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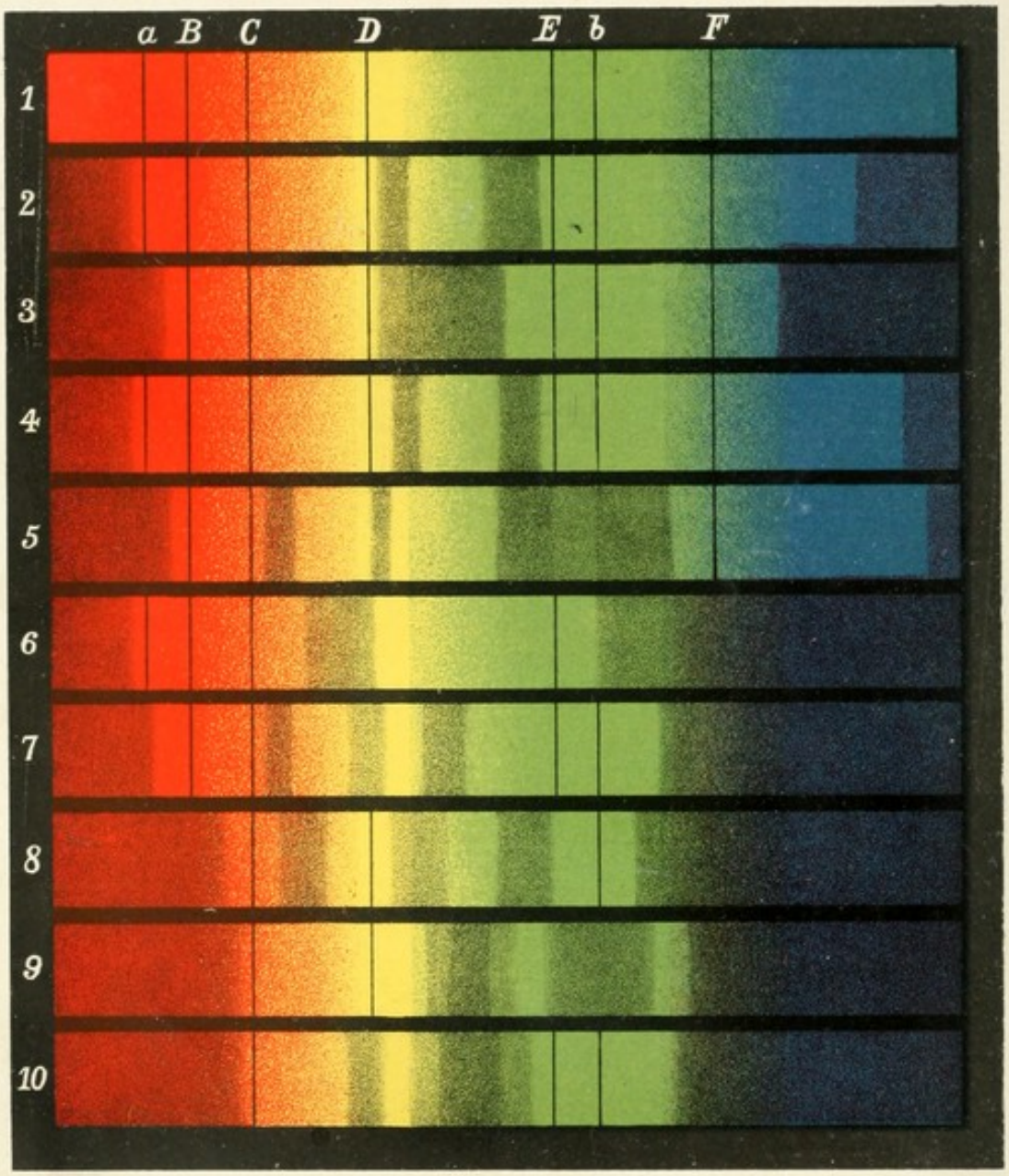
HAND-BOOK

OF

PHYSIOLOGY

BLOOD-SPECTRA COMPARED WITH SPECTRUM OF ARGAND-LAMP.



1 Spectrum of Argand-lamp with Fraunhofer's lines in position.
2 Spectrum of Oxyhæmoglobin in diluted blood.
3 Spectrum of Reduced Hæmoglobin.
4 Spectrum of Carbonic oxide Hæmoglobin.
5 Spectrum of Acid Hæmatin in etherial solution.
6 Spectrum of Alkaline Hæmatin.
7 Spectrum of Chloroform extract of acidulated Ox-Bile.
8 Spectrum of Methæmoglobin.
9 Spectrum of Hæmochromogen.
10 Spectrum of Hæmatoporphyrin.

Most of the above Spectra have been drawn from observations by Mr W. Lepraik F.C.S.

SACKETT & WILHELMS LITHO CO. NEW YORK

COLUMBIA UNIVERSITY

KIRKES' HANDBOOK

OF

PHYSIOLOGY

Revised and Rewritten by

CHARLES WILSON GREENE, A.M., Ph.D.
Professor of Physiology and Pharmacology
University of Missouri

Sixth American Revision

WITH FIVE HUNDRED AND SEVEN ILLUSTRATIONS,
INCLUDING MANY IN COLORS

NEW YORK
WILLIAM WOOD AND COMPANY
MDCCCCVII

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K63
1907

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PREFATORY NOTE

THE general organization of the Handbook has been retained in the present revision, but the anatomical discussions have been very greatly reduced. The text has been largely rewritten throughout, and many new illustrations of physiological experiments have been introduced. An entirely new feature is the introduction, at the end of the chapters, of directions for laboratory work. It is hoped that this will greatly increase the utility of the book both to the teacher and to the student. Acknowledgment is given my colleagues, Dr. C. M. Jackson for reading the manuscript on the Nervous System, and Miss Caroline McGill for similar criticism of the chapter on the Elementary Structure of the Tissues.

CHAS. W. GREENE.

COLUMBIA, MISSOURI, October 1, 1907.

CONTENTS

PAGE

CHAPTER I—The Phenomena of Life; Properties of Protoplasm, Structure of Protoplasm, ... 1

CHAPTER II—Cell Differentiation and the Structure of the Elementary Tissues; The Structure of the Cell, The Structure of the Elementary Tissues. I. The Epithelial Tissues. II. The Connective Tissues. III. Muscular Tissue. IV. Nervous Tissue, . 17

CHAPTER III—The Chemical Composition of the Body; The Nitrogenous Bodies, Classes of Proteids, Oils and Fats, Carbohydrates, Inorganic Principles, Laboratory Experiments, . . . 78

CHAPTER IV—The Blood; Quantity of the Blood, Coagulation of the Blood, Morphology of the Blood, Chemical Composition of the Blood, Globulocidal and Other Properties of Serum, The Character and Composition of Lymph, Laboratory Experiments, ... 101

CHAPTER V—The Circulation of the Blood; Anatomical Considerations, The Action of the Heart, The Regulative Influence of the Central Nervous System, The Circulation through the Blood-Vessels, The Pulse, The Peripheral Regulation of the Flow of Blood, Vaso-constrictor and Vaso-dilator Nerves for Individual Organs, Laboratory Experiments, ... 141

CHAPTER VI—Respiration; The Respiratory Apparatus, The Movements of the Respiratory Mechanism, Respiratory Changes in the Air Breathed, The Respiratory Changes in the Blood, The Nervous Regulation of the Respiratory Apparatus, The Effect of Respiration on the Circulation, Laboratory Experiments in Respiration, . 243

CHAPTER VII—Secretion in General; Organs and Tissues of Secretion, Secreting Glands, The Process of Secretion. Influence of the Nervous System on Secretion, ... 291

PAGE

CHAPTER VIII—Food and Digestion; Food and Food Principles, The Process of Digestion, Digestion in the Mouth, Deglutition, Nervous Mechanism of Deglutition, Digestion in the Stomach, Movements of the Stomach, Digestion in the Intestines, Movements of the Intestines, Laboratory Experiments in Digestion, Saliva and Salivary Digestion, Gastric Juice and Gastric Digestion, Pancreatic Juice and Pancreatic Digestion, ... 297

CHAPTER IX—Absorption; Absorption in the Stomach, Absorption in the Intestines, Absorption from the Skin, the Lungs, etc., . . . 361

CHAPTER X—Excretion; Structure and Function of the Kidneys, General Structure, The Urine, The Method of Excretion of Urine, The Discharge of the Urine, The Structure and Excretory Functions of the Skin, Laboratory Experiments in Excretion, . . . 371

CHAPTER XI—Metabolism, Nutrition, and Diet; Metabolism of Proteids, The Metabolism of Fats, The Metabolism of Carbohydrates, Requisites of a Normal Diet, The Influence of the Ductless Glands on Metabolism, ... 405

CHAPTER XII—Animal Heat; Heat-producing Organs, Variation in the Loss of Heat, Variation in the Production of Heat, Influence of the Nervous System on Heat Production, ... 433

CHAPTER XIII—Muscle-Nerve Physiology; Chemical Composition of Muscle, The Properties of Living Muscle, Single Muscle Contractions, Conditions which Affect the Irritability of the Muscle and the Character of the Contraction, Tetanic and Voluntary Muscular Contractions, The Type of Contraction in Involuntary Muscle and in Cilia, The Function of Nerve Fiber, Some Special Coordinated Motor Activities, Locomotion, The Production of the Voice, Laboratory Experiments on Muscle and Nerves, ... 440

CHAPTER XIV—The Nervous System; I. Function of the Nerve Cell. II. The Structure and Function of the Spinal Cord, The Arrangement of Nerve Cells in the Spinal Cord, Columns and Tracts in the White Matter of the Spinal Cord, The Reflex Arc and Reflex Action, Spinal Reflexes in Man and Mammals. III. The Brain Stem, The Medulla Oblongata or Bulb, The Pons Varolii, The Midbrain, The Optic Thalami, The Cranial Nerves. IV. The Cerebellum. V. The Cerebrum, Structure of the Cerebral Cortex, General Functions of the Cerebrum, Localization of the Motor Function of the Cerebral Cortex, Localization of Sensory Function in the Cerebral Cortex, Association Centers of the Cerebral Cortex, The Physiology of Sleep. VI. The Sympathetic System, ... 503

PAGE

CHAPTER XV—The Senses; I. The Senses of Touch, Pain, Temperature, and the Muscle Sense. II. Taste and Smell, The Sense of Taste, The Sense of Smell. III. Hearing and Equilibration, The Anatomy of the Ear, The Physiology of Hearing, The Sense of Equilibrium. IV. The Sense of Sight, The Eye, The Optical Apparatus, Accommodation, Defects in the Optical Apparatus, Visual Sensations from Excitation of the Retina, Color Sensations, Binocular Vision, Visual Judgments, Laboratory Directions for Experiments on the Sense Organs, ... 595

CHAPTER XVI—The Reproductive Organs; The Reproductive Organs of the Male, The Reproductive Organs of the Female, Ovulation and Menstruation, Menstrual Life, ... 679

CHAPTER XVII—Development; Changes which Occur in the Ovum Prior to Impregnation, Changes Following Impregnation, Circulation of Blood in the Fetus, Parturition, Lactation, ... 691

Index, ... 701

FAHRENHEIT and CENTIGRADE SCALES.

F.	C.
500°	260°
401	205
392	200
383	195
374	190
356	180
347	175
338	170
329	165
320	160
311	155
302	150
284	140
275	135
266	130
248	120
239	115
230	110
212	100
203	95
194	90
176	80
167	75
140	60
122	50
113	45
105	40.54
104	40
100	37.8
98.5	36.9
95	35
86	30
77	25
68	20
50	10
41	5
32	0
23	− 5
14	− 10
+ 5	− 15
− 4	− 20
− 13	− 25
− 22	− 30
− 40	− 40
− 76	− 60

1 deg. F. = .54° C.
1.8 " = 1° C.
3.6 " = 2° C.
4.5 " = 2.5° C.
5.4 " = 3° C.

To convert degrees F. into degrees C., subtract 32, and multiply by $\frac{5}{9}$.

To convert degrees C. into degrees F., multiply by $\frac{9}{5}$, and add 32°.

MEASUREMENTS.

FRENCH INTO ENGLISH.

LENGTH.

1 mètre, 10 décimètres, 100 centimètres, 1,000 millimètres = 39.37 English inches. (or 1 yd. and 3⅜ in.)

1 décimètre, 10 centimètres, 100 millimètres = 3.937 inches (or nearly 4 inches.)

1 centimètre, 10 millimètres = .3937 or about (nearly $\frac{3}{8}$ inch.)
1 millimètre = nearly $\frac{1}{25}$ inch.

OR,

ONE METRE = 39.37079 inches.

(It is the ten-millionth part of a quarter of the meridian of the earth.)

