since their range of length is far greater (41 μ at the base to 495 μ at the apex of the cochlea—Hensen); and while the structure of Corti's organ certainly suggests that some one or other of its elements may be endowed with such a function, the theory of peripheral analysis of pitch tends upon the whole rather to break down than to be strengthened as evidence gathers.

When two notes of different frequency are sounded together, they 'interfere' with each other. If two tuning-forks A and B, making 100 and 101 vibrations a second respectively, be started together, at the end of the first vibration of A, B will be $\frac{1}{100}$th of a vibration ahead, at the end of the second $\frac{2}{100}$ths of a vibration, at the end of the fiftieth half a vibration. Here the crest of B's wave will coincide with the trough of A's, and if the forks are vibrating with the same amplitude the resultant for this vibration will be zero, the wave will be blotted out. If the amplitudes are not the same, the wave will still be weakened. At the end of the hundredth vibration of A, B will have gained a whole vibration, the tops of the two waves will coincide, and the sound will be strengthened. We recognise the alternate changes in the amplitude of the interfering sound-waves by a change in the auditory sensation, which is called a *beat;* and in the case supposed there will be one beat a second. If the difference in the frequency of the forks is five there will be five beats a second. If the difference is twenty there will be twenty beats a second. As the difference is increased the beats will ultimately follow each other so rapidly that they will themselves be fused into a note—a beat-tone as it is called, whose pitch will correspond to the frequency of the beats. Now, Hermann has found that the ear may perceive a beat-tone which elicits no response from a resonator attuned to its note and readily set into vibration by the same note when sounded by a tuning-fork. This shows that the process by which pitch is appreciated, whatever it may be, is not entirely explicable on the theory of resonance.

(2) The second theory, in accordance with the simile used by Rutherford, to whom we owe it in its present form, may be conveniently labelled the 'telephone theory.' He supposes that the organ of Corti (or, at any rate, the hair-cells) is set into vibration as a whole by all audible sounds, and that its vibrations are translated into impulses in the auditory

nerve, which are the physiological counterpart of the aerial waves and the waves of increased and diminished pressure in the liquids of the labyrinth to which they give rise. Thus, a sound of 100 vibrations a second would start 100 impulses a second in the auditory nerve; a loud sound would set up impulses more intense than a feeble sound; and a complex wave, which is the resultant of several sounds of different vibration-frequency, would also in some way or other stamp the impress of its *form* on the auditory excitation-wave; just as in a telephone every wave in the air causes a swing of the vibrating plate, and thus sets up a current of corresponding intensity and duration in the wires. This theory evidently abandons the doctrine of specific energy for the particular case of the analysis of pitch, for it assumes that differences of auditory sensation are related to differences in the nature of the impulses travelling up the auditory nerve, and not merely to differences in the anatomical connections (peripheral and central) of the auditory nerve-fibres.

The statement of Ewald, that after extirpation of the membranous labyrinth on both sides pigeons can still hear, would have an important bearing on the question of the perception of pitch, if it could be definitely accepted, and particularly if it were shown that differences of pitch could still be appreciated. But it has not been proved beyond a doubt that the apparent reaction to sound is due to anything else than stimulation of tactile end-organs.

The **range of hearing** is very great. The highest audible tone corresponds to 30,000 to 40,000 vibrations a second, the lowest to about 30. Between these limits as many as 6,000 variations of pitch can be perceived.

Smell and Taste.

Smell was defined by Kant as 'taste at a distance'; and it is obvious that these two senses not only form a natural group when the quality of the sensations is considered, but are closely associated in their physiological action, especially in connection with the perception of the flavour of the food. The olfactory end-organs in the mucous membrane of the upper part of the nostrils, the so-called regio olfactoria, have been already described (p. 717). In cases of anosmia, in which the olfactory nerve is absent or paralyzed,

smell is abolished; but substances such as ammonia and acetic acid, which stimulate the ordinary sensory nerves (nasal branch of fifth) of the olfactory mucous membrane, are still perceived, though not distinguished from each other. In fact, the so-called pungent odour of these substances is no more a true smell than the sense of smarting they produce when their vapour comes in contact with a sensory surface like the conjunctiva or a piece of skin devoid of epidermis.

It was at one time believed that odoriferous particles could not be appreciated unless they were borne by the air into the nostrils; but this appears not to be the case, for the smell of substances dissolved in normal saline solution is distinctly perceived when the nostrils are filled with the liquid; and fish, as every line-fisherman knows, have no difficulty in finding a bait in the dark.

Beaunis has classified the substances which can affect the olfactory mucous membrane as follows:

1. Those which act only on the olfactory nerves:
   - (*a*) Pure scents or perfumes, without pungency.
   - (*b*) Odours with a certain pungency, *e.g.*, menthol.
2. Substances which act at the same time on olfactory nerves and on nerves of common sensation (tactile nerves), *e.g.*, acetic acid.
3. Substances which act only on the nerves of common sensation (tactile nerves), *e.g.*, carbon dioxide.

Electrical excitation of the olfactory mucous membrane causes a sensation like the smell of phosphorus. The sensation is experienced at the kathode on closure and the anode on opening.

Taste.—The sense of taste is not so strictly localized as the sense of smell. The tip and sides of the tongue, its root, the neighbouring portions of the soft palate, and a strip in the centre of the dorsum, are certainly endowed with the sense of taste; but the exact limits of the sensitive areas have not been defined, and, indeed, seem to vary in different individuals.

The nerves of taste are the glosso-pharyngeal, which innervates the posterior part of the tongue; and the lingual, which supplies its tip (see p. 722). The end-organs of the gustatory nerves are the taste-buds or taste-bulbs, which stud the fungiform and circumvallate papillæ, and are most characteristically seen in the moats surround-

ing the latter. They are barrel-like bodies, the staves of the barrel being represented by supporting cells; each bud encloses a number of gustatory cells with fine processes at their free ends projecting through the superficial end of the barrel. They are surrounded by the end arborizations of the fibres of the gustatory nerves.

As to the properties in virtue of which sapid substances are enabled to stimulate the gustatory nerve endings, we know that they must be soluble in the liquids of the mouth, and there our knowledge ends. An attempt has been made by various authors to connect the taste of such bodies with their chemical composition, but researches of this kind have not hitherto yielded much fruit. Sapid substances have been divided into four classes: 1, sweet; 2, acid; 3, bitter; 4, saline.

Sweet and acid tastes are best appreciated by the tip, and bitter tastes by the base, of the tongue.

Normal lymph, which bathes the gustatory end-organs, does not excite any sensation of taste, but when the composition of the blood is altered in disease or by the introduction of foreign substances, tastes of various kinds may be perceived. Sometimes this may be due to the stimulation of substances excreted in the saliva; but in other cases it seems that, without passing beyond the blood and lymph, foreign substances may excite the gustatory nerves.

When a constant current is passed through the tongue, an acid taste is experienced at the positive, and an alkaline taste at the negative, pole; and it is said that this is the case even when the current is conducted to and from the tongue by unpolarizable combinations, which prevent the deposition of electrolytic products on the mucous membrane (p. 542).

Flavour is a mixed sensation, in which smell and taste are both concerned, as is shown by the common observation that a person suffering from a cold in the head, which blunts his sense of smell, loses the proper flavour of his food, and that some nauseous medicines do not taste so badly when the nostrils are held.

In common speech, the two sensations are frequently confounded with each other and with tactile sensations. Thus the 'bouquet' of wines, which most people imagine to be a sensation of taste, is in reality a sensation of smell; the astringent 'taste' of tannic acid is not a taste at all, but a tactile sensation; the 'hot' taste of mustard is no more a true sensation of taste than the sensation produced by the same substance when applied in the form of a mustard poultice to the skin.

Tactile and Common Sensations.

Under the sense of touch it is usual to include a group of sensations which differ in quality—and that in some instances to as great an extent as any of the sensations which are universally considered as separate and distinct—but agree in this, that the end-organs by which they are perceived are all situated in the skin, the mucous membrane, or the subcutaneous tissue. Such are the common tactile sensations—including pressure and tickling—and the sensations of temperature, or, more correctly, of change of temperature. The sensation of pain, although it cannot, perhaps, be absolutely separated from these, ought not to be grouped along with them. It is called forth by the stimulation of afferent nerve-fibres in their course; and it may originate, under certain conditions, in internal organs which are devoid of tactile sensibility, and the functional activity of which in their normal state gives rise to no special sensation at all. The peculiar sensation associated with voluntary muscular effort, to which the name of the muscular sense has been given, also deserves a separate place; for although it may in part depend on tactile sensations set up through the medium of end-organs situated in muscle, tendon, or the structures which enter into the formation of the joints, other elements are, in all probability, involved.

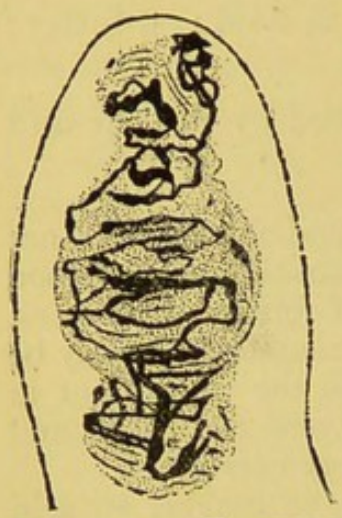

FIG. 327. — TACTILE CORPUSCLE FROM SKIN OF FINGER (SMIRNOW).

(Golgi preparation.) The winding and intersecting black lines are the non-medullated endings of the one or more nerve-fibres that enter the corpuscle.

The simplest form of tactile sensation is that of mere contact, as when the skin is lightly touched with the blunt end of a pencil. This soon deepens into the sensation of pressure if the contact is made closer; and eventually the sense of pressure merges into a feeling of pain. It is not easy to say whether these various sensations are due to the stimulation of different nervous elements, or to different grades of stimulation of the same elements. But there is some pathological evidence in favour of the former view, *e.g.*, it is said that the sensation of contact is abolished in cicatrices where

the true skin has been destroyed, although sensibility to pressure persists. The existence of different forms of sensory end-organs in the skin and other tissues (tactile or touch-corpuscles, corpuscles of Pacini, end-bulbs of Krause, etc.) is also, so far as it goes, in favour of the same view. The minimum pressure necessary to evoke a sensation of contact is not the same for every portion of the skin. The forehead and palm of the hand are most sensitive.

If two points of the skin are touched at the same time there is a double sensation when the distance between the points exceeds a certain minimum, which varies for different parts of the sensitive surface.

	Distance at which two points can be distinctly felt, in mm.
Point of tongue	1·1
Palmar surface of third phalanx of finger	2·2
Dorsal surface of third phalanx of finger	6·7
Tip of nose	6·7
Back	11·2
Eyelids	11·2
Skin over sacrum	40·5
Upper arm	67·6

Practice increases the acuity of touch. Even in a few hours it may be temporarily quadrupled on some parts of the skin. Since at the same time it is increased in the corresponding part of the opposite side of the body, it is argued that the modification takes place in the central nervous system, not in the end-organs themselves.

Few of the internal organs seem to be supplied with tactile nerves. The movements of a tapeworm in the intestines are not recognised as tactile sensations, nor the movements of the alimentary canal during digestion, nor the rubbing of one muscle on another during its contraction.

It would seem that **pressure** is only perceived when it affects two neighbouring areas to a different degree. Thus, the atmospheric pressure, bearing uniformly on the whole surface of the body, causes no sensation; we are so entirely unconscious of it that it needed the inspiration of genius to discover it, and the patience of genius to force the discovery on the world. When the finger is dipped in a trough of mercury at its own temperature, no sensation is perceived except a feeling of constriction at the surface of the liquid.

Sensations of Temperature.—When a body colder or hotter than the skin is placed on it, or when heat is in any other

way withdrawn from or imparted to the cutaneous tissues with sufficient abruptness, a sensation of cold or heat is experienced. And when two portions of the skin at different temperatures are put in contact, we feel that, relatively to one another, one is warm and the other cold. But it is worthy of remark that it is only difference of temperature, and not absolute height, that we are able to estimate by our sensations. Thus, a hand which has been working in ice-cold water will feel water at 10° as warm; whereas it would appear cold to a warm hand. When the temperature of the skin is raised above or diminished below a certain limit, the sensation of change of temperature gives place to one of pain; and this may be considered as due either to excessive stimulation of the end-organs of the temperature sense, or as due to stimulation of the ordinary sensory nerves, which are normally insensible to more moderate variations of temperature.

The recent researches of Blix, Goldscheider, and others have thrown new light upon the anatomical basis of the sensations which have their origin in the skin. They have found that the whole skin is not endowed with the capacity of distinguishing temperature. The temperature sense is confined to minute areas scattered over the cutaneous surface, some of which are 'cold' points, *i.e.*, respond to variations of temperature only by a sensation of cold, while others are 'warm' points and respond only by a sensation of heat. 'Cold' points are present in greater number than 'warm.' When a nerve is compressed, the sensibility of the tract supplied by it disappears for cold sooner than for heat.

The explanation of these facts seems to be that the skin is supplied with several kinds of nerve-fibres, anatomically as well as functionally distinct. Some fibres minister to the sensation of cold, others to that of heat, others to that of pressure, others, perhaps, to that of contact, and others still to pain. And just as stimulation of the optic nerve gives rise to a sensation of light, so stimulation of any one of the cutaneous nerves gives rise to the specific sensation proper to the group to which it belongs. But with the eyes closed a thermal may sometimes be mistaken for a tactile stimulus.

It is not only of physiological interest, but of practical importance,

that most mucous membranes are in comparison with the skin but slightly sensitive to changes of temperature; some, as the mucous membrane of the greater portion of the alimentary canal, seem to be entirely devoid of nerves of temperature. Only towards its ends in the mouth, pharynx and rectum, and to some extent in the stomach, does a blunted sensibility appear. The uterus, too, is quite insensible to heat; and hot liquids may be injected into its cavity at a temperature higher than that which can be borne by the hand, without causing inconvenience—a fact which finds its application in the practice of gynæcology and obstetrics. It is, indeed, obvious that in the greater number of the internal organs the conditions necessary for stimulation of temperature nerves, even if such were present, could hardly ever exist.

It has already been mentioned that changes of external temperature exert a remarkable influence on the intensity of metabolism (p. 510), and it has been supposed that this is brought about by afferent impulses travelling up the cutaneous nerves. We have also seen that for certain kinds of stimuli the excitability of nerve-fibres is increased by cooling (p. 594). It is possible that this is the case for the fibres in the skin which are concerned in the regulation of the production of heat, and it has been suggested that this fact may have a bearing on the reflex regulation of temperature (Lorrain Smith).

The Muscular Sense.

Voluntary muscular movements are accompanied with a peculiar sensation of effort, graduated according to the strength of the contraction, and affording data from which a judgment as to its amount and direction may be formed. To these sensations the name of the muscular sense has been given.

Some writers have supposed that the muscular sense does not depend upon afferent impulses at all, but that the nervous centres from which the voluntary impulses depart, take cognizance, retain a record, so to speak, of the quantity of outgoing nervous force; that the effort which we feel in lifting a heavy weight is an effort of the cells of the motor centres from which the innervation of the groups of muscles takes origin, and not of the muscles themselves.

But although this feeling of central effort or outflow (we can hardly say of central fatigue) may play a part in the muscular sense, it cannot be doubted that the brain is kept in touch with the contracting muscle by impulses of various kinds which reach it by different afferent channels.

The corpuscles of Pacini, which exist in considerable numbers in the neighbourhood of joints and ligaments, and in the periosteum of bones, would seem well fitted to play the part of end-organs for the tactile sensations caused by the movements of flexion, extension, or rotation of one bone on another, which form so large a portion of all voluntary muscular movements. And it has been stated that paralysis of these bodies in the limbs of a cat by section of the nerves going to them causes a characteristic uncertainty of movement which suggests that something necessary to normal co-ordination has been taken away. Tendons also possess afferent nerve-fibres, which terminate by breaking up into reticulated end-plates (Fig. 328). We have already seen that the skeletal muscles possess

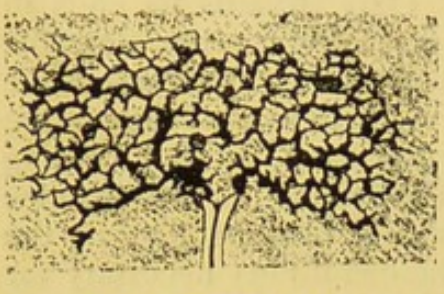

FIG. 328.—NERVE-ENDING IN TENDON NEAR THE INSERTION OF THE MUSCULAR FIBRES (GOLGI).

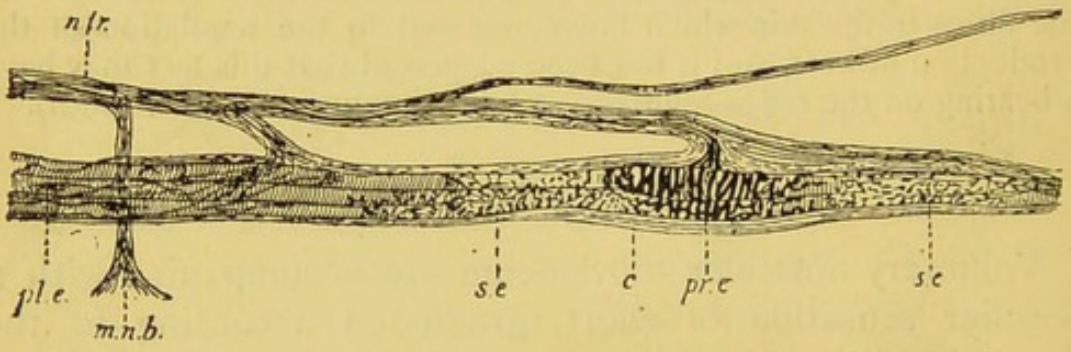

FIG. 329.—MUSCLE SPINDLE (HALLIBURTON, AFTER RUFFINI).

c, sheath of the spindle; *n.tr.*, trunk of nerve, which sends fibres through the sheath into the spindle, where they form endings (*pr.e.*, *s.e.*, *pl.e.*) of various kinds; *m.n.b.*, bundle of motor fibres.

numerous afferent fibres (p. 731). Some of these must be nerves of ordinary sensation. For although, when a muscle is laid bare in man and stimulated electrically, the sensation does not in general amount to actual pain, it is capable, under the influence of strong stimuli, of taking on a painful character. And nobody who has felt the severe and sometimes almost intolerable pain of muscular cramp would be likely to deny the existence of sensory muscular nerves. But after deducting these, we must assume that a large proportion of the afferent nerves of muscle have other functions, and among them may be the conveyance of impulses connected with the muscular sense. The muscle-spindles or neuro-muscular spindles (Fig. 329), peculiar structures which occur in large numbers in most of the skeletal muscles, and have been carefully studied by Huber, Sihler, Ruffini, and other observers, are the terminations of many of the sensory fibres. They are long narrow bodies, with a thick sheath of connective tissue enclosing fine striped muscular fibres. Medullated nerve-fibres enter the spindle, and

there, dividing into branches and losing their medullary sheath, form endings of various kinds around and between the muscular fibres. It is probable that in contraction of the muscles the nerve-fibres in the spindles are compressed, and thus mechanically stimulated.

In the spinal cord these impulses are conducted up through the posterior column; and, although nothing is known as to the paths they follow in the higher parts of the central nervous system, it is certain that there is some afferent bond of connection between the cortical motor areas and the muscles which they control (p. 754).

Tactile sensations set up in the skin or mucous membrane lying over contracting muscles may also help the nervous motor mechanism in appreciating and regulating the amount of contraction; but the fact that, in anæsthesia of the mucous membrane covering the vocal cords produced by cocaine, the voice is not at all impaired, shows that muscular contractions of extreme nicety can be carried on without any such aid.

Pain.

Pain has been defined as 'the prayer of a nerve for pure blood.' The idea is not only true as poetry, but, with certain deductions and limitations, true as physiology. That is to say, pain, as a rule, is a sign that something has gone wrong with the bodily machinery; freedom from pain is the normal state of the healthy body. Physiologically, pain acts as a danger-signal; it points out the seat of the mischief, and even, in certain cases, by compelling rest, favours the process of repair. Thus, the surgeon has sometimes looked upon pain as 'Nature's splint.' But as a matter of fact, a certain amount of pain occurring at intervals is not incompatible with high health; and probably nobody, even when accidents and indiscretions of all kinds are avoided, is entirely free from pain for any considerable time. Sometimes, indeed, the mere fixing of the attention on a particular part of the body is sufficient to bring out or to detect a slight sensation of pain in it; and it is matter of common experience that a dull continuous pain, like that of some forms of toothache, is aggravated by thinking of it, and relieved when the attention is diverted.

In general, the skin is far more sensitive to pain than the deeper structures. The most painful part of an operation is generally the stitching of the wound. The cutting of healthy muscle causes no pain. In an operation in which an artificial connection was established between the stomach and the small intestine (gastro-enterostomy), and in which no anæsthetic was administered, the only pain of which the patient complained was produced by the incision in the skin (Senn). The spasmodic contraction of the intestines and stomach causes the intense pain of colic and gastralgia. Labour is an example of a strictly physiological function which is the occasion of severe pain. Tissues normally insensible to pain may become acutely painful when inflamed.