1 Décimètre = 4 in.
1 Centimètre = $\frac{4}{10}$ in.
1 Millimètre = $\frac{1}{25}$ in.
Décamètre = 32.80 feet.
Hectomètre = 109.36 yds.
Kilomètre = 0.62 miles.
One inch = 2.539 Centimètres.
One foot = 3.047 Décimètres.
One yard = 0.91 of a Mètre.
One mile = 1.60 Kilomètre.

The cubic centimètre (15.432 grains—1 gramme) is a standard at 4° C., the grain at 16°.66 C.

WEIGHT.

(One gramme is the *weight* of a cubic centimètre of water at 4° C. at Paris).

1 gramme, 10 décigrammes, 100 centigrammes, 1,000 milligrammes = 15.432349 grs. (or nearly 15½).

1 décigramme, 10 centigrammes, 100 milligrammes = rather more than 1½ grain.

1 centigramme, 10 décigrammes = rather more than $\frac{3}{20}$ grain.

1 milligramme = rather more than $\frac{3}{200}$ grain.

OR

1 Décigramme = 2 dr. 34 gr.
1 Hectogrm. = 3½ oz. (Avoir.)
1 Kilogrm. = 2 lb. 3 oz. 2 dr. (Avoir.)

A grain equals about 1.16 gram., a Troy oz. about 31 gram., a lb. Avoirdupois about ½ Kilogrm., and 1 cwt. about 50 Kilogrms.

CAPACITY.

1,000 cubic décimètres, 1,000,000 cubic centimètres = 1 cubic mètre.

1 cubic décimètre or 1,000 cubic centimètres = 1 litre.

OR

ONE LITRE = 1 pt. 15 oz. 1 dr. 40.

(For simplicity, *Litre* is used to signify 1 cubic décimètre, a little less than 1 English quart.)

Décilitre (100 c.c.)	= 3½ oz.
Centilitre (10 c.c.)	= 2⅜ dr.
Millilitre (1 c.c.)	= 17 m.
Décalitre	= 2⅛ gal.
Hectolitre	= 22 gals.
Kilolitre (cubic mètre)	= 27½ bushels.

A cubic inch = 16.38 c.c.; a cubic foot = 28.315 cubic déc., and a gallon = 4.54 litres.

CONVERSION SCALE.

To convert GRAMMES to OUNCES avoirdupois, multiply by 20 and divide by 567.

To convert KILOGRAMMES to POUNDS, multiply by 1,000 and divide by 454.

To convert LITRES to GALLONS, multiply by 22 and divide by 100.

To convert LITRES to PINTS, multiply by 88 and divide by 50.

To convert MILLIMETRES to INCHES, multiply by 10 and divide by 254.

To convert METRES to YARDS, multiply by 70 and divide by 64.

SURFACE MEASURE.

1 square mètre = about 1550 sq. inches. Or 10,000 sq. centimètres, or 10.75 sq. ft.
1 sq. inch = about 6 4 sq. centimètres.
1 sq. foot = " 930 " "

ENERGY MEASURE.

1 kilogrammètre = about 7.24 ft. pounds.
1 foot pound = " .1381 kgm.
1 foot ton = " 310 kgm.

HEAT EQUIVALENT.

1 kilocalorie = 424 kilogrammètres.

ENGLISH MEASURES.

Apothecaries Weight.

7000 grains = 1 lb.

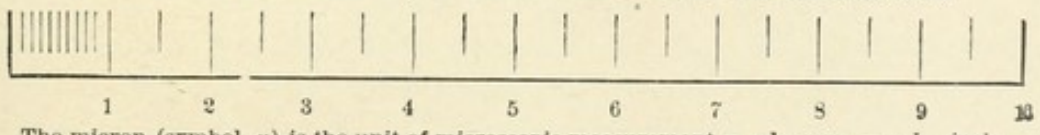
Or

437.5 grains = 1 oz.

Avoirdupois Weight.

16 drams = 1 oz.
16 oz. = 1 lb.
28 lbs. = 1 quarter.
4 quarters = 1 cwt.
20 cwt. = 1 ton.

Measure of 1 décimètre, or 10 centimètres, or 100 millimètres.



The micron (symbol, μ) is the unit of microscopic measurement = $\frac{1}{1000}$ mm. = $\frac{1}{25000}$ inch.

HANDBOOK OF PHYSIOLOGY

CHAPTER I

THE PHENOMENA OF LIFE

PHYSIOLOGY is the science which treats of the various processes or changes which take place in the organs and tissues of the body during life. These processes, however, must not be considered as by any means peculiar to the human organism, since, putting aside the properties which serve to distinguish man from other animals, the changes which go on in the tissues of man go on in much the same way in the tissues of all other animals as long as they live. Furthermore it is found that similar changes proceed in all living vegetable tissues; they indeed constitute what are called *vital phenomena*, and are those properties which mark out living from non-living material.

The lowest types of life, whether animal or vegetable, are found to consist of minute masses of a jelly-like substance, which is generally known under the name of *protoplasm*. Each such living mass is called a cell, so that these minute elementary organisms are designated *unicellular*.

Not only is it true that the lowest types of life are made up of cells, but it has also been shown that the tissues of which the most complex organisms are composed consist of cells.

The phenomena of life are exhibited in cells, whether existing alone or developed into the organs and tissues of animals and plants. It must be at once evident that a correct knowledge of the nature and activities of the cell forms the very foundation of physiology; cells being, in fact, physiological no less than morphological units.

The prime importance of the cell as an element of structure was first established by the researches of the botanist Schleiden, and his conclusions, drawn from the study of vegetable histology, were at once extended by Theodor Schwann to the animal kingdom. The earlier observers defined a cell as a more or less spherical body limited by a membrane, and containing a smaller body termed a *nucleus*, which in its turn incloses one or more still smaller bodies or *nucleoli*. Such a definition applied admirably to most vegetable cells, but the more extended investigation of animal tissues soon showed that in many cases no limiting membrane or cell-wall could be demonstrated.

The presence or absence of a cell-wall, therefore, was then regarded as quite a secondary matter, while at the same time the cell-substance came

gradually to be recognized as of primary importance. Many of the lower forms of animal life, the Rhizopoda, were found to consist almost entirely of matter very similar in appearance and chemical composition to the cell-substance of higher forms; and this from its chemical resemblance to flesh was termed *Sarcode* by Dujardin. When recognized in vegetable cells it was called *Protoplasm* by Mulder, while Remak applied the same name to the substance of animal cells. As the presumed formative matter in animal tissues it was termed *Blastema*, and in the belief that, wherever found, it alone of all substances has to do with generation and nutrition, Beale has named it *Germinal matter* or *Bioplasm*. Of these terms the one most in use at the present day, as we have already said, is protoplasm, and inasmuch as all life, both in the animal and vegetable kingdoms, is associated with protoplasm, we are justified in describing it, with Huxley, as the "physical basis of life," or simply "living matter."

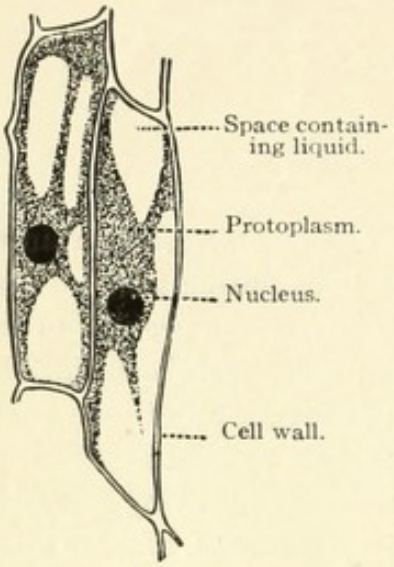


FIG. 1.—Vegetable Cells.

Properties of Protoplasm. Protoplasm is a semi-fluid substance, which absorbs but does not mix with water. It is transparent and generally colorless, with refractive index higher than that of water but lower than that of oil. It is neutral or weakly alkaline in reaction, but may under special circumstances be acid, as, for example, after activity. It undergoes heat-coagulation at a temperature of about 54.5° C. (130° F.), and hence no organism can live when its own temperature is raised above that point. It is also coagulated and therefore killed by alcohol, by solutions of many of the metallic salts, by strong acids and alkalies, and by many other chemical substances.

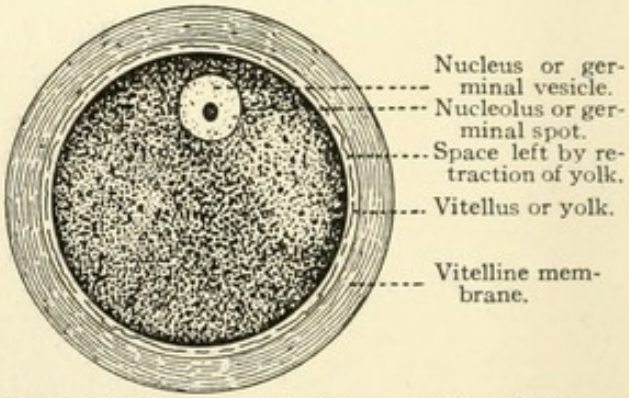


FIG. 2.—Semidiagrammatic Representation of a Human Ovum, showing the parts of an animal cell. (Cadia.)

Under the microscope it is seen almost universally to be granular, the granules consisting of different substances, albuminous, fatty, or carbohydrate matter. The granules are not equally distributed throughout the whole cell-mass, as they are sometimes absent from the outer part or layer, and very numerous in the interior. In addition to granules, protoplasm generally exhibits spaces or vacuoles, usually globular in shape, excepting during movement, when they may be irregular, and filled with a watery

fluid. These vacuoles are more numerous and pronounced in vegetable than in animal cells. Gas bubbles also sometimes exist in cells.

It is impossible to make any definite statement as to the exact chemical composition of living protoplasm, since the methods of chemical analysis necessarily imply the death of the cell; it is, however, stated that protoplasm contains 75 to 85 per cent of water, and of the 15 to 25 per cent of solids the most important part belongs to the class of substances called *proteids* or *albumins*. Proteids contain the chemical elements carbon, hydrogen, nitrogen, oxygen, sulphur, and phosphorus, the last two in very small quantities only. A proteid-like substance, *nuclein*, found in the nuclei of cells, contains phosphorus in greater abundance. In the cell nucleus a compound of nuclein with proteid, called nucleoproteid, forms the most abundant proteid substance. Other bodies are frequently found associated with the proteids, such

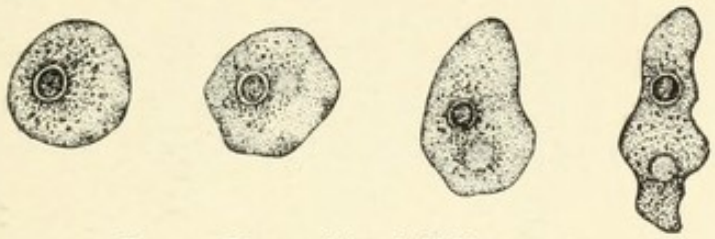


FIG. 3.—Phases of Ameboid Movement.

as *glycogen*, *starch*, *cellulose*, which contain the elements carbon, hydrogen, and oxygen, the last two in the proportion to form water, and hence are termed *carbohydrates; fatty bodies*, containing carbon, hydrogen, and oxygen, but not in proportion to form water; *lecithin*, a complicated fatty body containing phosphorus; *cholesterin*, a monatomic alcohol; *chlorophyll*, the coloring matter of plants; *inorganic salts*, particularly the chlorides and phosphates of calcium, sodium, and potassium; *ferments*, and other substances.

The Physiological Characteristics of Protoplasm. The properties of protoplasm may be well studied in the microscopic animal called the ameba, a unicellular organism found chiefly in fresh water. These properties may be conveniently studied under the following heads:—

The Power of Spontaneous Movement. When an ameba is observed with a high power of the microscope, it is found to consist of an irregular mass of protoplasm containing one or more nuclei, the protoplasm itself being more or less granular and vacuolated. If watched for a minute or two, an irregular projection is seen to be gradually thrust out from the main body; other masses are then protruded until gradually the whole protoplasmic substance is, as it were, drawn over to a new position, and when this is repeated several times we have locomotion in a definite direction, together with a continual change of form. These movements, figure 3, when observed in other cells, such as the colorless blood-corpuscles of higher animals, in the branched corneal cells of the frog and elsewhere, are termed *ameboid*.

The remarkable movement of pigment granules observed in the branched pigment cells of the frog's skin by Lister are also probably due to ameboid movement. These granules are seen at one time distributed uniformly through the body and branched processes of the cell, while at another time they collect in the central mass leaving the branches quite colorless.

This movement within the pigment cells might also be considered an example of the so-called *streaming* movement not infrequently seen in certain of the protozoa, in which the mass of protoplasm extends long and fine processes, themselves very little movable, but upon the surface of which freely moving or streaming granules are seen. A *gliding* movement has also been noticed in certain animal cells; the motile part of the cell being composed of protoplasm bounding a central and more compact mass. By means of the free movement of this layer, the cell may be observed to move along.