Whether the sensation of pain can be caused by excessive stimulation of the nerves of common tactile sensibility or not, there can be little doubt that afferent 'pain' fibres exist which are anatomically distinct from the fibres of tactile sensation. For the conducting paths in the spinal cord appear not to be the same for tactile and for painful impressions. And in certain cases of disease sensibility to pain may be lost, while tactile sensations are still perceived; or, on the other hand, pain may be felt in cases where tactile sensibility is abolished. Loss of temperature sensation, however, is almost always accompanied by loss of sensibility to pain.

Localization of Sensations.—We not only perceive sensations of touch, temperature, pain, etc., but are able, more or less accurately, to localize the part of the body from which the sensory impressions come. This power of localization is not equal for all portions of the body nor for all kinds of sensations. It is best developed for touch (in the restricted sense), and all the varieties of common sensation are better localized on the skin than in any of the deeper structures. The precise mechanism of the localization is unknown. But we must suppose that each peripheral area is 'represented' in the brain, so that the arrival of afferent impulses from it affects particularly the related cerebral area. The brain, therefore, so to speak, associates excitation of a given cerebral area with stimulation of the corresponding peripheral area, and thus not only recognises the quality and quantity of the resultant sensation, but also localizes it; just as a waiter who watches the bell indicator not only learns how a bell has been rung, whether once or twice, peremptorily or languidly, but also in what room it has been rung. If, to pursue the illustration a little farther, he is aware that two rooms are connected with one bell, but that one of the rooms is scarcely ever occupied, he associates the ringing of the bell with a summons from the other room even when it happens to be rung from the usually vacant room. In like manner the brain seems to connect the arrival of sensory impulses from the internal organs, which have few sensory fibres, and these perhaps not often stimulated, with excitation in a related cutaneous region, from which it is constantly receiving sensory impressions. The fact already mentioned (p. 699), that in disease of internal organs the pain is referred to some portion of the skin, may be thus explained.

Relation of Stimulus to Sensation.

It is impossible to measure sensation in terms of stimulus. All that we can do is to compare differences in the intensity of stimuli and differences in the resultant sensations, or, in other words, to compare stimuli together and to compare sensations together. And when we determine the amount by which a given stimulus must be increased or diminished in order that there may be a just perceptible increase or diminution in the sensation, it is found that (with certain limitations) the two are connected by a simple law: *Whatever the absolute strength of a stimulus of given kind may be, it must be increased by the same fraction of its amount in order that a difference*

in the sensation may be perceived (sometimes called *Weber's law*). Thus, a light of the strength of one standard candle must be increased by $\frac{1}{100}$th candle, a light of 10 candles by $\frac{10}{100}$ths, and a light of 100 candles by a candle, in order that the eye may perceive that an increase has taken place, just as the weight necessary to turn a balance increases with the amount already in the pans. The fraction varies for the different senses. It is about $\frac{1}{100}$ for light, $\frac{1}{3}$ for sound. But it would appear that Weber's law does not hold for the pressure sense, nor for the other senses above and below certain limits. Fechner, making various assumptions, has thrown Weber's law into the form $y = k \frac{\log x}{x_0}$, where y is the intensity of sensation, x the intensity of stimulation, x_0 the smallest intensity of stimulus which can be perceived (liminal intensity), and k, a constant. This so-called psycho-physical law of Fechner states that the sensation varies as the logarithm of the stimulus. But Fechner's law has been subjected to serious criticism, and the subject cannot be further pursued here.

PRACTICAL EXERCISES ON CHAPTER XIII.

1. **Formation of Inverted Image on the Retina.**—Fix the eye of an ox or of a dog or rabbit (preferably an albino), after removal of part of the posterior surface of the sclerotic, in a hole cut in a blackened box. Place a candle in front of the eye. Look from behind, and observe the inverted image of the candle formed on the retina. Move the candle until the image is as sharp as possible. Now bring between the candle and the eye a concave lens. The image becomes blurred, the candle must be put farther away to render it distinct, and perhaps no position of the candle can be found which will give a sharp image. If the lens is convex, the candle must be brought nearer, and a sharp image can always be formed by bringing it near enough. If both a convex and a concave glass be placed in front of the eye, they will partially or wholly neutralize each other.

2. **Helmholtz's Phakoscope** (Fig. 330).—This instrument is employed in studying the changes that take place in the curvature of the lens during accommodation. It is to be used in a dark room. A candle is placed in front of the two prisms P, P'. The observer looks through the hole B ; the observed eye is placed at a hole opposite the hole A. The candle or the observed eye is moved till the observer sees three pairs of images, one pair, the brightest of all, reflected from the anterior surface of the cornea ; another, the largest of the three, but dim, reflected from the anterior surface of the lens; and

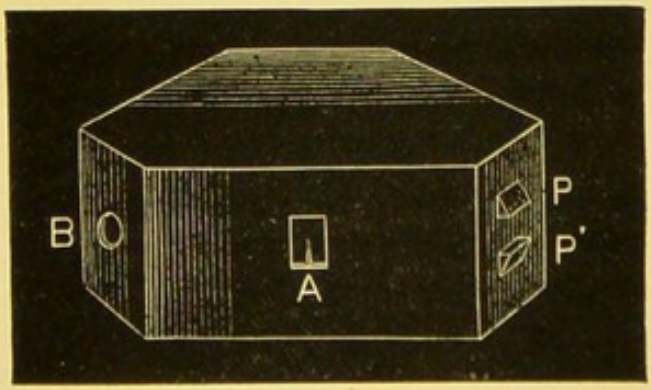

FIG. 330.—PHAKOSCOPE.

a third pair, the smallest of all, reflected from the posterior surface of the lens (Fig. 292). The last two pairs can, of course, only be seen within the pupil. The observed eye is now focussed first for a distant object (it is enough that the person should simply leave his eye at rest, or imagine he is looking far away), and then for a near object (an ivory pin at A). During accommodation for a near object no change takes place in the size, brightness, or position of the first or third pair of images; therefore the cornea and the posterior surface of the lens are not altered. The middle images become smaller, somewhat brighter, approach each other, and also come nearer to the corneal images. This proves (*a*) that the anterior surface of the lens undergoes a change; (*b*) that the change is increase of curvature (diminution of the radius of curvature), for the virtual image reflected from a convex mirror is smaller the smaller is its radius of curvature. (The third pair of images really undergo a

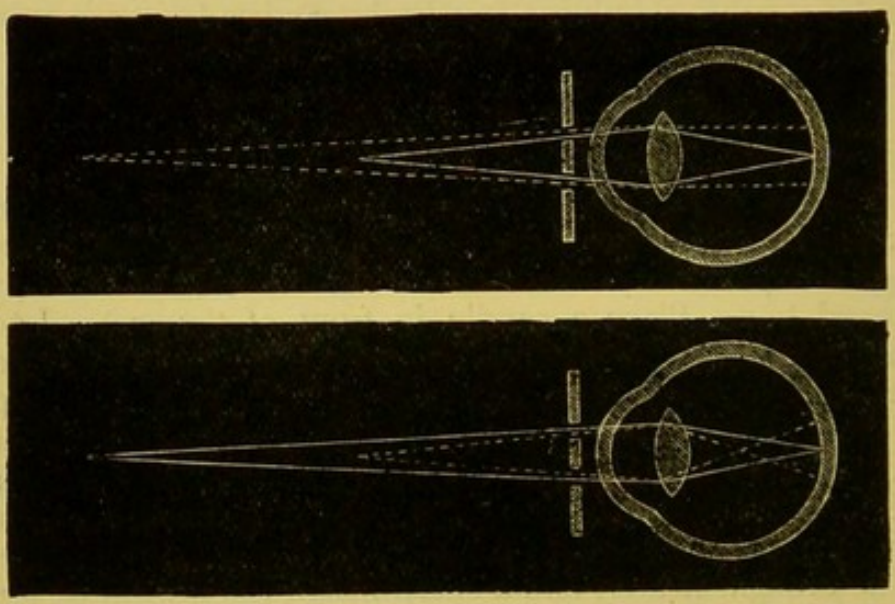

FIG. 331.—SCHEINER'S EXPERIMENT.

In the upper figure the eye is focussed for a point farther away than the needle; in the lower, for a nearer point. The continuous lines represent rays from the needle, the interrupted lines rays from the point in focus. But the lines *inside* the eye, which by an error in engraving are drawn as continuous lines, ought to be interrupted, and *vice versâ*.

slight change, such as would be caused by a small increase in the curvature of the posterior surface of the lens; but the student need not attempt to make this out.)

3. **Scheiner's Experiment.**—Two small holes are pricked with a needle in a card, the distance between them being less than the diameter of the pupil. The card is nailed on a wooden holder, and a needle stuck into a piece of wood is looked at with one eye through the holes. When the eye is accommodated for the needle, it appears single; when it is accommodated for a more distant object, or not accommodated at all, the needle appears double. The two images approach each other when the needle is moved away from the eye, and separate out from each other when it is moved towards the eye. When the eye is accommodated for a point nearer than the needle, the image is also double; the images approach each other when the

needle is brought closer to the eye, and move away from each other when it is moved away from the eye. If while the needle is in focus one of the holes be stopped by the finger, the image is not affected. When the eye is focussed for a greater distance than that of the needle, stopping one of the holes causes the image on the other side of the field of vision to disappear; if the eye is focussed for a smaller distance, the image on the same side as the blocked hole disappears (Fig. 331).

4. **Kühne's Artificial Eye.**— This is an elongated box provided with a glass lens to represent the crystalline, and a ground-glass plate to represent the retina. The box is filled with water to which a little eosin has been added. The water must be perfectly clear. If the tap water is turbid it should be filtered or allowed to settle, or distilled water should be used. A beam of sunlight or electric light, or, in case these are not available, a beam from an oil stereopticon, is made to pass through the box. Many of the facts of vision can be illustrated by means of this piece of apparatus.

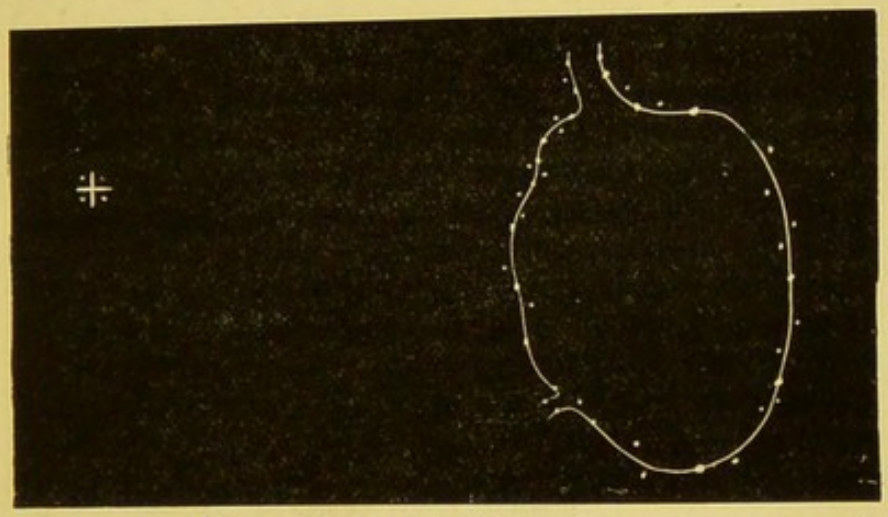

FIG. 332.—MAP OF BLIND SPOT (REDUCED BY ONE-HALF).
Right eye. Distance of eye from paper, 12 inches.