In vegetable cells the protoplasmic movement can be well seen in the hairs of the stinging-nettle and Tradescantia and in the cells of Vallisneria and Chara; it is marked by the movement of the granules nearly always embedded in it. For example, if part of a hair of Tradescantia, figure 5, be viewed under a high magnifying power, streams of protoplasm containing crowds of

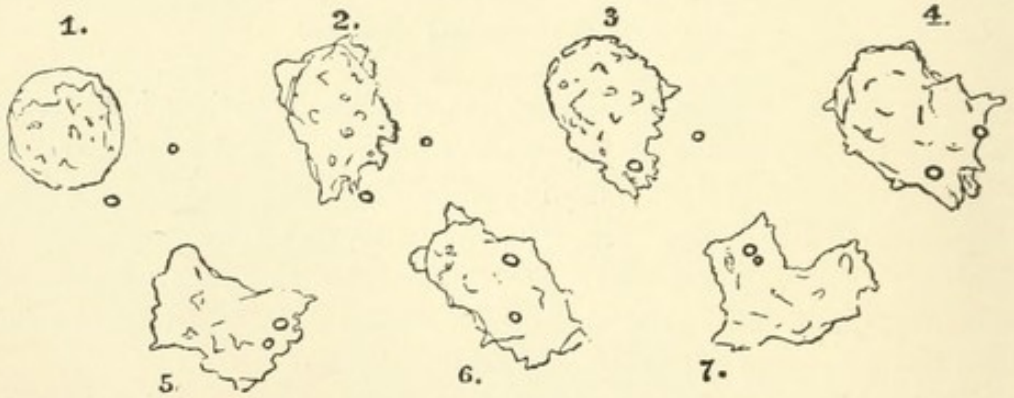


FIG. 4.—Changes of Form of a White Corpuscle, Sketched at Brief Intervals. The figures show also the ingestion of two small granules. (Schäfer.)

granules hurrying along, like the foot-passengers in a busy street, are seen flowing steadily in definite directions, some coursing round the film which lines the interior of the cell-wall, and others flowing toward or away from the irregular mass in the center of the cell-cavity. Many of these streams of protoplasm run together into larger ones and are lost in the central mass, and thus ceaseless variations of form are produced. The movement of the protoplasmic granules to or from the periphery is sometimes called vegetable *circulation*, whereas the movement of the protoplasm round the interior of the cell is called *rotation*.

The first account of the movement of protoplasm was given by Rösel in 1755, as occurring in a small Proteus, probably a large fresh-water ameba. His description was followed twenty years later by Corti's demonstration of the rotation of the cell sap in characeæ, and in the earlier part of the century

by Meyer in Vallisneria, 1827; Robert Brown, 1831, in "Staminal Hairs of Tradescantia." Then came Dujardin's description of the granular streaming in the pseudopodia of Rhizopods and movements in other cells of animal protoplasm (Planarian eggs, von Siebold, 1841; colorless blood-corpuscles, Wharton Jones, 1846).

The Power of Response to Stimuli, or Irritability. Although the movements of the ameba have been described above as spontaneous, yet they may be increased under the action of external agencies which excite them and are therefore called *stimuli*, and if the movement has ceased for the time, as is the case if the temperature is lowered beyond a certain point, movement may be set up by raising the temperature. Contact with foreign bodies, gentle pressure, cer-

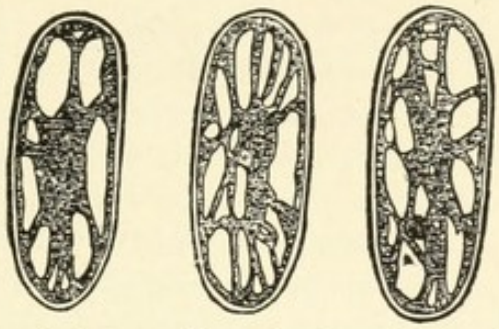


FIG. 5.—Cell of Tradescantia Drawn at Successive Intervals of two Minutes.—The cell-contents consist of a central mass connected by many irregular processes to a peripheral film, the whole forming a vacuolated mass of protoplasm, which is continually changing its shape. (Schofield.)

tain salts, and electricity produce or increase the movement in the ameba. The protoplasm is, therefore, sensitive or irritable to stimuli, and shows its irritability by movement or contraction of its mass.

The effects of some of these stimuli may be thus further detailed:—

a. Changes of Temperature. Moderate heat acts as a stimulant; the movement stops below 0° C. (32° F.), and above 40° C. (104° F.); between these two points the movements increase in activity; the optimum temperature is about 37° to 38° C. Exposure to a temperature even below 0° C. stops the movement of protoplasm, but does not prevent its reappearance if the temperature is raised; on the other hand, prolonged exposure to a temperature of over 40° C. kills the protoplasm and causes it to enter into a condition of coagulation or *heat rigor.*

b. Mechanical Stimuli. When gently squeezed between a cover and object-glass under proper conditions, a colorless blood-corpuscle contracts and ceases its ameboid movement.

c. Nerve Influence. By stimulation of the nerves of the frog's cornea, contraction of certain of its branched cells has been produced.

d. Chemical Stimuli. Water generally stops ameboid movement, and by imbibition causes great swelling and finally bursting of the cells. In some cases, however (myxomycetes), protoplasm can be almost entirely dried up, but remains capable of renewing its movements when again moistened.

Dilute salt-solution and many dilute acids and alkalies stimulate the movements temporarily. Strong acids or alkalies permanently stop the movements; ether, chloroform, veratrium, and quinine also stop it for a time.

Movement is suspended in an atmosphere of hydrogen or carbonic acid and resumed on the admission of air or oxygen, but complete withdrawal of oxygen will after a time kill the protoplasm.

e. Electrical. Weak currents stimulate movement, while strong currents cause the cells to assume a spherical form and to become motionless.

The Power of Digestion, Respiration, and Nutrition. This consists in the power which is possessed by the ameba and similar animal cells of taking in food, modifying it, building up tissue by assimilating it, and rejecting what is not assimilated. These various processes are effected in some one-celled animals by the protoplasm simply flowing around and enclosing within itself minute organisms such as diatoms and the like. From these it extracts what it requires, and then rejects or *excretes* the remainder, which has never formed part of the body. This latter proceeding is done by the cell withdrawing itself from the material to be excreted. The assimilation constantly taking place in the body of the ameba is for the purpose of replacing waste of its tissue consequent upon manifestation of energy. The respiratory process of absorbing oxygen goes on at the same time.

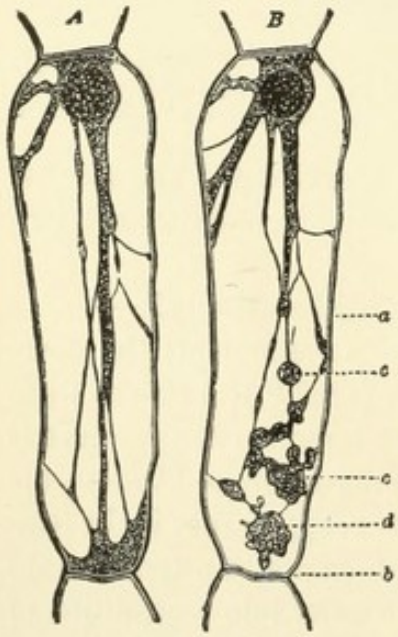


FIG. 6.—Cells from the Staminal Hairs of Tradescantia. *A*, Fresh in water; *B*, the same cell after slight electrical stimulation; *a*, *b*, region stimulation; *c*, *d*, clumps and knobs of contracted protoplasm. (Kühne.)

The processes which take place in cells, both animal and vegetable, are summed up under the term *metabolism* (from μεταβολη, change). The changes which go on are of two kinds, viz., *assimilation*, or building up, and *disassimilation*, or breaking down; they may be also called, using the nomenclature of Gaskell, *anabolism* or constructive metabolism, and *catabolism* or destructive metabolism. In the direction of anabolism two processes occur, viz., the building up of materials which it takes in, and secondly, the building up of its own substance by those or other materials. As we shall see in a subsequent paragraph, the process of anabolism differs to some extent in vegetable and animal cells. The catabolism of the cell consists in chemical changes which occur in the cell-substance itself, or in substances in contact with it.

The destructive metabolism of a cell is increased by its activity, but goes on also during quiescence. It is probably of the nature of oxidation, and results in the evolution of carbon dioxide and water on the one hand, and in the

formation of various more complex chemical substances on the other, some of which may be stored up in the cell for future use, and are called *secretions*, and others, like carbon dioxide, for example, and bodies containing nitrogen, are eliminated as *excretions*.

The Power of Growth. In protoplasm it is seen that the two processes of waste and repair go on side by side, and so long as they are equal the size of the animal remains stationary. If, however, the building up exceed the waste, then the animal *grows;* if the waste exceed the repair, the animal

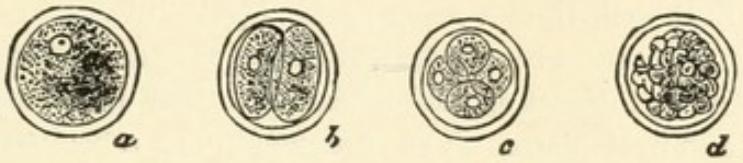


FIG. 7.—Diagram of an Ovum (*a*) Undergoing Segmentation. In (*b*) it has divided into two, in (*c*) into four; and in (*d*) the process has ended in the production of the so-called "mulberry mass." (Frey.)

decays; and if decay go on beyond a certain point, life becomes impossible, and the animal dies.

The power of increasing in size, although essential to our idea of life, is not, it must be recollected, confined to living beings. A crystal of common salt, for example, if placed under appropriate conditions for obtaining fresh material, will increase in size in a fashion as definitely characteristic and as easily to be foretold as that of a living creature; but the growth of a crystal takes place merely by additions to its outside; the new matter is laid on particle by particle, and layer by layer, and, when once laid on, it remains unchanged. In a living structure, where growth occurs, it is by addition of new matter, not to the surface only, but throughout every part of the mass, and this matter becomes an intimate part of the living substance.

The Power of Reproduction. The ameba, to return to our former illustration, when the growth of its protoplasm has reached a certain point, manifests the power of reproduction, by splitting up into (or in some other way producing) two or more parts, each of which is capable of independent existence. The new amebæ manifest the same properties as the parent, perform the same functions, grow and reproduce in their turn. This cycle of life is being continually passed through.

In more complicated structures than the ameba, the life of individual protoplasmic cells is probably very short in comparison with that of the organism they compose; and their constant decay and death necessitate constant reproduction. The mode in which this takes place has long been the subject of controversy.

It is now very generally believed that every cell is descended from some pre-existing mother cell. This derivation of cells from cells takes place by *gemmation*, which essentially consists in the budding off and separation of a portion of the parent cell; or by *fission* or *division*.

The exact manner of the division of cells is a matter of some difficulty, and will not be described until the subject of the structure of protoplasmic cells has been considered.

STRUCTURE OF PROTOPLASM.

Elemental Structure. Protoplasm was formerly thought to be homogeneous. It is now generally found to consist of the elemental divisions called cells. Each cell, from a morphological point of view, consists of differentiated parts, the most constant of which are the cell nucleus and the cell cytoplasm. The cytoplasm is differentiated further into two substances, spongioplasm and hyaloplasm. The *spongioplasm* or *reticulum* forms a fine network, increases in relative amount as the cell grows older, and has an affinity for staining reagents. The *hyaloplasm* is less refractile, elastic, or extensile, and has little or no affinity for stains; it predominates in young cells

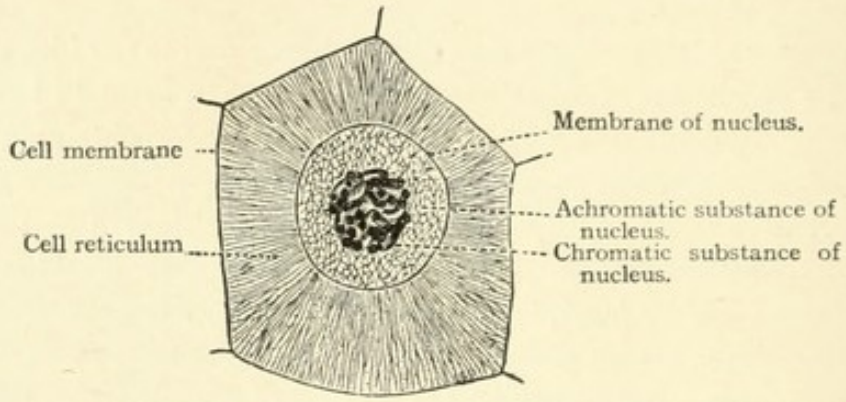


FIG. 8.—Cell with its Reticulum Disposed Radially; from the intestinal epithelium of a worm. (Carnoy.)

is thought to be fluid, and fills the interspaces of the reticulum. The nodal points of the reticulum, with the granular *microsomes*, found in the protoplasm, cause the granular appearance.

The arrangement of the reticulum varies considerably in different cells, and even in different parts of the same cell. Sometimes, for example, figure 8, the meshwork has an elongated radial arrangement from the nucleus; at others, the meshwork is more evenly disposed, as in figure 9. At the junctions of the fibrils there are usually slight enlargements or nodes.

In some cells, particularly in plants, but also in some animal cells, there is a tendency toward a formation of a firmer external envelope, constituting in vegetable cells a membrane distinct from the more central and more fluid part of the protoplasm. In such cases the reticulum at the periphery of the cell is made up of very fine meshes. The membrane when formed is usually pierced with pores by which fluid may pass in, or through which protrusion of the protoplasmic filaments forming the cell's connection with other cells surrounding it may take place.

It is an exceedingly interesting question whether in cells the one part of the protoplasm can exist without the other. Schäfer summarizes the matter thus: "There are cells, and unicellular organisms both animal and vegetable, in which no reticular structure can be made out, and these may be formed of hyaloplasm alone. In that case, this must be looked upon as the essential part of protoplasm. So far as ameboid phenomena are concerned it is certainly so; but whether the chemical changes which occur in many cells are effected by this or by spongioplasm is another matter."

The Cell Nucleus. All cells at some period of their existence possess *nuclei*. The origin of a nucleus in a cell is the first trace of the differentiation of protoplasm. The existence of nuclei was first pointed out in the

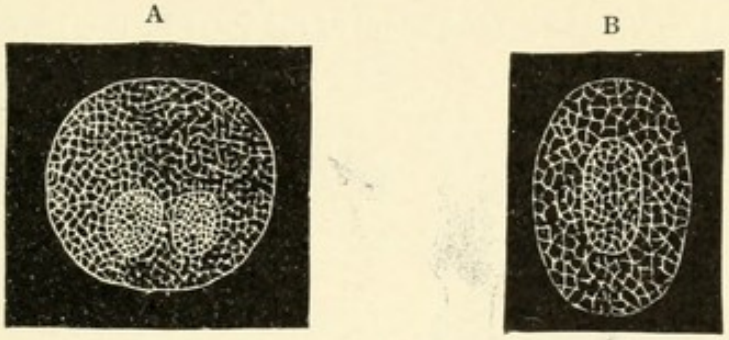


FIG. 9.—A: The Colorless Blood-Corpuscle, Showing the Intracellular Network, and two nuclei with intranuclear network. B: Colored blood-corpuscle of newt showing the intracellular network of fibrils. Also oval nucleus composed of limiting membrane and fine intranuclear network of fibrils. × 800. (Klein and Noble Smith.)

year 1833 by Robert Brown, who observed them in vegetable cells. They are either small transparent vesicular bodies containing one or more smaller particles called nucleoli, always when in the resting condition bounded by a well-defined envelope. In their relation to the life of the cell they are certainly hardly second in importance to the cytoplasm itself, and thus Beale is fully justified in comprising both under the term "germinal matter." They control the nutrition of the cell, and probably initiate the process of subdivision. If a cell be mechanically divided, that portion not containing the nucleus dies.

Histologists have long recognized certain important characters of nuclei. One is their power of resisting the action of various acids and alkalies, particularly acetic acid, by which their outlines are more clearly defined, and they are rendered more easily visible. Another is their quality of staining in solutions of carmine, hematoxylin, etc. This indicates some chemical difference between the cytoplasm of the cells and their nuclei, as the former is destroyed by these reagents.

Nuclei are most commonly oval or round, and do not necessarily conform to the diverse shapes of the cells; they are altogether less variable elements than cells, even in regard to size, of which fact one may see a good example in the uniformity of the nuclei in cells so multiform as those of epithelium. But sometimes nuclei occupy almost the whole of the cell, as in the lymph corpuscles

of lymphatic glands, and in some small nerve cells. Their position in the cell is very variable. In many cells, especially where active growth is progressing, two or more nuclei are present.

Cell Division and Growth. The division of a cell is preceded by division of its nucleus, which may be either direct or indirect. Direct or simple division, amitosis or akinesis, see figure 10, occurs without any change in the arrangement of the intranuclear network. A constriction develops at the center of the nucleus, possibly preceded by division of the nucleoli, and gradually divides it into two equal daughter nuclei. A similar constriction of the protoplasm of the cell occurs between the daughter nuclei and divides it into two parts.

Indirect division, mitosis, or karyokinesis is the usual method, and consists of a series of changes in the arrangement of the intranuclear network, resulting

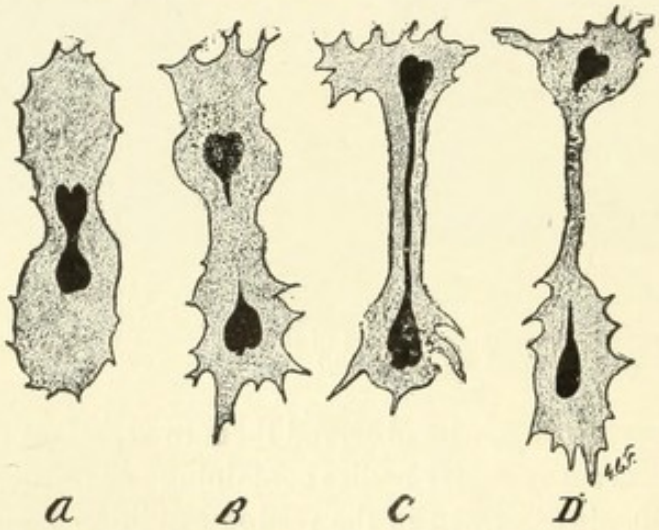


FIG. 10.—Akinesis, Amitosis, or Direct Cell Division. *A*, Constriction of nucleus; *B*, division of nucleus and constriction of cell body; *C*, daughter nuclei still connected by a thread, division being delayed; *D*, division of cell body nearly complete. (After Arnold.)

in the exact division of the chromatic fibers into two parts, which form the chromoplasm of the daughter nuclei. The changes follow a closely similar course in both plant and animal cells.

Differences between Animals and Plants. Having considered at some length the vital properties of protoplasm, as shown in cells of animal as well as of vegetable organisms, we are now in a position to discuss the question of the *differences between plants and animals*. It might at the outset of our inquiry have seemed an unnecessary thing to recount the distinctions which exist between an animal and a vegetable as they are in many cases so obvious, but, however great the differences may be between the higher animals and plants, in the lowest of them the distinctions are much less plain.

In the first place, it is important to lay stress upon the differences between vegetable and animal *cells*, first as regards their structures and next as regards their functions.

It has been already mentioned that in animal cells an envelope or cell-wall is by no means always present. In adult vegetable cells, on the other hand, a well-defined wall is highly characteristic; this is composed of cellulose, is non-nitrogenous, and thus differs chemically as well as structurally from the contained protoplasmic mass. Moreover, in vegetable cells, figure 12, B, the

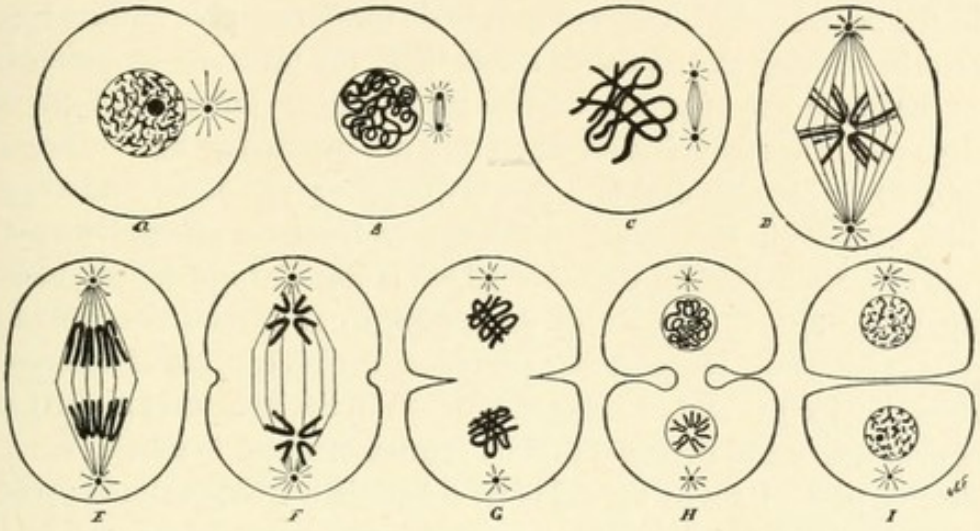


FIG. 11.—Karyokinesis, Mitosis, or Indirect Cell Division (diagrammatic). *A*, Cell with resting nucleus; *B*, wreath, daughter centrosomes and early stage of achromatic spindle; *C*, chromosomes; D, monaster stage, achromatic spindle in long axis of nucleus, chromosomes dividing; *E*, chromosomes moving toward centrosomes; *F*, diaster stage, chromosomes at poles of nucleus, commencing constriction of cell body; *G*, daughter nuclei beginning return to resting state; *H*, daughter nuclei showing monaster and wreath; *I*, complete division of cell body into daughter cells whose nuclei have returned to the resting state. (After Böhm and von Davidoff.)

protoplasmic contents of the cell fall into two subdivisions: 1, a continuous film which lines the interior of the cellulose wall; and, 2, a reticulate mass containing the nucleus and occupying the cell-cavity. The interstices are filled with fluid. In young vegetable cells such a distinction does not exist; a

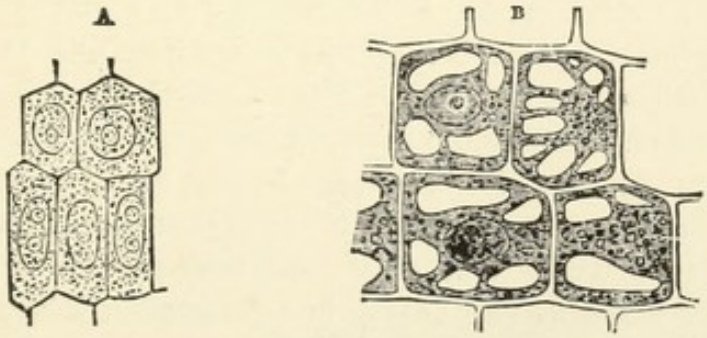


FIG. 12.—A. Young Vegetable Cells, Showing Cell-Cavity Entirely Filled with Granular Protoplasm Enclosing a Large Oval Nucleus, with one or more Nucleoli. B. Older cells from same plant, showing distinct cellulose-wall and vacuolation of protoplasm.

finely granular protoplasm occupies the whole cell-cavity, figure 12, A. As regards the respective functions of animal and vegetable cells, one of the most important differences consists in the power which vegetable cells possess of being able to build up new complicated nitrogenous and non-nitrogenous

bodies out of very simple chemical substances obtained from the air and from the soil. They obtain from the air oxygen, carbon dioxide, and water, as well as traces of ammonia gas; and from the soil they obtain water, ammonium salts, nitrates, sulphates, and phosphates in combination with such bases as potassium, calcium, magnesium, sodium, iron, and others. The majority of plants are able to work up these elementary compounds into other and more complicated bodies. This they are able to do in consequence of their containing a certain coloring matter called *chlorophyll*, the presence of which is the cause of the green hue of plants. In all plants which contain chlorophyll two processes are constantly going on when they are exposed to light: one, which is called *true respiration* and is a process common to animal and vegetable cells alike, consists in the taking of the oxygen from the atmosphere and the giving out of carbon dioxide; the other, which is peculiar apparently to bodies containing chlorophyll, consists in the taking in of carbon dioxide and the giving out of oxygen. It seems that the chlorophyll is capable of decomposing the carbon dioxide gas and of fixing the carbon in the structures in the form of new compounds, one of the most rapidly formed of which is *starch*.

Vegetable protoplasm by the aid of its chlorophyll is able to build up a large number of bodies besides starch, the most interesting and important being proteid or albumin. It appears to be a fact that the power which bodies possess of being able to synthesize is to a large extent dependent upon the chlorophyll they contain. Thus the power is present to a marked extent only in the plants in which chlorophyll is found, and is absent in those which do not possess it. It is probably present only in slight degree as one of the properties of animal protoplasm.

It must be recollected, however, that chlorophyll without the aid of the light of the sun can do nothing in the way of building up substances, and a plant containing chlorophyll when placed in the dark, while it continues to live, and that is not as a rule long, acts as though it did not contain any of that substance. It is an interesting fact that certain of the bacteria have the chlorophyll replaced by a similar pigment which is able to decompose carbon dioxide gas.

Animal cells do not possess the power of building up or synthesizing from simple materials; their activity is chiefly exercised in the opposite direction, viz., they have brought to them as food the complicated compounds produced by the vegetable kingdom. With these foods they are able to perform their complex functions, setting free energy in the direction of heat, motion, and electricity, and at the same time eliminating such bodies as carbon dioxide and water, and producing other bodies, many of which contain nitrogen, but are derived from decomposition.