(*a*) Let the rays of light pass through an arrow-shaped slit in a piece of cardboard. An inverted image of the arrow is formed on the retina. Move the retina nearer to or farther from the lens to make the image sharp. In the eye, accommodation is not brought about by a change in the distance of retina and lens, but by a change of curvature in the lens.

(*b*) Remove the lens. The focus is now far behind the retina. This illustrates the state of matters after the lens has been removed for cataract. The arrow can again be sharply focussed on the retina by putting a convex lens in front of the artificial eye. But this must be much weaker than the lens which has been removed, for if the latter be placed in front of the eye, the image is formed a little behind the cornea.

(*c*) Replace the lens. Move the retina so far back that the image is focussed in front of it. This is the condition in the myopic eye.

Put a weak concave lens in front of the eye; the image now falls more nearly on the retina. Move the retina forward, so that the focus is behind it. This corresponds to the hypermetropic eye. Put a weak convex lens in front of the eye to correct the defect.

(*d*) Observe that a plate with a hole in it, placed in front of the eye, renders an indistinctly focussed image somewhat sharper by cutting off the more divergent peripheral rays.

(*e*) Fill with water the chamber in front of the curved glass that

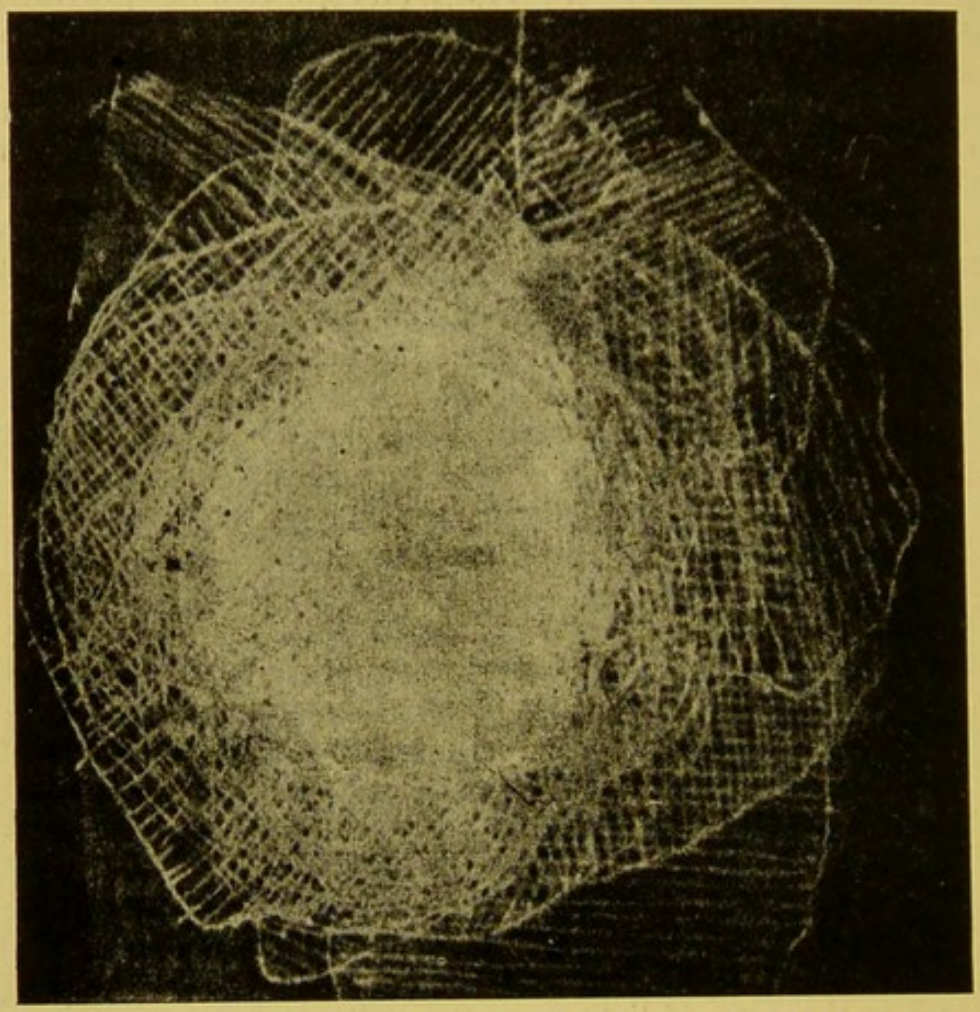

FIG. 333.—COMPOSITE PICTURE OF BLIND SPOT (NOT REDUCED).

The blind spot of the right eye was mapped by 31 men, the eye being always at a distance of 12 inches from the paper. The maps were then superposed. The amount of white at any point of the figure is intended to correspond to the number of maps which overlapped at that point. Although the mechanical process of reproduction gives rather an imperfect view of the composite map, the area in the centre of the figure where the white is most continuous, and which represents the shape of the majority of the blind spots, evidently bears a general resemblance to the outline in Fig. 332.

represents the cornea. The focus is now behind the back of the eye altogether. Refraction by the cornea is here abolished, as is the case in vision under water. An additional lens inside the eye, or a weaker one in front of it, corrects the defect. Fishes have a much more nearly spherical lens than land animals, and a flat cornea.

(*f*) Fill the hollow cylindrical lens with water, and place it in front of the artificial eye. It is now astigmatic. A point of light is focussed on the retina, not as a point, but as a line. The vertical and hori-

zontal limbs of a cross cut out of a piece of cardboard and placed in the path of the beam of light cannot be both focussed at the same time.

5. **Mapping the Blind-spot.**—Make a black cross on a piece of white paper attached to the wall, the centre of the cross being at the height of the eye in the erect position. Stand about 12 inches from the wall, the chin supported on a projecting piece of wood. Fix the centre of the cross with one eye, the other being closed, and move over the paper a pencil covered, except at the point, with white paper, until the point just disappears. Make a mark on the paper at this point, and repeat the observation for all diameters of the field. The blind-spot is thus marked out (Fig. 332). Its shape is not the same in all eyes (Fig. 333). Its size and distance from the fovea centralis can be calculated from the construction given in Fig. 291.

6. **Ophthalmoscope**—(1) **Human Eye** (p. 800).—Let A be the observer, and B the person whose eye is to be examined. A and B are seated facing each other. Suppose that the right eye of B is to be examined. Close to the left ear of B is a lamp on a level with his eyes: the room is otherwise dark. For a clinical examination, the pupil should be dilated by putting into the eye a drop of a ·5 per cent. solution of atropia sulphate, but this is not indispensable for the experiment.

(*a*) *Direct Method.*—A takes the mirror in his right hand, and, holding it close to his own eye, looks through the central hole, and throws a beam of light into B's eye. A red glare, the so-called 'reflex' from the choroidal vessels, is now seen. A then brings the mirror to within 2 or 3 inches of B's eye, keeping his own eye always at the aperture. A and B both relax their accommodation, as if they were looking away to a distance. If both eyes are emmetropic, the retinal vessels will be seen. B should now look away past the little finger of A's right hand. This causes slight inward rotation of B's eye, and brings into view the white optic disc with the central artery and vein of the retina crossing it.

(*b*) *Indirect Method.*—A takes the mirror in his right hand to examine B's right eye, places his own eye behind the aperture as before at a distance of about 18 inches from B, and throws a beam of light into B's eye. Then A takes a small biconvex lens in his left hand, and places it 2 or 3 inches in front of B's eye, keeping it steady by resting his little finger on B's temple. A now moves the mirror until he sees the optic disc.

(2) Examine a rabbit's eye by the direct and indirect method. Dilate the pupil by a drop or two of atropia solution.

For practice, before doing (1) and (2) the student should examine an artificial 'eye' by both methods, so as to get a clear view of what represents the retina. A substitute for the artificial eye may be made by unscrewing the lower lens of the eyepiece of a microscope, and fastening in its place a piece of paper with some printed matter on it. The letters must be made out with the ophthalmoscope.

7. **Pupillo-dilator and Constrictor Fibres.**—(*a*) Set up an induction machine arranged for tetanus, and connect a pair of electrodes

through a short-circuiting key with the secondary. Etherize a cat by putting it into a large vessel with a lid, slipping into the vessel a piece of cotton-wool soaked with ether, and waiting till the movements of the animal inside the vessel have ceased. Then quickly put the cat on a holder and maintain anæsthesia with ether. Expose the sympathetic in the neck (p. 190); the carotid is taken as the guide to it. Ligature the nerve, and cut below the ligature. On stimulating the upper (cephalic) end, the pupil of the corresponding eye dilates.