With reference to the substance chlorophyll it is necessary to say a few words. It has been noted that the synthetical operations of vegetable cells are peculiarly associated with the possession of chlorophyll and that these operations are dependent upon the light of the sun. It has been further shown that

a solution of chlorophyll has a definite absorption spectrum when examined with the spectroscope, and that it is particularly those parts of the solar spectrum corresponding to these absorption bands which are chiefly active in the decomposition of carbon dioxide. In the synthetical processes of the plant then, by aid of its chlorophyll, the radiant energy of the sun's rays becomes stored up or rendered potential in the chemical products formed. The potential energy is set free, or is again made kinetic, when these products simply by combustion produce heat, or when they are taken into the animal organism and used as food and to produce heat and motion.

The influence of light is not an absolute essential to animal life; indeed, it is said not to increase the metabolism of animal tissue to any great extent, and the animal cell does not receive its energy directly from the sun's light, nor yet to any extent from the sun's heat, but from the potential energy of the food stuffs. But it must be always kept in mind that anabolism is not peculiar to vegetable, or katabolism to animal cells; both processes go on in each. Some of the lowest forms of vegetable life, *e.g.*, the bacteria, will live only in a highly albuminous medium, and in fact seem to require for their growth elements of food stuffs which are essential to animal life. In their metabolism, too, they very closely approximate animal cells, not only requiring an atmosphere of oxygen, but giving out carbon dioxide freely, and secreting and excreting many very complicated nitrogenous bodies, as well as forming proteid, carbohydrates, and fat, requiring heat but not light for the due performance of their functions. Certain bacteria grow only in the absence of oxygen.

There is, commonly, a difference in general chemical composition between vegetables and animals, even in their lowest forms; for associated with the protoplasm of the former is a considerable amount of *cellulose*, a substance closely allied to starch and containing carbon, hydrogen, and oxygen only. The presence of cellulose in animals is much rarer than in vegetables, but there are many animals in which traces of it may be discovered, and some in which it is found in considerable quantity. The presence of starch in vegetable cells is very characteristic, though, as we have seen above, it is not distinctive, and a substance, *glycogen*, similar in composition to starch, is very common in the organs and tissues of animals.

Inherent power of movement is a quality which we so commonly consider an essential indication of animal nature that it is difficult at first to conceive of its existence in any other. The capability of simple motion is now known, however, to exist in so many vegetable forms that it can no longer be held as an essential distinction between them and animals, and ceases to be a mark by which the one can be distinguished from the other. Thus the zoöspores of many of the Cryptogams exhibit ciliary or ameboid movements of a like kind to those seen in amebæ; and even among the higher orders of plants, many, *e.g.*, *Dionæa muscipula* (Venus's fly-trap), and *Mimosa sensitiva* (Sensitive plant) exhibit such motion, either at regular times or on the applica-

tion of external irritation, as might lead one, were this fact taken by itself, to regard them as sentient beings. Inherent power of movement, then, although especially characteristic of animal nature, is, when taken by itself, no proof of it.

Cell Differentiation and the Functions of Organized Cells. As we proceed upward in the scale of life from the unicellular organisms, we find another phenomenon exhibited in the life history of the higher forms, namely, that of *development*. The one-celled ameba comes into being derived from a previous ameba; it manifests the properties and performs the functions of its life which have been already enumerated. In the higher organisms it is different. Each, indeed, begins as a single cell, but the cells which result from division and subdivision do not form so many independent organisms, but adhere in one differentiated community which ultimately forms the complex but co-ordinated whole, in man the human body.

Thus, from the ovum, or germ cell which forms the starting-point of animal life, in a comparatively short time there is formed a complete membrane of cells, polyhedral in shape from mutual pressure, called the *Blastoderm;* and

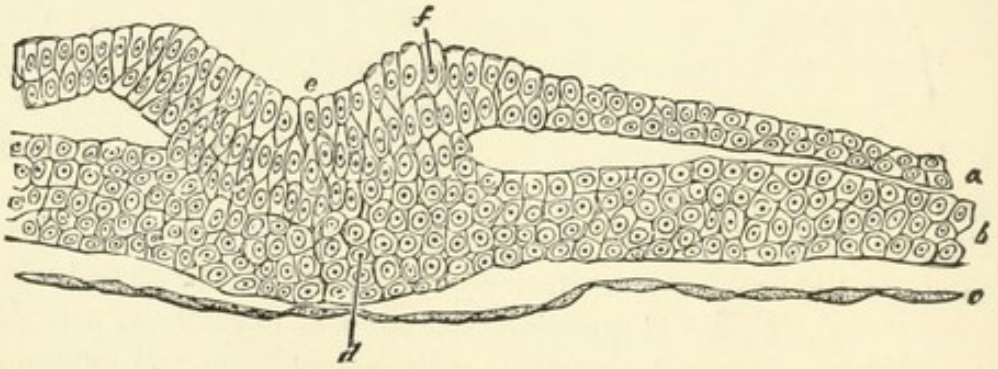


FIG. 13.—Transverse Section through Embryo Chick (26 hours). *a*, Epiblast; *b*, mesoblast; *c*, hypoblast; *d*, central portion of mesoblast, which is here fused with epiblast; *e*, primitive groove; *f*, dorsal ridge. (Klein.)

this speedily differentiates into two and then into three layers, chiefly from the rapid proliferation of the cells of the first single layer. These layers, figure 13, are called the *Epiblast*, the *Mesoblast*, and the *Hypoblast*. In the further development of the animal it is found that from each of these layers is produced a very definite part of the completed body. For example, from the cells of the epiblast are derived, among other structures, the skin and the central nervous system; from the mesoblast the muscles and connective tissue of the body, and from the hypoblast the epithelium of the alimentary canal, some of the chief glands, and so on.

It is obvious that the tissues and organs so derived will exhibit in a varying degree the primary properties of protoplasm. The muscles, for example, derived chiefly from certain cells of the mesoblast are particularly contractile and respond to stimuli readily, while the cells of the liver, although possibly contractile to a certain extent, have to do chiefly with the processes of nutrition.

As the cells of the embryo increase in number in development there is a corresponding differentiation of function among the groups of cells. The various functions which the original cell may be supposed to discharge, and the various properties it may be supposed to possess, become divided among groups of cells in which the work of each group is specialized. As a result of this division of labor the functions and properties are developed and made more perfect, with a view to the more economic and effective accomplishment of the activities of the body as a whole.

In studying the functions of the human body it is necessary first of all to know of what it is composed, of what tissues and organs it is made up; this can of course be ascertained only by the dissection of the dead body, and thus it comes that *Anatomy*, the science which treats of the structure of organized bodies, is closely associated with physiology, which treats of the function of the same structures. So close, indeed, is the association that *Histology*, which is especially concerned with the minute or microscopic structure of the tissues and organs of the body, and which is strictly speaking a department of anatomy, is often included in works on physiology. There is much to be said in favor of such an arrangement, since it is impossible to consider the changes which take place in any tissue during life, apart from the knowledge of the structure of the tissues themselves. There is indeed an almost inseparable relation between the structure and the function of the differentiated animal body in which the one is made the means to a knowledge of the other as an end, and *vice versa*, according to the aims and purposes of the student.

An equally important essential to the right comprehension of the changes which take place in the living organism is a knowledge of the chemical composition of the body. Here, however, we can deal directly only with the composition of the dead body, and it is well at once to admit that there may be many chemical differences between living and non-living tissues; but as it is impossible to ascertain the exact chemical composition of the living tissues, the next best thing which can be done is to find out as much as possible about the composition of the same tissues after they are dead. This is the assistance which the science of *Chemistry* can afford to the physiologist.

Having mastered the structure and composition of the body, we are brought face to face with physiology proper, and have to investigate the vital changes which go on in the tissues, the various actions taking place as long as the organism is at work. The subject includes not only the observation of the manifest processes which are continually taking place in the healthy body, but the conditions under which these are brought about, the laws which govern them and their effects.

Sources and Utilization of Physiological Material. It may be well to mention as a preliminary that the physiological information which we have at our disposal has been derived from many sources, the chief of which are as follows: From actual observation of the various phenomena occurring in

the human body from day to day, and from hour to hour, as, for example, the estimation of the amount and composition of the ingesta and egesta, the respiration, the beat of the heart, and the like; from observations upon other animals, the bodies of which we are taught by comparative anatomy approximate the human body in structure and may be supposed to be similar in function; from observations of the changes produced by experiment upon the various processes in such animals, or in the organs and tissues of animals; from observations of the changes in the working of the human body produced by diseases; from observations upon the gradual changes which take place in the functions of organs when watched in the embryo from their earliest beginnings to their completed development.

The physiologist, in order to utilize the sources of material, must be familiar with the gross structure of the animals or parts of animals which he proposes to use in experimental procedure. So simple a matter as the determination of arterial blood pressure involves familiarity with extensive anatomical structure. Experimental procedure must also draw on the field of microscopic structure or histology, and many of the most instructive bodies of physiological knowledge have come directly from the utilization of the facts of comparative anatomy and of biology. The problems in animal nutrition which are under such extensive investigation at the present time require for their solution not only the use of the most complex methods of chemistry, both analytical and synthetical, but also the principles and methods of physics. Indeed, since the work of Helmholz, the interpretation of physiological phenomena by means of physical laws and methods has contributed more than any other means toward the prominent scientific position of physiology at the present time. In a word, physiology must utilize the facts of anatomy, histology, biology, physics, and chemistry to interpret the phenomena of life.

CHAPTER II

CELL DIFFERENTIATION AND THE STRUCTURE OF THE ELEMENTARY TISSUES

A CAREFUL examination of the human body shows that the functional unit for the various and complicated life phenomena is the microscopical structure, the cell. The cell, alone or in combination, is capable of all the activities manifested by the living body. As a basis for brief review of the elementary structures of the body we shall first discuss the structure and development of the cell.

THE STRUCTURE OF THE CELL.

The typical tissue cell is a spherical or ovoid mass of protoplasm. Its structure is quite complex, but the most general differentiation is into the cell mass or *cytoplasm*, and its contained *nucleus*. The cytoplasm is sometimes bounded by a definite cell membrane, but in differentiated animal tissues this membrane is usually not present.

The Cell Body. The cell body or cytoplasm is a complex semi-fluid mass, the detailed structure of which has presented problems of many difficulties. It is usually described as having a framework of *spongioplasm* or formed elements, and a homogeneous *hyaloplasm*. In some cells there are formed materials resulting from the cellular activity called *metaplasm*, figure 14. These structural features are made more evident by their affinity for certain staining reagents.

The spongioplasm or reticulum varies greatly in different types of cells, and even in different parts of the same cell. It has considerable affinity for stains which exhibit a fine network, the reticulum. It increases in amount in older cells and also in constancy in the type of arrangement.

The hyaloplasm is more fluid, less refractile, and stains with great difficulty. It fills the interspaces of the spongioplasm. In this material may be embedded such substances as the metaplasts mentioned above.

Structure of the Nucleus. The nucleus when in a condition of rest is bounded by a distinct membrane, the nuclear membrane, possibly derived from the spongioplasm of the cell, which encloses the nuclear contents, *nucleoplasm* or *karyoplasm*. The membrane consists of an inner, or chromatic, and of an outer, or *achromatic layer*, so called from their reaction to stains. The nucleoplasm is made up of a reticular network, or *chromoplasm*, whose interspaces are filled by the karyolymph, or *nuclear matrix*, a homogeneous sub-

stance which is rich in proteids, has but slight affinity for stains, and is supposed to be fluid.

The network is composed of *linin* or achromatin, a transparent unstainable framework; and of *chromatin*, which stains deeply. It is supported by the linin, and occurs sometimes in the form of granules, but usually as irregular anastomosing threads, both thicker primary fibers and thinner connecting branches. The threads often form thickened nodes, karyosomes or false nucleoli, at their points of intersection. It is now quite generally believed that

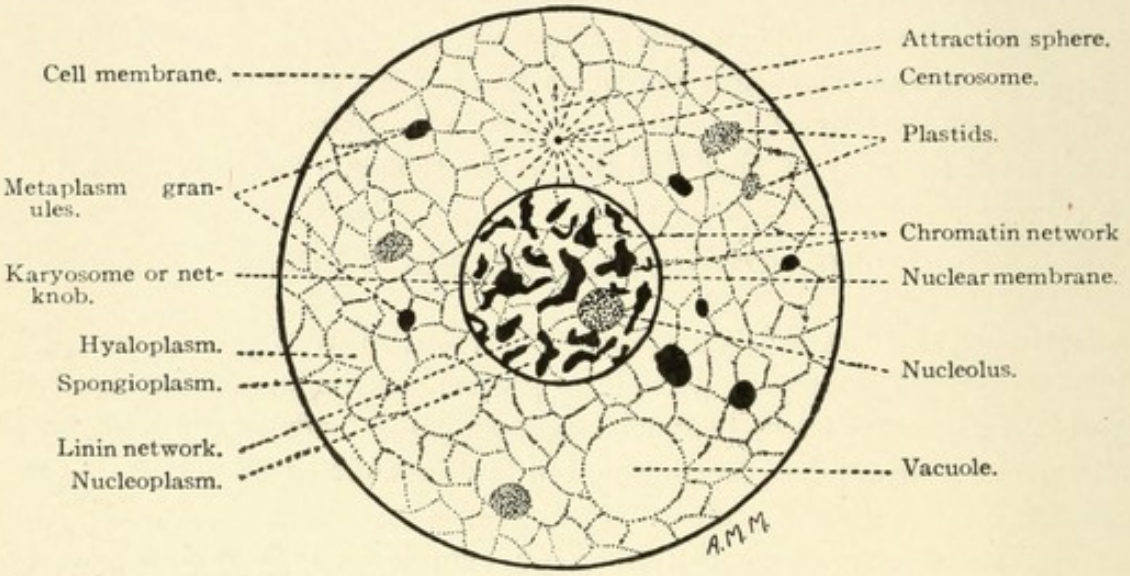


FIG. 14.—Diagram of a Typical Cell. (Bailey.)

the chromatin occurs as short, rodlike, and highly refractive masses, which are embedded in the linin in a regular series.

The *nucleoli*, or plasmosomes, are spherical bodies which stain deeply, and may either lie free in the nuclear matrix or be attached to the threads of the network.

The Centrosome and Attraction Sphere. In addition to the nucleus, a minute spherical body called the *centrosome* is believed to be constantly present in animal cells, though sometimes too small to be demonstrated. The centrosome is smaller than the nucleus, close to which it lies, and exerts a peculiar attraction for the protoplasmic filaments and granules in its vicinity, so that it is surrounded by a zone of fine radiating fibrils, forming the *attraction sphere* or archoplasm. Some authorities assert that the centrosome lies within the nucleus in the resting state, and passes into the cell proper only in the earlier stages of cell division. The attraction sphere is most distinctly seen in cells about to divide. It plays an important rôle in nuclear division, but it is doubted if it gives the initial impulse to the process.

Cell Multiplication. Cells increase in number by a process known as cell division, of which the first act is nuclear division. In fact the nucleus is the center of control of the cell-mass in the process of division. Cell multi-

plication takes place by two recognized methods, direct (amitosis), in which there is little disturbance of the nuclear network, and indirect (mitosis), in which there is a complex series of nuclear network changes. These mitotic changes result in the division of the chromatin filaments into the two new parts which form the chromoplasm of the daughter nuclei.

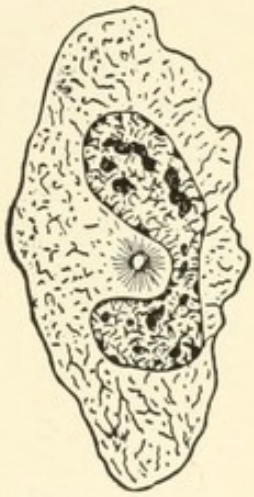


FIG. 15.—Leucocyte of Salamander Larva, Showing Attraction Sphere. (After Flemming.)

The process may be divided into the following stages:—

Prophase. The resting nucleus becomes somewhat enlarged, and the centrosome (according to those who regard it as lying normally within the nucleus) migrates into the cell protoplasm. The centrosome then divides into two daughter centrosomes which lie near the nucleus but are separated by a considerable interval. Each is surrounded by the radiating fibrils of the attraction sphere, and some of these fibrils pass continuously from one centrosome to the other, forming the *achromatic spindle.* At the same time the intranuclear network becomes converted into a fine convoluted coil (*spirem* or *skein*) which may be either continuous or else broken up into several threads. The thread or threads then shorten and become thicker, while the convolutions, which have become less numerous, arrange themselves in a series of connecting loops, forming the *wreath.* The nuclear membrane and the nucleolus disappear, the latter passing at times into the cell protoplasm and disintegrating. The wreath then breaks up into V-shaped segments, the *chromosomes,* of which each species of animal has a constant and characteristic number. This varies in the different animals, but is sixteen in man.

The two centrosomes migrate to the poles of the nucleus, while the achromatic spindle which connects them occupies the long axis of the nucleus. The

FIG. 16.—Early Stages of Karyokinesis. A. The thicker primary fibers remain and the achromatic spindle appears. B. The thick fibers split into two and the achromatic spindle becomes longitudinal. (Waldeyer.)

chromosomes, becoming much shorter and thicker, gather around the spindle in its equatorial plane, with their angles directed toward the center, forming the *aster* or *monaster.*

Metaphase. The actual division of the nucleus is begun at this time by the splitting of each chromosome longitudinally into halves which lie at first close

together so that each seems doubled. Soon afterward the fibrils of the achromatic spindle begin to contract, and thus separate the halves of the chromosomes in such a way that one-half of each is turned toward one pole, and the other half toward the other. As this continues, the two groups, which are equal in

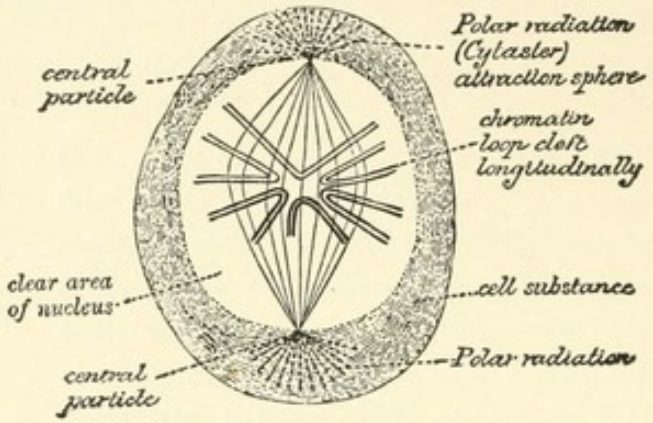


FIG. 17.—Monaster Stage of Karyokinesis. (Rabl.)

size, draw away from each other and from the equator, each group being formed of daughter chromosomes.

Anaphase. The two groups (daughter chromosomes) now gradually approach their respective poles, or centrosomes, and the equator becomes free. On reaching the pole, each group gathers in a form which is similar in arrangement to the monaster and is known as the *diaster.* During this time the cell body becomes slightly constricted by a circular groove at its equatorial plane.

Telophase. Soon afterward the fibrils of the chromatic spindle which connect the two groups begin to grow dim and finally disappear. The daugh-

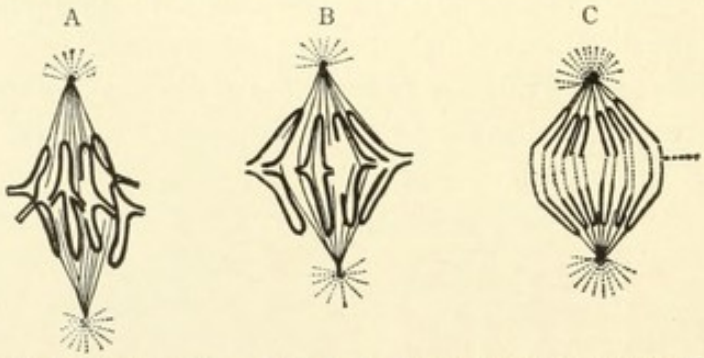


FIG. 18.—Stages of Karyokinesis. (Rabl.) A. Commencing separation of the split chromosomes. B. The separation further advanced. C. The separated chromosomes passing along the fibers of the achromatic spindle.

ter chromosomes assume the form of threads twisted in a coil and develop each a nuclear membrane and a nucleolus, forming a daughter nucleus. The nuclei enlarge and the nuclear threads assume the appearance of the resting state of the nucleus. Meanwhile, the constriction about the body of the cell has become deeper and deeper until the protoplasm is divided into two equal parts, or daughter cells, each with its daughter nucleus, and the process of karyokinesis is completed.

The Cell Types. All of the elementary tissues consist of cells and of their altered equivalents. It will be as well therefore to indicate some of the differences between the cells of the body. They are named in various ways, according to their *shape*, *origin*, and *functions*.

From their *shape*, cells are described as *spherical* or *spheroidal*, which is the typical shape of the free cell; this may be altered to *polyhedral* when the pressure on a mass of cells in all directions is nearly the same; of this the primitive segmentation cells afford an example. The *discoid* form is seen in blood-corpuscles, and the *scale-like* form in superficial epithelial cells. Some cells have a jagged outline and are then called *prickle cells*. Cells of *cylindrical*, *conical*, or *prismatic* form occur in various places in the body. Such cells may taper at one or both ends into fine processes, in the former case being *caudate*, in the latter *fusiform*. They may be greatly elongated so as to become fibers.

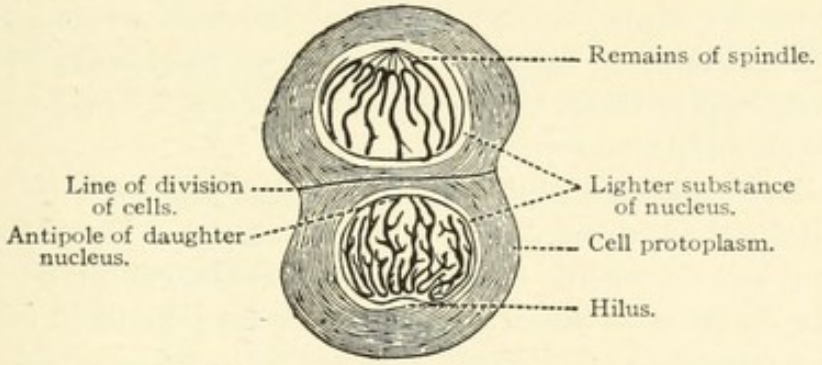


FIG. 19.—Final Stages of Karyokinesis. In the lower figure the changes are still more advanced than in the upper. (Waldeyer.)

Cells with hair-like processes, or *cilia*, projecting from their free surfaces, are a special variety. The cilia vary greatly in size, and may even exceed in length the cell itself. Finally, cells may be *branched* or *stellate* with long outstanding processes.

From their *function* cells are called *secreting*, *protective*, *sensitive*, *contractile*, and the like.

From their *origin* cells are called *epiblastic* and *mesoblastic* and *hypoblastic* (ectodermic, mesodermic, and endodermic).

Modes of Cell Connection. Cells are connected together to form tissues in various ways.

They are connected by means of a cementing intercellular substance. This is probably always present as a transparent, colorless, viscid, albuminous substance, even between the closely apposed cells of epithelium; while in the case of cartilage it forms the main bulk of the tissue, and the cells only appear as embedded in, not as cemented together by, the intercellular substance. This intercellular substance may be either homogeneous or fibrillated. In many cases, *e.g.*, the cornea, it can be shown to contain a number of irregular branched cavities, which communicate with each other, and in which branched

cells lie. Nutritive fluids can find their way through these branching spaces into the very remotest parts of a non-vascular tissue. The basement membrane (*membrana propria*) must be mentioned as a special variety of intercellular substance which is found at the base of the epithelial cells in most mucous membranes, and especially as an investing tunic of gland follicles which determines their shape.

Cells are connected by anastomosis of their processes. This is the usual way in which stellate cells, *e.g.*, of the cornea, are united. The individuality of each cell is thus to a great extent lost by its connection with its neighbors to form a reticulum. As an example of a network so produced we may cite the anastomosing cells of the reticular tissue of lymphatic glands.

Derived Elements. Besides the cell, which may be termed the primary tissue element, there are materials which may be termed secondary or derived elements or formed materials. Examples of this type of structure are found in the matrix of cartilage, the fibers of connective tissue, bone, etc.

Decay and Death of Cells. There are two *chief* ways in which the comparatively brief existence of cells is brought to an end, by mechanical abrasion and by chemical transformation.

The various epithelia furnish abundant examples of mechanical abrasion. As it approaches the free surface, the cell becomes more and more flattened and scaly in form and more horny in consistency, till at length it is simply rubbed off as in the epidermis. Hence we find free epithelial cells in the mucus of the mouth, intestine, and in the genito-urinary tract.

In the case of chemical transformation the cell-contents undergo a degeneration which, though it may sometimes be pathological, is very often a normal process. Thus we have cells by *fatty* metamorphosis producing oil-globules in the secretion of milk, fatty degeneration of the muscular fibers of the uterus after the birth of the fetus. *Calcareous* degeneration is common in the cells of many cartilages.

THE STRUCTURE OF THE ELEMENTARY TISSUES.

There are certain elementary structures formed in the process of differentiation which alone or when combined in varying proportions form the whole of the organs and tissues of the body. These elementary tissues are: *The Epithelial*, *The Connective*, *The Muscular*, and *The Nervous Tissues*. To these four some would add a fifth, looking upon the *Blood* and *Lymph*, containing, as they do, formed elements in a fluid menstruum, as a distinct tissue.

I. THE EPITHELIAL TISSUES.

Epithelium is a tissue composed almost wholly of cells, with a very small amount of intercellular substance which glues the cells together. In general it includes all those cellular membranes which cover either an external or

an internal free surface, together with the cellular portions of the glands which are connected with, or developed from, these free surfaces.