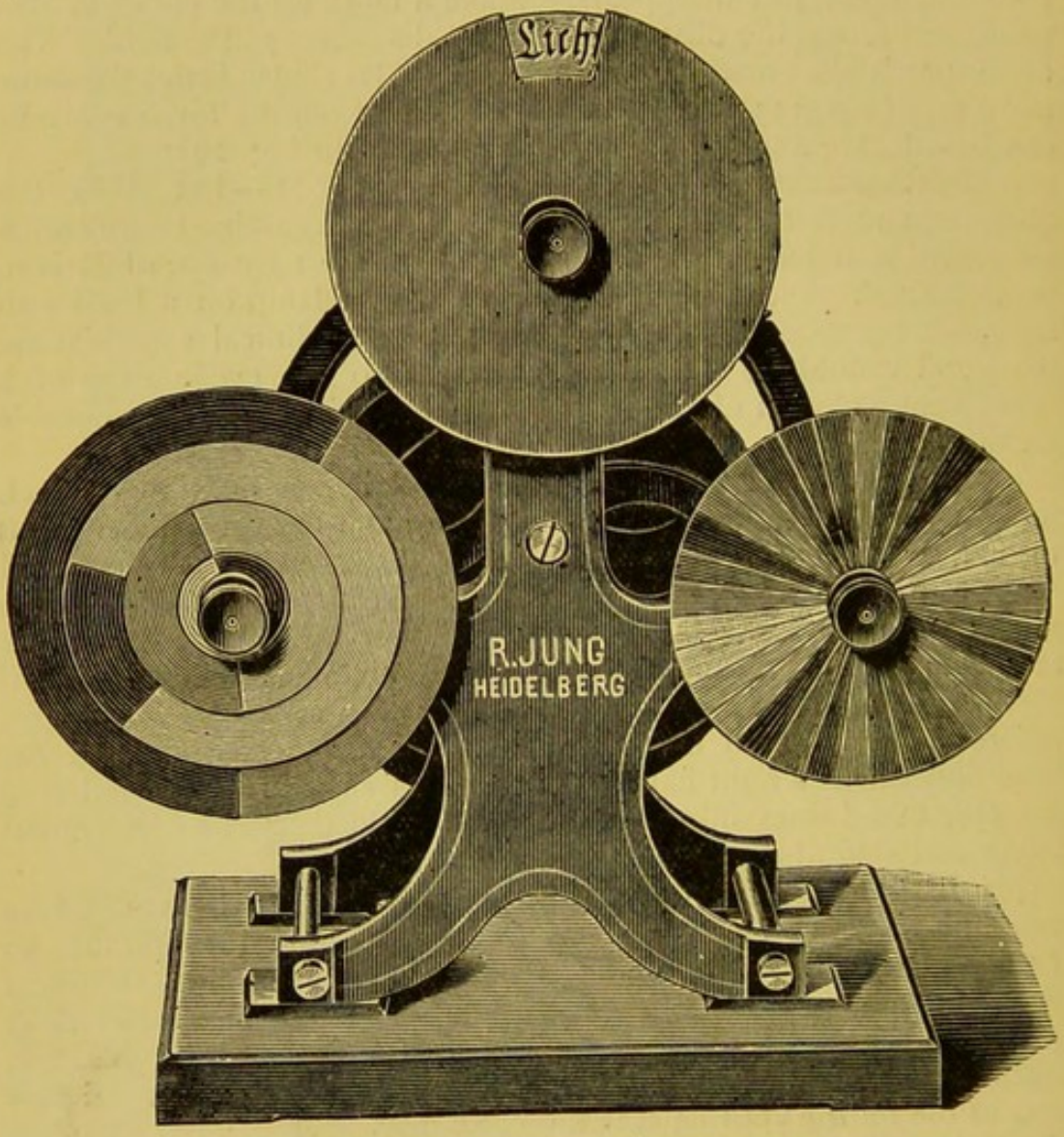

FIG. 334.—APPARATUS FOR COLOUR-MIXING.

(*b*) Observe in the eye of a fellow-student, or, by means of a looking-glass, in your own eye, that when light falls on one eye both pupils contract.

(*c*) Observe that when the eye is accommodated for a near object the pupil contracts, and that it dilates when a distant object is looked at.

8. **Colour-mixing.**—(*a*) Arrange a red and a bluish-green disc on one of the steel discs of the colour-mixing apparatus shown in

Fig. 334, so that a part of each is seen. On another arrange a violet and a yellow disc, and on the third an orange and a blue disc. By adjustment of the proportions of the two colours a uniform grey can be obtained from each of these combinations (complementary colours) when the discs are rapidly rotated.

(*b*) Mix two colours that are not complementary, *e.g.*, blue and red; grey or white cannot be obtained by any adjustment of proportions; the result is always a mixed colour, the precise hue depending on the amount of each ingredient.

(*c*) Take papers of any three colours from widely-separated parts of the spectrum, *e.g.*, blue, green, and red, and arrange them on one of the rotating discs. By varying the proportions white can be produced, and any other coloured paper fastened on another of the rotating discs can be matched by adding white to the three colours.

9. **Talbot's Law.**—Rotate a disc one sector of which is black and the rest white, or a disc like that in Fig. 315. A uniform shade is produced as soon as a speed of about 25 revolutions a second has been attained, and this is not altered by further increase in the speed.

10. **Purkinje's Figures.**—(*a*) Concentrate a beam of sunlight by a lens on the sclerotic at a point as far as possible from the corneal margin, passing the ray through a parallel-sided glass trough filled with a solution of alum to sift out the long heat-rays. The eye is turned towards a dark ground. The field of vision takes on a bronzed appearance, and the retinal bloodvessels stand out on it as a dark network, which appears to move in the same direction as the spot of light on the sclerotic. A portion of the field corresponding to the yellow spot is devoid of shadows (p. 810).

(*b*) Direct the eyes to a dark ground while a flame held at the side of the eye, and at a distance from the visual line, is moved slightly to and fro. A picture of branching bloodvessels appears. This experiment is performed in a dark room (p. 811).

(*c*) Immediately on awaking look at a white ceiling for an instant; a pattern of branched bloodvessels is seen. If the eye be at once closed, and then opened with a blinking movement, this may be observed again and again. Ultimately the appearance fades away.

11. **Monochord.**—Study by means of the monochord, a stretched string with a movable stop, the relation between the pitch of the note given out by a vibrating string, and its length and tension.

12. **Beats.**—Cause two tuning-forks of nearly equal pitch to vibrate at the same time. Make out the beats, and count their number per second.

13. **Aesthesiometry.**—Measure on different parts of the skin and accessible mucous membranes the distances at which the points of a pair of compasses must be held apart in order that two distinct sensations may be experienced (p. 851) (*aesthesiometer*).

CHAPTER XIV.

REPRODUCTION.

Regeneration of Tissues.—Since cells are constantly dying within the body, they must be constantly reproduced. In some tissues the process by which this is accomplished is more evident, and therefore better known, than in others. The most highly-organized tissues are with difficulty repaired, or not at all. The epidermis is always wearing away at its surface, and is being constantly replaced by the multiplication of the cells of the stratum Malpighii. In the corneous layer we have only dead cells ; in the Malpighian layer we have every histological gradation from squames to columns, and every physiological gradation from cells which are about to die to cells that have just been born. The corpuscles of the blood undoubtedly arise at first, and are recruited throughout life, by the proliferation of mother-cells. The gravid uterus grows by the formation of new fibres from the old, and by the enlargement of both old and new. A severed muscle is generally united only by connective or scar tissue, but under favourable conditions a complete muscular 'splice' may be formed. A broken bone is regenerated by the proliferation of cells of the periosteum, which become bone-corpuscles. We do not know whether there is any new formation of nerve-cells in the adult organism (but see p. 749), but peripheral nerve-fibres which have been destroyed by accident or operation are readily regenerated by the growth of new processes from the cells that originally produced them ; and the end-organs of efferent nerves may share in this regeneration.

In lower forms of animals, and in all or most vegetables, the power of regeneration is much greater than in man. The starfish can not only repair the loss of an arm, but from a severed arm a complete animal can be developed. A newt can reproduce an amputated toe, and every tissue—skin, muscle, nerves, bone—will be in its place. After extraction of the crystalline lens in triton larvæ, a new lens is formed from the iris epithelium.

Thus, in a sense, reproduction is constantly going on within the bodies even of the higher animals. But since the whole organism eventually dies, as well as its constituent cells, a reproduction of the whole, a regeneration *en masse*, is required.

A cell of the stratum Malpighii can only, so far as we know, reproduce a similar cell, and this is characteristic of cells that have

undergone a certain amount of differentiation, especially in the higher animals. The fertilized ovum, on the other hand, has the power of reproducing not only ova like itself, but the counterparts of every cell in the body. And this is only the highest development of a power which is in a smaller degree inherent in other cells in lower forms. Plants and the lowest animals are far less dependent upon reproduction by means of special cells. A piece of a Hydra separated off artificially or by simple fission becomes a complete Hydra, as was shown by Trembley a century and a half ago. A cutting from a branch, a root, a tuber, or even a leaf of a plant, may reproduce the whole plant. It is as if each cell in these lowly forms carried within it the plan of the complete organism, from which it built up the perfect plant or animal. But the special bias or trend of growth characteristic of each form is not a rigid rule. It can be modified; it is modified in every garden and pond by influences coming from without. The inborn rule of life for many plants is to grow straight up; but this rule is often traversed by circumstances—by differences in the amount of sunshine, for example, caught by one side or the other, or by the position of neighbouring objects which hinder or help a vertical growth. And in animals Pflüger has shown that the direction of the lines of cleavage of the ovum of a frog depends on the direction in which gravity acts, although Driesch and Hertwig find that the nucleus can even be made artificially to change its place with reference to the yolk, without hindering the development of a normal animal. Artificial mouths, surrounded by tentacles, can be formed in Cerianthus, an animal belonging to the same group as the sea-anemones, merely by making a cut in the body-wall and preventing it from closing. In an Ascidian, too (the *Cynone intestinalis*), artificial openings in the branchial sac, surrounded by numerous pigmented points similar to the eye-spots around the natural mouth and anus, have been produced (Loeb). Even in Amphioxus, the lowest of the vertebrates, the eggs have been broken up by shaking, and a complete animal evolved from as little as one-eighth of an ovum. If the separation was incomplete a kind of Siamese twins, or even triplets, could be obtained (Wilson and Mathews).

Reproduction in the Higher Animals.—In all the higher animals reproduction is sexual, and the sexes are separate.

In regard to the secretions of the reproductive glands, all that is necessary to be said here is that, unlike other secretions, their essential constituents are living cells. The spermatozoa in the male have, indeed, diverged far from the primitive type. Certain (spermatogenous) cells in the tubules of the testicle divide so as to form spermatoblasts. Each spermatoblast becomes a spermatozoon, the head of the latter representing the nucleus of the former; and it is this nucleus which is the essential contribution of the male to the reproductive process. The tail of the spermatozoon is simply, from the physiological point of view, a motile arrangement, whose function it is to carry the nucleus of the spermatoblast, freighted with all that the father can transmit to the offspring, into the neighbourhood of the female reproductive element or ovum.

The ovum also begins as a typical cell with nucleus (germinal vesicle) and nucleolus (germinal spot), and it forms, by its repeated subdivision, all the cells of the fœtal body. But, except in some (*parthenogenetic*) forms, it never awakens to this reproductive activity till fecundation has occurred; and fecundation essentially consists in the union of the male with the female element, or rather in the union of the male and female nucleus.

From time to time a Graafian follicle, over-distended by its liquor folliculi, bursts on the surface of the ovary and discharges an ovum. The frayed end of the Fallopian tube, rising up finger-like from the dilatation of its bloodvessels, grasps the ovum, and it is passed slowly along the tube by the downward-lashing cilia which line it. If not impregnated, it soon perishes amid the secretions of the uterus—how soon has been matter of discussion, and can hardly be considered as settled. If, however, impregnation occurs, the ovum becomes fixed in one of the crypts or pouches of the uterine mucous membrane (*decidua serotina*), which grows round it as the *decidua reflexa*.

Menstruation.—In the mature female, from puberty, the age at which the reproductive power begins (thirteenth to fifteenth year), on till the time of the *menopause* (fortieth to fiftieth year), at which it ceases, an ovum—or it may be in some cases more than one—is discharged at regular intervals of about four weeks. This discharge is accompanied by certain constitutional symptoms and local signs that last for a variable number of days. The genital organs are congested, and a quantity of blood, which varies in different individuals, but is usually from 100 to 200 grammes—that is to say, $\frac{1}{40}$th to $\frac{1}{20}$th of the whole of the blood in the body—is shed. At the same time, the whole or a portion of the mucous membrane of the uterus is cast off.