Epithelium clothes (1) the whole exterior surface of the body, forming the *epidermis* with its appendages; becoming continuous at the chief orifices of the body—nose, mouth, anus, and urethra—with (2) the epithelium which lines the whole length of the respiratory, alimentary, and genito-urinary tracts, together with the ducts and secretory cells of their various glands. Epithelium also lines the cavities of (3) the brain and the central canal of the spinal cord, (4) the serous and synovial membranes, and (5) the interior of blood-vessels and lymphatics.

Epithelial cells vary in size and shape, pressure being the main factor in this variation. The protoplasm may be granular, reticular, or fibrillar in appearance. The nucleus is spherical or oval, usually there is only one, but there may be two or more, present.

Epithelial tissues are non-vascular, that is to say, do not contain blood-vessels, but in some varieties minute channels exist between the cells of certain layers. Nerve fibers are supplied to the cells of many epithelia.

CLASSIFICATION OF EPITHELIA.

As to form and arrangement of cells.

I. Epithelia in the form of membranes (covering surfaces).
  1. Simple epithelium. Cells only one layer in thickness.
    (1) Squamous or pavement. Cells flattened.
      (a) Non-ciliated. Alveoli of lungs, also includes endothelium, lining the blood-vessels, and mesothelium, lining the large serous spaces.
      (b) Ciliated. The peritoneum of some forms at breeding season.
    (2) Cubical epithelia. Cells with the three dimensions approximately equal, mainly glandular.
      (a) Non-ciliated. The usual type. It is found lining both ducts and secretory portions of most glands, the pigmented layer of the retina, etc.
      (b) Ciliated. Not common. Lining of some of the smaller bronchial tubes.
    (3) Columnar. Cells may be cylindrical, conical, or goblet shaped.
      (a) Non-ciliated. Intestinal.
      (b) Ciliated. Fallopian tube and uterus.
      (c) Pseudo-stratified. Smaller bronchi, nasal duct, etc.
  2. Stratified epithelia. Cells more than one layer in thickness.
    (1) Squamous. Surface cells flattened.
      (a) Non-ciliated. Skin, mouth, vagina, etc.
      (b) Ciliated. Pharynx of embryo.

(2) Columnar. Surface cells columnar.
  (a) Non-ciliated. Portions of male urethra.
  (b) Ciliated. Trachea, bronchi, etc.

II. Epithelia not in the form of membranes, but in solid masses or cords, usually glandular.
  (1) Cells spheroidal, ova.
  (2) Cells polyhedral, liver, suprarenal, etc.

Epithelia, classified mainly as to function.

I. Protective. Skin, mouth, alimentary canal.
  1. Cornified. Skin, nails, hair.
  2. Cuticular border. Columnar cells of intestine.

II. Glandular.
  1. Secretory. Cells of salivary glands, pancreas, etc.
  2. Execretory. Cells of kidney.
  3. Absorptive. Cells of alimentary canal.

III. Sensory Epithelium. Cells of olfactory membrane, organ of Corti, taste buds, etc.

IV. Reproductive. Sex cells.

V. Pigmented. Pigmented layer of retina.

VI. Ciliated. Trachea, uterus, Fallopian tube, etc.

Only a few of the more important of the above-mentioned types of epithelium will be described here.

Simple Epithelium. *Simple Squamous.* This form of epithelium is found arranged in a single layer of flattened cells, for example, the lining of the alveoli of the lungs and of the descending arm of Henle's loop of the kidney tubule. Aside from endothelium as mesothelium it has very limited distribution in man. Endothelium and mesothelium are typical simple squamous

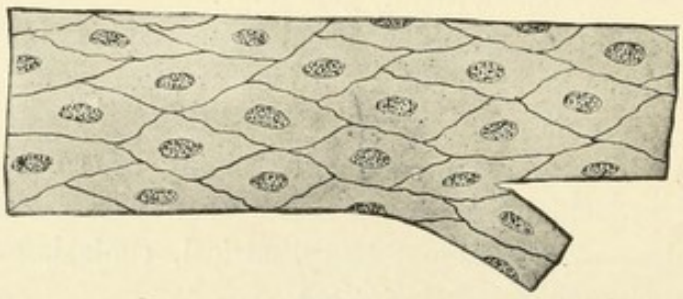


FIG. 20.—The Endothelium of a Small Blood-vessel. Silver-nitrate stain. × 350.

epithelia. They consist of much flattened cells with clear or slightly granular protoplasm and oval bulging nuclei, the edges of the cells are peculiarly wavy or serrated.

The presence of endothelium in any locality may be demonstrated by staining with silver nitrate, which brings into view the intercellular cement sub-

stance. When a small portion of a perfectly fresh serous membrane, for example, figure 20, is immersed for a few minutes in a solution of silver nitrate, and exposed to the action of light, the silver is precipitated in the in-

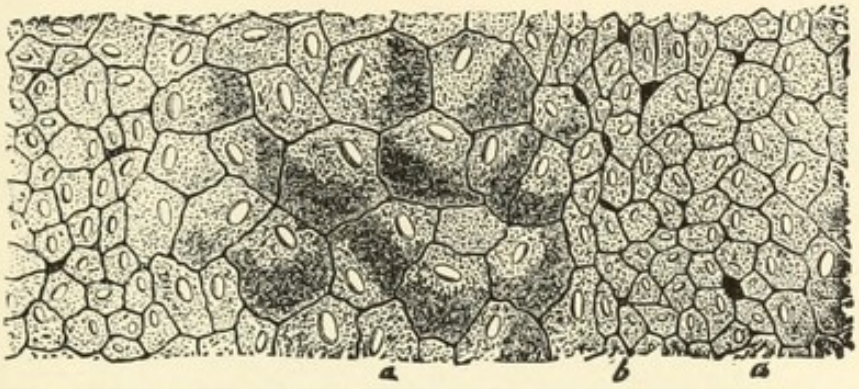


FIG. 21.—Abdominal Surface of Central Tendon of the Diaphragm of Rabbit, showing the general polygonal shape of the endothelial cells; each cell is nucleated. (Klein.) × 300.

tercellular cement substance, and the endothelial cells are thus mapped out by fine, dark, and generally sinuous lines of extreme delicacy.

Endothelial cells in certain situations may be ciliated, *e.g.*, those of the mesentery of the frog, especially during the breeding season.

On those portions of the peritoneum and other serous membranes in which lymphatics abound, apertures, figure 22, are found surrounded by small, more or less cubical, cells. These apertures are called *stomata*. They are particularly well seen in the anterior wall of the great lymph sac of the frog,

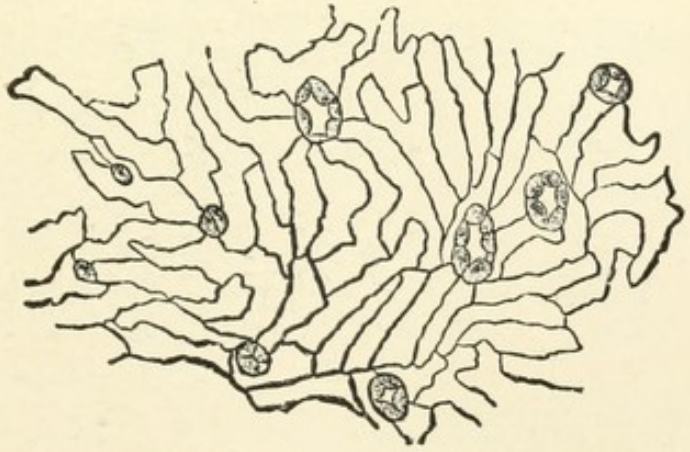


FIG. 22.—Peritoneal Surface of a Portion of the Septum of the great Lymph-Sac of Frog. The stomata, some of which are open, some collapsed, are surrounded by endothelial cells. (Klein.) × 160.

figure 22, and in the omentum of the rabbit. These are really the open mouths of lymphatic vessels or spaces, and through them lymph-corpuscles and the serous fluid from the serous cavity pass into the lymphatic system.

Simple Non-Ciliated Columnar Epithelium, figure 23, lines, *a*, the mucous membrane of the stomach and intestines as a single layer, from the cardiac

orifice of the stomach to the anus, and *b*, wholly or in part all the ducts of the glands opening on its free surface, and *c*, many gland-ducts in other regions of the body, *e.g.*, mammary, salivary, etc. The intracellular and intranuclear networks are well developed, and in some cases the spongioplasm is arranged

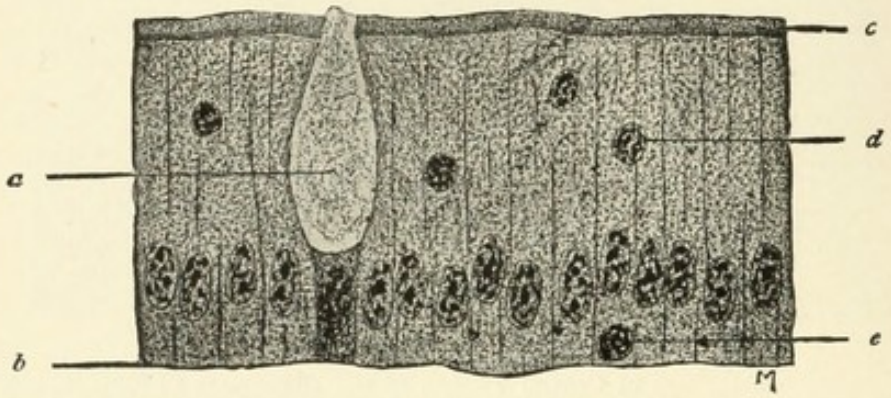


FIG. 23.—Simple Columnar Ephithelial Cells from the Human Intestinal Mucous Membrane. *a*, Mucous (goblet) cell; *b*, basement membrane; *c*, cuticle; *d*, leucocyte nucleus; *e*, germinating cell. (Bailey.)

in rods or longitudinal striæ at one part of the cell, as in the cells of the ducts of salivary glands. The protoplasm of columnar cells may be vacuolated and may also contain fat or other substances seen in the form of granules. Certain columnar cells transform a large part of their protoplasm into mucin, goblet cells, figure 24, which is discharged by the open mouth of the goblet, leav-

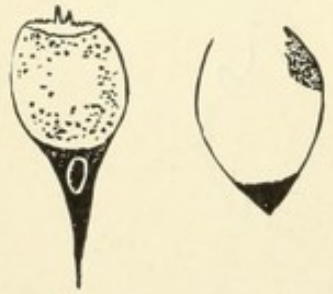


FIG. 24.

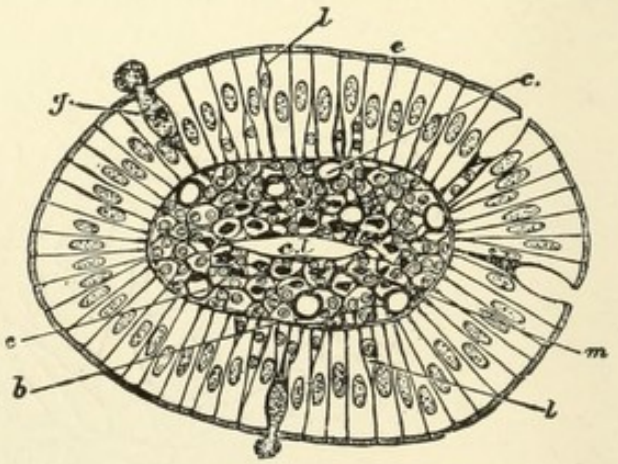


FIG. 25.

FIG. 24.—Goblet Cells. (Klein.)

FIG. 25.—Cross-section of a Villus of the Intestine. *e*, Columnar epithelium with striated border; *g*, goblet cell, with its mucus partly extruded; *l*, lymph-corpuscles between the epithelial cells; *b*, basement membrane; *c*, sections of blood-capillaries; *m*, section of plain muscle fibers; *c.l*, central lacteal. (Schäfer.)

ing only a nucleus surrounded by the remains of the protoplasm in its narrow stem. This transformation is a normal process which is continually going on during life, the cells themselves being supposed to regenerate into their original shape.

Stratified Epithelium. The term stratified epithelium is employed to describe the type found in the skin or its derivatives in which the cells forming the epithelium are arranged in a considerable number of superimposed layers. The shape and size of the cells of the different layers, as well as the number of layers, vary in different situations. Thus the superficial cells may be either squamous or columnar in shape and the deeper cells range from polygonal to columnar in form.