As to the physiological meaning of this *menstruation*, as it is called, opinion is divided. Two chief theories have been proposed to account for it, both of which agree in considering the phenomenon to be connected with a preparation of the uterus for the reception of the ovum. But according to the theory of Pflüger the mucous membrane is stripped off (by a process analogous to the 'freshening' or paring of the indurated edges of a wound by the surgeon, in order that union may occur when they are brought together) *on the chance, so to speak, that an impregnated ovum may arrive.* On the alternative theory, this change takes place *because* the ovum has not been impregnated, and the bed prepared for it is therefore not required (Reichert, Williams, etc.).

Development of the Ovum.—Before fecundation, and apparently as a preparation for it, the ovum is the seat of remarkable changes, which have been most fully studied in the eggs of certain invertebrate animals. A spindle-shaped structure appears stretching between the nucleus and the surface of the ovum; at its outer end a small round body, the first polar body, rises up from the surface of the egg as if it were being squeezed out of it, and is finally extruded. In most cases the process is repeated; a new spindle forms and a second polar body or directive corpuscle is cast out. As to the significance of

these changes there has been much discussion. It seems to be agreed that the spindle is formed in part, at any rate, from the nucleus or germinal vesicle, and that the result of the process is the expulsion of a portion of the chromatin skein (p. 18), which is restored by the male pronucleus when it arrives and penetrates the ovum.*

Not till all these events have taken place—extrusion of the two polar bodies, or *maturation*, penetration of the spermatozoon and blending of its head (the male pronucleus) with the remnant of the nucleus of the ovum (female pronucleus), or *fecundation*—not till then does the ovum begin to divide. The germinal spot, or nucleus, splits into two, and the yolk being also cleft by a corresponding furrow, two complete nucleated cells make their appearance. These divide in turn, till at length (in the mammal) the embryo is represented by a hollow sphere or vesicle, with a cellular crust. During division the upper or outer cells have always been larger than the inner and lower, and have multiplied more rapidly; and thus it comes about that the hollow sphere of large cells encloses a mass of smaller cells, along with remnants of broken-down yolk and of fluid derived by absorption from the contents of the uterus. The smaller cells continue to multiply and arrange themselves as a lining to the sphere already formed, so that in a short time it becomes double, and we have already differentiated two of the primary embryonic layers, the *epiblast*, or superficial, and the *hypoblast*, or deep layer. The whole sphere is called the *blastoderm*, or the blastodermic vesicle.

While this inner shell of hypoblastic cells is gradually creeping on to completion, there appears at a part where it is already fully formed a small opaque whitish disc, the germinal area or *embryonal shield*. This represents the stocks on which the framework of the embryo is to be laid down. The area elongates; at its posterior end appears a thickened line, the *primitive streak*, soon furrowed by a longitudinal groove, the *primitive groove*, that marks the direction in which the long axis of the future embryo will lie, but is not itself a permanent line in the building, and ultimately vanishes. The appearance of the primitive streak is the signal that a rapid proliferation of the cells of the germinal area, and especially of the epiblast, has begun; and this goes on until a third layer is formed intermediate in position to the original two, and therefore named the *mesoblast*. While this is pushing its way over the germinal area and into the rest of the blastodermic vesicle, the epiblast in front of the primitive streak rises up in two lateral ridges, enclosing between them the *medullary groove*. The medullary groove is the beginning of the cerebro-spinal

* Loeb has lately made a contribution of far-reaching importance to our knowledge of the significance of fertilization by the discovery that the unfertilized egg of the sea-urchin can develop in sea-water to which magnesium chloride has been added in a certain proportion, just as if a spermatozoon had entered the egg. From his experiments he deduces the conclusion that the unfertilized egg of the sea-urchin contains all the elements essential for development, and that 'the only reason which prevents it from developing parthenogenetically is the constitution of the sea-water.'

axis; its walls first come to overhang the furrow, and then to coalesce; and the medullary groove has now become the neural canal. Immediately under it the mesoblast forms a rod of cells, the *notochord*, which is the forerunner of the vertebral column; around this the bodies of the vertebræ are afterwards developed from cubical masses of mesoblastic cells, arranged in pairs along the notochord, and called the *protovertebræ*. The rest of the mesoblast, running out on each side from the protovertebræ, splits into two layers, an *upper or somatic layer*, which unites with the epiblast, and a *lower or splanchnic layer*, which unites with the hypoblast. Between the two layers is a space called the cœlom, or pleuro-peritoneal cavity (Fig. 335).

Up to the present, apart from the enclosure of the neural canal, all this formative activity is buried beneath the surface of the blastoderm, and has not showed itself by any external token; the embryo still appears as a portion of the germinal area, and lies in its plane. But now a pocket, or crease, or moat, beginning at the head as the head-fold, then pushing under the tail, gradually creeps round and undermines the whole embryo, which is raised above the general level, and, as it were, scooped out from the rest of the blastoderm; till at length it lies on the latter, something like an upturned canoe, enclosing a tube, complete in front and behind, but still open in the middle, where it communicates with the interior of the yolk-vesicle. Since this tube has been formed by the tucking in of the three ancestral layers of the blastoderm, it follows that it is lined by hypoblast, supported externally by the splanchnic sheet of mesoblast. So that now the body consists of a dorsal tube (the neural canal), essentially of epiblastic origin, a ventral tube (the alimentary canal), essentially of hypoblastic origin, and between the two a massive double layer of mesoblastic tissue, which contributes supporting elements to both. At this point it may be well to emphasize the fact that this embryological distinction of the three primitive layers has a deep and fundamental meaning, and corresponds to a physiological distinction that endures throughout life. The hypoblast, the lowest layer in position, may also be described as the lowest in the physiological hierarchy. It furnishes the epithelial lining of the alimentary canal from the beginning of the œsophagus to near the end of the rectum, as well as the epithelium of the organs which arise from diverticula of the primitive intestine, viz., the digestive glands with the exception of the salivary glands, the lungs, and the passages leading to them, the thyroid, and the greater part of the thymus gland in its primitive condition before the lymphoid tissue derived from the mesoblast has as yet grown into it. According to some authorities, the notochord is also derived from the hypoblast.

Upon the whole, it may be said that the tissues of hypoblastic origin are essentially concerned in chemical labours, in the absorption of food material and excretion of waste products, The mesoblastic tissues are essentially concerned in mechanical labour; they are the tissues of movement and of passive support. The epiblastic tissues are at the top of the pyramid; they govern the rest.

From the mesoblast arise the muscles, the entire vascular system with its blood and lymph corpuscles, the bones and connective tissues; and the Wolffian body and its appendages, which are the predecessors of the genital glands and ducts, and of the chief portion of the renal apparatus.

The epiblast forms the epidermis and its appendages, the epithelial end-organs of the nerves of special sense, and the nervous system, cerebro-spinal and sympathetic. The salivary glands and the mucous lining of the mouth and anus are developed from the epiblast, which is indented to meet the intestinal canal and give it access to the exterior at either end.

It is not possible here to trace in detail the development of all the organs of the embryo. Its nutrition and metabolism not only distinctly belong to the physiological domain, but, carried on as they are under conditions that seem so strange, and even so bizarre, to one acquainted only with adult physiology, are calculated to throw light on the metabolic processes of the fully developed body. And they cannot be understood without reference to the peculiarities of the vascular system in fœtal life. These we shall accordingly describe, but for further details as to the anatomy of the embryo the student is referred to some standard anatomical text-book, such as Quain's 'Anatomy.'

Physiology of the Embryo.—In the first period of its development the ovum, nestling in the pouch formed by the decidua serotina and reflexa, is fed simply by imbibition through the hollow finger-like processes or villi with which its external layer, the zona pellucida, becomes studded. Soon the heart appears as a tube (at first double), formed by cells belonging to the splanchnic layer of the mesoblast. It begins to pulsate in the chick as early as the middle of the second day, although it as yet contains neither nerve-cells nor fully-formed muscular fibres. In the mammal pulsation is late in making its appearance, in man about the beginning of the third week. A bloodvessel grows out from the anterior end of the heart and divides into two primitive aortic arches, from each of which a vessel (omphalo-mesenteric or *vitelline artery*, runs out in the mesoblast covering the umbilical vesicle or yolk-sac. The blood is returned to the heart by the *vitelline veins* coursing in on the walls of the vitelline duct. In this way the store of nutriment in the umbilical vesicle of the chick, which is the only solid or liquid food it receives or needs during the whole period of development, is tapped, and a regular channel of supply established. Oxygen is at the same time absorbed through the porous shell; but later on this respiratory function is taken over by the second or allantoic circulation. In the mammal the circulation on the umbilical vesicle is of much less consequence, for the quantity of material left over after the formation of the blastoderm is exceedingly small; it is only with a few days' provision in its haversack that the embryo starts out on its developmental march. And the vitelline vessels deriving their further supply of food and oxygen from the tissues of the mother in contact with the ovum, cease to be of use as soon as the second and more

perfect placental circulation is established, and soon shrivel up and disappear, as the umbilical vesicle shrinks.

The *second circulation* of the embryo is developed in connection with a remarkable off-shoot from the hind-gut called the *allantois*, which, before the fifth day in the chick and during the second week in man, pushes its way out between the somatic and splanchnic layers of the mesoblast, *i.e.*, in the pleuro-peritoneal cavity, and grows through the umbilicus, carrying bloodvessels along with it in its mesoblastic layer. Still earlier, and, indeed, while the embryo is being separated off from and raised above the level of the rest of the blastoderm by the deepening of the ditch around it, the further banks of this furrow, formed of epiblast and somatic mesoblast, have risen up on every side and, growing over the back of the embryo, have finally coalesced and enclosed it in a double-walled pouch (Fig. 335). The superficial layer of the pouch is called the *false amnion;* it soon blends with the tufted chorion or common outer envelope of the ovum. The inner layer persists as the *true amnion;* a liquid, the *amniotic fluid*, is secreted in the cavity which it encloses; and the embryo, loosely anchored for the rest of its intra-uterine life by the umbilical cord alone, floats freely within it. The amniotic fluid acts as a water jacket or cushion, to break the force of the inevitable shocks and jars transmitted from the mother to the fœtus and from the fœtus to the mother.

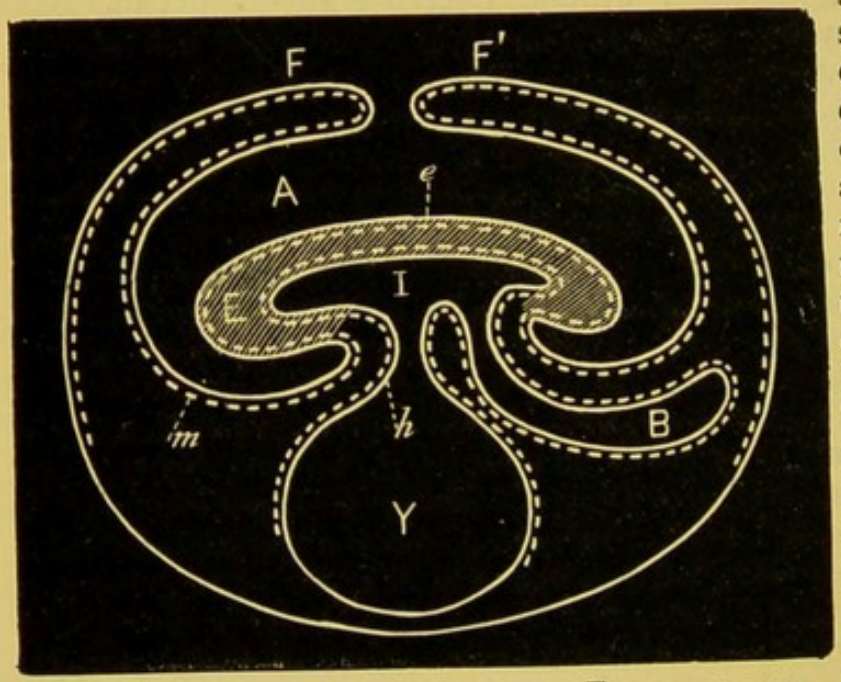

FIG. 335.—DIAGRAM TO ILLUSTRATE FORMATION OF AMNION.

A, cavity of true amnion; F, F', folds about to coalesce and complete the amniotic cavity; *m*, mesoblastic layer of amnion; B, allantois; I, intestinal cavity of embryo; Y, yolk-sac; *h*, hypoblastic layer; *e*, epiblastic layer of embryo. The embryo is the shaded portion in the middle of the figure. E is placed over the head region. No attempt is made to delineate its actual form. The mesoblast is represented by the interrupted line.

The allantois, growing out at the umbilicus, in the manner described, insinuates itself between the true and false amnion and soon blends with the latter. For a time the secretion of the primitive kidneys continues to be poured into the cavity of the allantois, so that it serves in part as an excretory organ, while in the bird it also performs the function of respiration; and in the mammal both food and oxygen are carried by its vessels to the fœtus during the greater part of intra-uterine life. But later on the outgrowth

atrophies and disappears, all except its origin from the alimentary canal, which dilates and persists as the urinary bladder, and its bloodvessels, which grow in the form of tufts or loops into the chorionic villi. The vessels are fed by two umbilical arteries which arise from the hypogastric arteries and run out at the umbilicus on the allantois. The blood is returned by an umbilical vein, whose further course we shall have soon to trace. The shrivelled stalk of the allantois, projecting through the umbilicus, takes part, with its bloodvessels, in the formation of the umbilical cord, which contains also the remains of the yolk-sac and is clothed externally by a layer of the amnion. Continuous with the umbilical cord, and stretching from the umbilicus to the urinary bladder, is a portion of the allantois which is represented in extra-uterine life by a thin cord-like structure, the urachus. The vascular tufts of the chorion, which at first cover the whole surface of the ovum and suck up food and oxygen from decidua serotina and reflexa alike, disappear in the region of the reflexa, hypertrophy all over the serotina—that is, where the ovum is in actual contact with the uterine wall—and this part of the chorion is now distinguished as the chorion frondosum. The giant villi of the chorion frondosum push their way into the thickened decidua serotina, and ultimately penetrate into the great capillaries or sinuses of the uterine mucous membrane. At the same time the tissue of the villi external to the vessels becomes reduced to a mere film, so that, except for a thin covering of decidual cells, the fœtal vessels are bathed in maternal blood. By this interweaving of decidua and chorion frondosum is formed the *placenta*, which for the rest of intra-uterine life acts as the great respiratory, alimentary and excretory organ of the fœtus. The maternal blood, as it streams through the colossal capillaries of the decidua, gives up to the fœtal blood oxygen and food substances, and receives from it carbon dioxide and in all probability urea. It is true that the blood in the uterine sinuses is not itself fully oxygenated; it is not bright red arterial blood. But it yet contains more oxygen than the purest blood of the fœtus, and is, therefore, able to part with some of the surplus to the dark stream of oxygen-impoverished blood brought by the umbilical arteries to the placenta. Thus, it has been found that while the blood of the umbilical artery of the fœtus of a sheep had 47 volumes per cent. of carbon dioxide, and only 2·3 of oxygen, that of the umbilical veins had 6·3 volumes of oxygen, and only 40·5 of carbon dioxide (Kuntz and Cohnstein). This, although far from the level of ordinary arterial blood, is yet the best the fœtus ever gets; and by a series of contrivances it is assured that this best should go first to the most important parts, the liver, the heart and the head, while the legs and most of the abdominal organs have to put up with an inferior supply. This is brought about mainly by the existence of three short-cuts for the blood, which disappear in the adult circulation, the ductus venosus, the ductus arteriosus and the foramen ovale (Fig. 336).

The blood of the umbilical vein, rich in oxygen for fœtal blood, passes partly through the circulation of the liver, but a part takes the

route of the ductus venosus, and empties itself directly into the inferior vena cava. The latter gathers up the more or less vitiated blood from the inferior extremities and the renal and hepatic veins, and pours its mixed but still fairly oxygenated contents into the right auricle. By means of the Eustachian valve, the jet coming from the mouth of the inferior vena cava is directed into the left auricle through the foramen ovale in the inter-auricular septum. There it is joined by the trickle of blood which is creeping through the unexpanded lungs. The left ventricle propels its contents through the aorta,

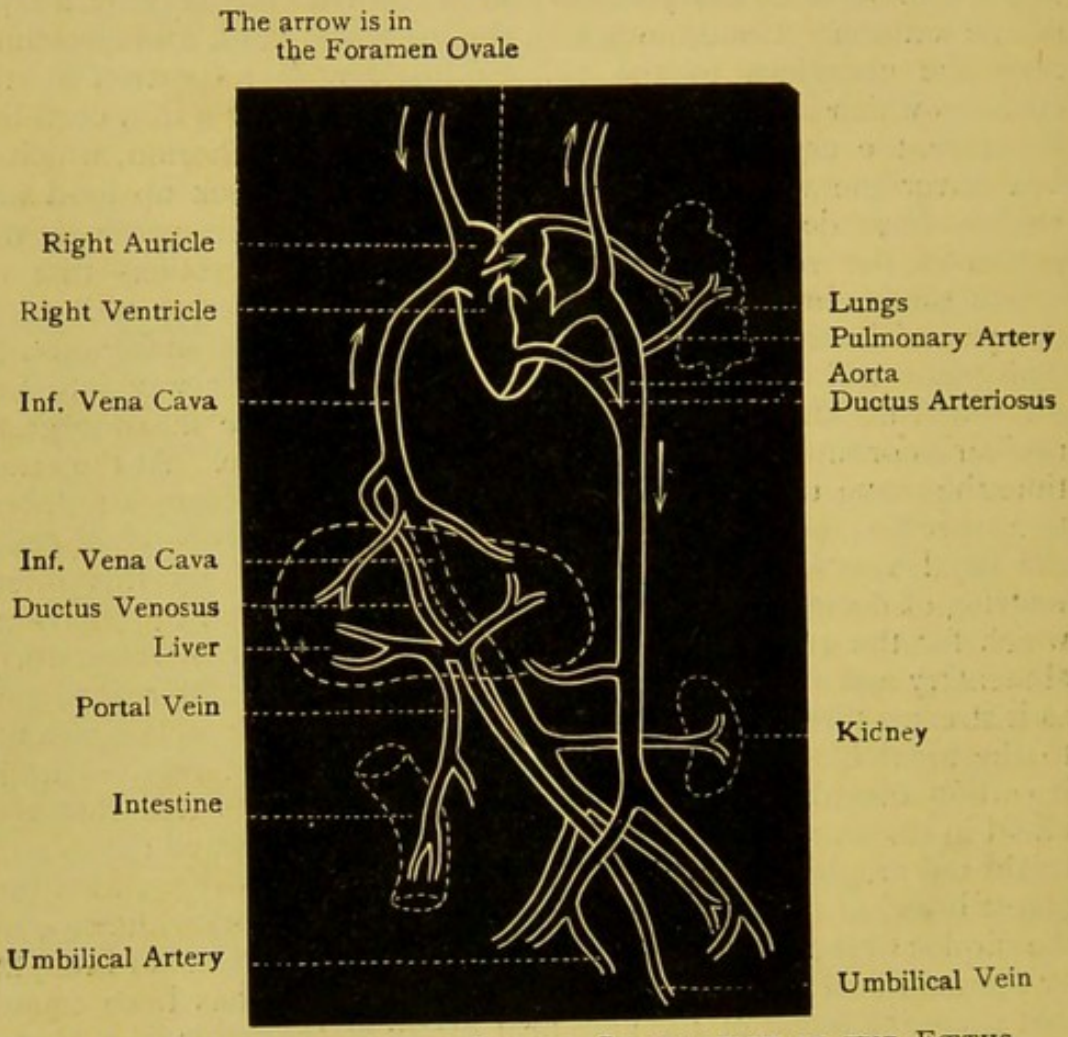

FIG. 336.—DIAGRAM OF THE SECOND CIRCULATION IN THE FŒTUS.
The arrows show the direction of the blood-flow.

and thus a large part of this comparatively pure or second-best blood is sent to the head and upper extremities. It returns in a vitiated state by the superior vena cava into the right auricle, and owing to the position of the Eustachian valve and the direction of the current, it flows now not through the foramen ovale, but into the right ventricle. Thence it is driven through the pulmonary artery, but only a small quantity of it finds its way through the lungs; the main stream is short-circuited through the ductus arteriosus, and mingles with the contents of the thoracic aorta below the origin of the cephalic and brachial vessels.

We may now give something more of precision to the statements that different parts of the body receive blood of different quality; and it is possible roughly to divide the organs in this respect into four categories: (1) The liver, which partakes both of the best and the worst, the purified blood of the umbilical veins and the vitiated blood of the intestines and spleen; (2) the heart, head, and upper limbs, which receive the blood from the inferior extremities and kidneys, mixed with the pure blood of the venous duct; (3) the legs, trunk, intestines, and kidneys, which are fed chiefly by the off-scourings of the cephalic end, mitigated, however, by a proportion of mixed blood from the inferior cava; (4) the lungs, which receive only a feeble stream of unmixed venous blood.

These peculiarities of the embryonic circulation are in obvious correspondence with the physiological events taking place in the fœtal body. The liver is not only the greatest gland in the embryo, as it continues to be in the adult, but its activity seems to dwarf that of all the other glands put together, and is in striking contrast with the functional torpor of the lungs. From the third month of intra-uterine life the secretion of bile begins and the intestines gradually fill with *meconium*, of which the principal constituent is bile. Accordingly the liver is most lavishly supplied with blood, while the lungs are stinted. And since the liver has, as we have already learnt, other and, in the adult at least, even more important labours than excretion, a large portion of the blood it receives is of the best quality: it enters the gland comparatively rich in oxygen, and passes out comparatively poor; while the lungs, which have to be nourished only for their own sake, and are of no use whatever till the child is born and respiration has begun, must be content with the poorest fare—with the crumbs that fall from the table of fœtal nutrition. The full-fed cephalic end of the embryo grows far more rapidly than the half-starved inferior extremities, and the head of the new-born child is large in proportion to the rest of the body.

There are some other points in the physiology of intra-uterine life which call for remark; and, to sum up in a few words the grand distinction between fœtal and adult life, we may say that growth is the keynote of the former, work (functional activity) of the latter. Thus, the muscles at an early period in their development become the seat of a great accumulation of glycogen, an accumulation which would entirely unfit them for the labours of fully-formed muscles, but which seems to be intimately connected with their own growth, and perhaps also with the growth of other tissues. Later on, when the muscles have been formed, their powers still lie dormant, but for the infrequent and feeble movements, generally regarded as reflex, but possibly to some extent originated in the cerebral cortex, which gives the mother the sensation of 'quickening.' But the store of glycogen now becomes reduced to its permanent amount, and the liver takes on its glycogenic function. It can hardly be doubted that the glycogen found in the placenta (bitch) is also deposited there in the interest of the rapidly growing fœtal tissues, as a kind of current account on which they can operate at any moment of emergency,

when the more distant maternal reserves cannot be drawn upon in time.

The excretory glands of the embryo, except the liver, scarcely awaken to activity during fœtal life. Urine may, indeed, be sometimes found in the bladder at birth, but it is often absent; and although a portion of the amniotic fluid, which contains traces of urea and salts, in addition to small quantities of albumin, may be secreted by the renal tubules, and find its way through the still open urachus into the amniotic sac, this contribution cannot imply more than a very slight degree of glandular action. The experiments of Kuntz, indeed, go far to show that this liquid comes essentially from the mother rather than from the child. He found that sulphindigotate of sodium injected into the bloodvessels of a pregnant animal (sheep) coloured the amniotic fluid and the placental tissues, but not the fœtus; while after injection into the latter the fœtal kidneys contained particles of the pigment, while the amniotic fluid remained uncoloured. The sebaceous glands have certainly begun their work by the secretion of the vernix caseosa, an oily material which covers the skin and serves to protect it from the continual irritation of the fluid in which the embryo floats.

The nervous system is even less active than the glandular tissues, and not more active than the muscles. There is evidently no scope for the exercise of the special senses. Psychical activity of every kind must be at the lowest ebb. Consciousness, if it exists at all, must be dull and muffled. And if motor impulses are discharged from the cortex, the psychical accompaniments of such discharge are doubtless widely different from those which we associate with voluntary effort.

This functional calm, broken only by the beat of the heart, is accompanied by a very feeble metabolism. The amount of oxygen carried to the tissues of an embryo sheep weighing 3·6 kilos, by the blood of the umbilical vein, was only 1·7 c.c. per minute; 2·8 c.c. of carbon dioxide per minute was given up to the blood of the mother in the placenta (Kuntz and Cohnstein). The gaseous exchange was, therefore, not one-tenth as much as in the adult sheep. In fact, the heat-production of the fœtus, sheltered as it is from loss except by the placental circulation, is only sufficient to raise its temperature by a small fraction of a degree above that of the mother. And it is not difficult to see that a large portion of this production must be due to the action of the heart. This beats at the rate of about 140 times a minute at full term.* The blood-pressure in the umbilical artery of

* It has not been finally determined whether the rate of the heart varies with the size, or what probably comes to the same thing, with the sex of the fœtus. As we have seen, the variation of the rate in the adult with the size of the body is associated with a corresponding variation in the metabolism and heat-loss, which are proportionally greater in a small than in a large animal. If this is a causal connection we should not expect that in the embryo *in utero*, where the conditions as regards heat-loss are entirely different, such a relation should exist, at any rate within the same species.

the mature embryo (sheep) varies from 60 to 80 mm. of mercury; but at the beginning of the aorta it will be more. The pressure in the pulmonary trunk must be about equal to that in the aorta, since the comparatively short and easy circuit through the lungs does not as yet exist; and in accordance with this equality of pressure (of work to be done) is the equality of thickness (of working power) in the walls of the two sides of the heart.

Suppose, now, that the embryo contains 60 grammes of blood for every kilo of body-weight, and that the whole of the blood passes through the circulation in twenty seconds. Then in twenty-four hours 259·2 kilos of blood will be forced through the heart for every kilo of body-weight against a pressure of, say, 80 mm. of mercury, or 1 metre of blood. This is equivalent, in round numbers, to 260 kilogramme-metres of work, or 600 small calories. Now, taking the total heat-production of the heart at three times the equivalent of its mechanical work, we get 1,800 calories per kilo of body-weight in twenty-four hours (see p. 503), or about $\frac{1}{20}$ of the heat-production of a resting adult.

So low is the intensity of metabolism in the embryo, so slight the demand for oxygen, that not only is even the purest blood, as has already been stated, far from saturated with that gas, but the relative proportion of hæmoglobin, the oxygen-carrier, is less than in the adult; and although constantly increasing in amount from the moment of its first appearance, it is still somewhat deficient, even at full term, but leaps sharply up at birth. At an early period of development the embryo also contains much more water than the adult; the specific gravity of its tissues increases as development goes on.

The remarkable vitality of the fœtus, and its resistance to asphyxia, are related to the feebleness of its metabolism and to the comparatively slight excitability of nervous centres like the respiratory, vasomotor, and cardio-inhibitory. Even when totally deprived of oxygen, as by pressure on the umbilical cord during delivery, the child does not perish in the two or three minutes which decide the fate of the asphyxiated adult; nor are the convulsions, rise of blood-pressure, and slowing of the heart-beat, associated with asphyxia in the latter, so readily induced, nor premature and fatal efforts at respiration easily excited *in utero*. But although in such a case the embryo behaves as a separate organism, governed by its own laws, there are circumstances in which it becomes merely a part of the mother and participates in her fate. Thus, the stream of oxygen which normally passes from the maternal to the fœtal blood is turned back if asphyxia threatens the mother; the blood of the umbilical arteries, instead of being purified in the placenta, loses the little oxygen it holds to the blood of the uterine sinuses, and the sluggish tissues of the embryo are impoverished to feed the more active metabolism of the maternal organs. In the same way, the phenomena of starvation have taught us that the nutrition of the organism is not subject to the rules of red tape. In normal circumstances the flow of nutriment follows definite lines: the blood feeds the tissues through its intermediary, the lymph, and recoups itself from the contents of the

alimentary canal. But when the normal sources of nutrient material fail, the body falls back upon its stores. The organs immediately necessary to life are kept, as far as possible, on full diet; organs of secondary importance have to be content with half-rations; organs less important still are drawn upon for supplies.

At birth, great changes take place in the circulation, and these are intimately connected with the commencement of the respiratory activity of the lungs. The causes of the first respiration are: (1) The increasing venosity of the blood circulating in the bulb, which stimulates the respiratory centre when the umbilical cord has been cut or tied and the placental circulation thus interfered with; (2) the stimulation of the skin by the air, which, as we have seen, acts reflexly upon the respiratory centre. That both of these factors may be involved is shown by the fact that either compression of the umbilical cord alone, or exposure of the fœtus by opening the uterus of an animal without interference with the circulation, has been observed to be followed by attempts at breathing. Once distended, the lungs never again completely collapse—not even after death, nor when the chest is opened. The aspiration caused by the elevation of the chest-walls in inspiration (for the respiration of the new-born child is mainly costal) sucks blood into the thorax, and expands the vessels of the lungs for its reception; and in the measure in which the blood passing through the pulmonary trunk finds an easy way through the lungs, the quantity which takes the route of the ductus arteriosus diminishes. The pulmonary veins, and consequently the left auricle, are better filled; and the increasing pressure on this side of the septum tends to oppose the passage of blood through the foramen ovale, to approximate its valve, and to close its orifice.

By the second or third day the ductus arteriosus has usually become obliterated. The umbilical arteries and vein and the ductus venosus become impervious soon after the interruption of the placental circulation. The vein and venous duct remain in the adult as the round ligament of the liver, the arteries as the lateral ligaments of the bladder.

Although from birth onwards the young mammal obtains its oxygen and gets rid of its carbon dioxide through its own pulmonary surface instead of through the placenta, it still lives, as regards its food proper, on the tissues of the mother, and that in as literal a sense as when it drew its supplies directly from the maternal blood. *Milk*, indeed, represents in large part the fragments of cells lining the alveoli of the mammary glands, which have undergone a fatty change and been bodily broken down. This is particularly the case with the first milk of each lactation, the *colostrum* as it is called, which consists of little else than the débris of fattily degenerated cells. In addition to the fat, which when milk is allowed to stand rises to the top as cream, milk contains a considerable quantity of a nucleo-proteid, casein, to whose coagulation, under the influence of the lactic acid produced from the lactose, or milk-sugar, by certain bacteria, spontaneous curdling is due. Another proteid, lact-albumin

(Halliburton), a large amount of water, and some inorganic salts, are the most important of its remaining constituents.

Pregnancy is accompanied with vascular dilatation and hypertrophy of the mammary glands, but the mechanism by which these changes are produced is unknown. Precisely similar phenomena are occasionally seen in animals which have not been impregnated and even in men. Humboldt relates the case of an Indian father, who so well understood the responsibilities of paternity, and was so capable of fulfilling them, that he suckled his child for five months on the death of the mother.

APPENDIX.

COMPARISON OF METRICAL WITH ENGLISH MEASURES.

Measures of Length.

1 millimetre = 0·03937 inch.
1 centimetre = 0·39371 „
1 decimetre = 3·93708 inches.
1 metre = 39·37079 „

1 inch = 25·3995 millimetres.

Measures of Weight.

1 gramme = 15·432349 grains.
1 kilogramme = 2·2046213 pounds.

1 ounce = 28·3495 grammes.
1 pound = 453·5926 grammes.

Measures of Volume.

1 cubic centimetre = 0·061027 cubic inch.
1 litre (1,000 cubic centimetres) = 61·027052 cubic inches.
= 1·760773 pints.
= 0·22009668 gallon.

1 cubic inch = 16·3861759 cubic centimetres.
1 cubic foot = 28·3153119 cubic decimetres (or litres).
1 pint = 0·567932 litres.
1 gallon = 4·5434579 litres.

Measures of Work.

1 kilogrammetre = about 7·24 foot-pounds.
1 foot-pound = 0·1381 kilogrammetre.

Temperature Scales.—To convert degrees Fahrenheit into degrees Centigrade, subtract 32, and multiply the remainder by $\frac{5}{9}$. To convert degrees C. into degrees F. multiply by $\frac{9}{5}$, and add 32 to the result.

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THE END.

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