Stratified Squamous. The intermediate cells are polygonal in shape and approach more to the flat variety the nearer they are to the surface, and to the

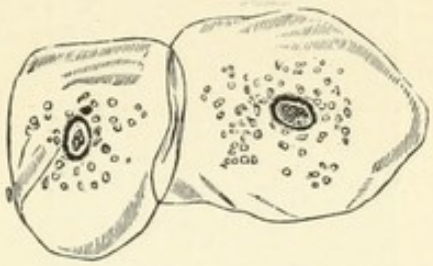


FIG. 26.—Squamous Epithelium Scales from the Inside of the Mouth. × 260. (Henle.)

columnar as they approach the lowest layer. In many of the deeper layers of epithelium in the mouth and skin, the outline of the cells is very irregular, in consequence of processes passing from cell to cell across these intervals. Such cells, figure 28, are termed "prickle" cells. These "prickles" are the intercellular bridges which run across from cell to cell, the interstices being filled by the transparent intercellular lymph. When this increases in quantity

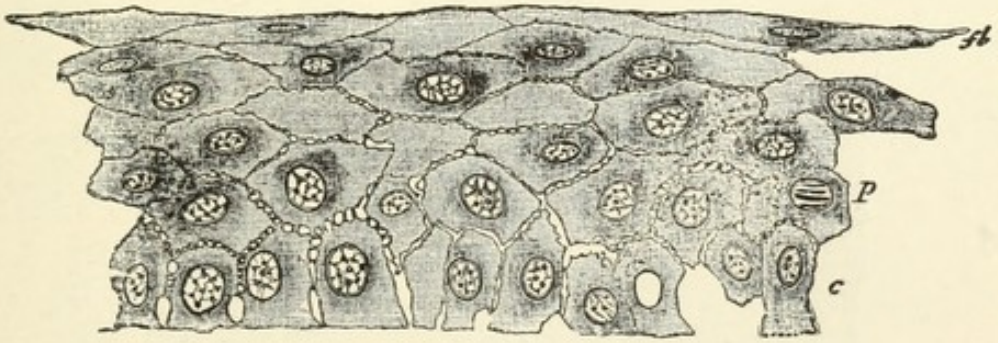


FIG. 27.—Vertical Section of the Stratified Epithelium Covering the Front of the Cornea. Highly magnified. (Schäfer.) *c*, Lowermost columnar cells; *p*, polygonal cells above these; *fl*, flattened cells near the surface. The intercellular channels, bridged by minute cell processes, are well seen.

in inflammation the cells are pushed further apart, and the connecting fibrils or "prickles" are elongated and more clearly visible.

The columnar cells of the deepest layer are distinctly nucleated; they multiply rapidly by division; and as new cells are formed beneath, they press the older cells forward, to be in turn pressed forward themselves toward the surface, gradually altering in shape and chemical composition until they die and are cast off from the surface.

Stratified squamous epithelium is found in the following situations: 1. Forming the epidermis, covering the whole of the external surface of the body; 2. Covering the mucous membrane of the nose, tongue, mouth, pharynx, and esophagus; 3. As the conjunctival epithelium, covering the cornea; 4. Lining the vagina and the vaginal part of the cervix uteri.

Stratified Columnar Epithelium. In this type of epithelium, the surface cells alone are columnar, the deeper cells being irregular in shape. From

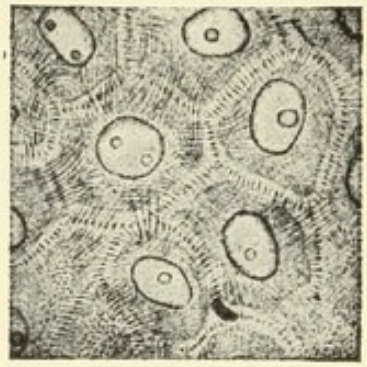


FIG. 28.—Epithelial Cells from the Stratum Spinosum of the Human Epidermis, Showing "Intercellular Bridges." × 700. (Szymonowicz.)

the surface cells long processes extend down among the underlying cells. This type of epithelium is usually ciliated, as in the trachea, bronchi, etc., but may be non-ciliated, as in portions of the human male urethra.

Transitional Epithelium. This is a stratified epithelium consisting of only three or four layers of cells. The superficial cells are large and flat, often

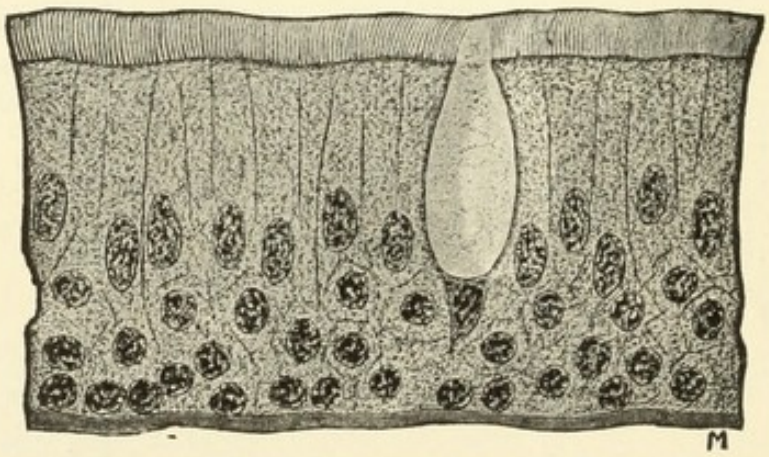


FIG. 29.—Stratified Columnar Ciliated Epithelium from the Human Trachea. A mucous (goblet) cell also is present.

containing two nuclei. The under surfaces of these cells are hollowed out, and into these depressions fit the large ends of the pyriform cells which form the next layer. Beneath the layer of pyriform cells are from one to four layers of polyhedral cells. This type of epithelium occurs in the bladder, ureter, and pelvis of the kidney.

Specialized Epithelium. Glandular Epithelium forms the active secreting agent in the glands; the cells are usually spheroidal, but may be polyhedral from mutual pressure, or even columnar; their protoplasm is generally occupied by the materials which the gland secretes. Examples of glandular

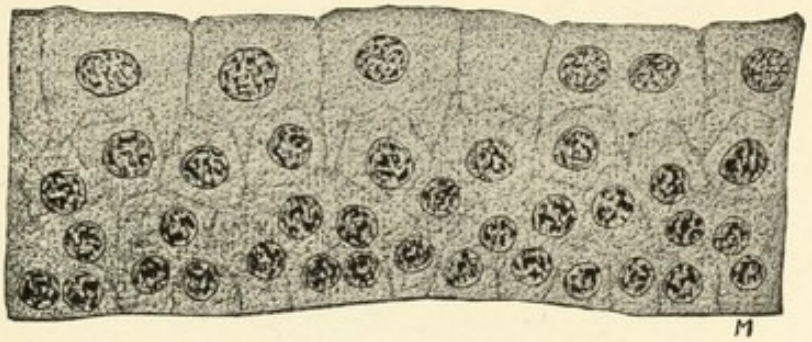


FIG. 30.—Transitional Epithelium from the Human Bladder. (Bailey.)

epithelium are to be found in the liver, figure 31, in the secreting tubes of the kidney, and in the salivary, figure 32, and gastric glands.

Ciliated epithelium consists of cells which are generally cylindrical in form, figures 29, 30, but may be spheroidal or even squamous.

This form of epithelium lines: *a*. The mucous membrane of the respiratory tract beginning just beyond the nasal aperture, and completely covers the nasal passages, except the upper part to which the olfactory nerve is distributed,

FIG. 31

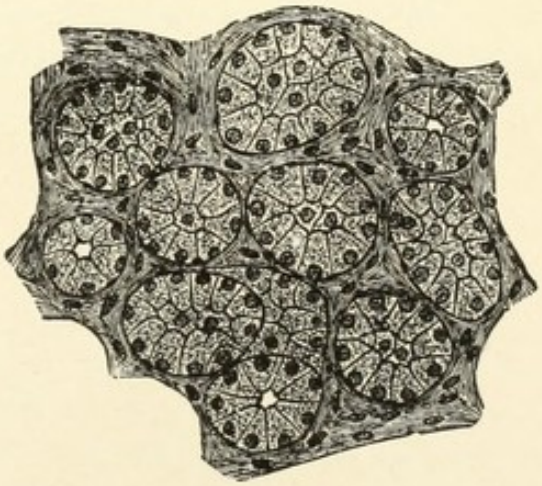


FIG. 32.

FIG. 31.—A Small Piece of the Liver of the Horse. (Cadiat.)

FIG. 32.—Glandular Epithelium. Small lobule of a mucous gland of the tongue, showing nucleated glandular cells. × 200. (V. D. Harris.)

and also the sinuses and ducts in connection with it and the lachrymal sac, the upper surface of the soft palate and the naso-pharynx, the Eustachian tube and tympanum, the larynx, except over the vocal cords, to the finest subdivisions of the bronchi. In part of this tract, however, the epithelium is in several layers, of which only the most superficial is ciliated, so that it should

more accurately be termed transitional, page 28, or stratified. *b*. Some portions of the generative apparatus in the male, viz., lining the "vasa efferentia" of the testicle, and their prolongations as far as the lower end of the epididymis, and much of the vas deferens; in the female, *c*, commencing about the middle

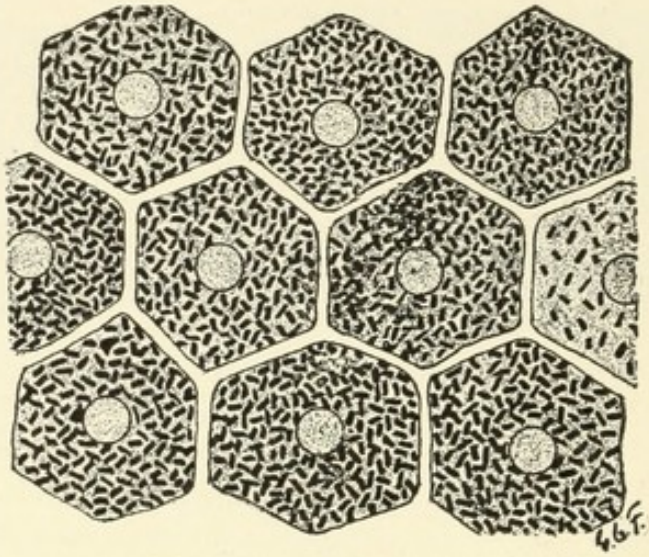


FIG. 33.—Specialized Pigmented Epithelial Cells of Retina.

of the neck of the uterus, and extending throughout the uterus and Fallopian tubes to their fimbriated extremities, and even for a short distance on the peritoneal surface of the latter. *d*. The ventricles of the brain and the central canal of the spinal cord are clothed with ciliated epithelium in the child, but in the adult this epithelium is limited to the central canal of the cord.

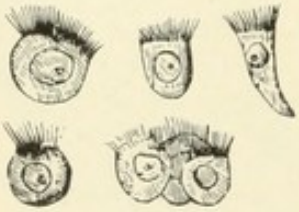


FIG. 34.

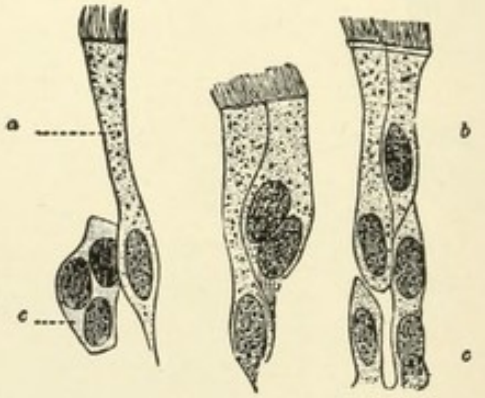


FIG. 35.

FIG. 34.—Spheroidal Ciliated Cells from the Mouth of the Frog. × 300 diameters. (Sharpey.)

FIG. 35.—Ciliated Epithelium from the Human Trachea. *a*, Large, fully formed cell; *b*, shorter cell; *c*, developing cells with more than one nucleus. (Cadiat.)

The cilia themselves are fine rounded or flattened homogeneous processes. According to some observers these processes are connected with longitudinal fibers which pass to the other end of the cell, but which are not connected with the nucleus.

Functions of Epithelium. According to function, epithelial cells may be classified as: 1, *protective*, *e.g.*, in the skin, mouth, blood-vessels, etc.; 2, *protective and motive*, ciliated epithelium; 3, *secreting*, glandular epithelium; 4, *germinal*, as epithelium of testicle producing spermatozoa; 5, *absorbing and secreting*, *e.g.*, epithelium of intestine; 6, *sensory*, *e.g.*, olfactory cells, organ of Corti.

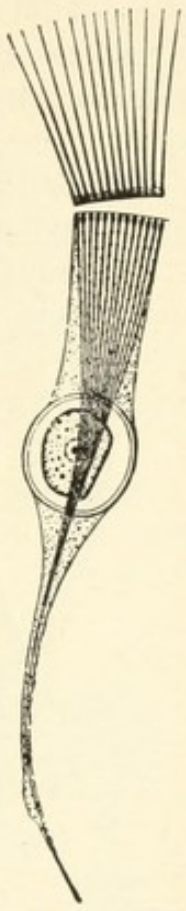


FIG. 36.—Ciliated Cell of the Intestine of a Mollusk. (Engelmann.)

Epithelium forms a continuous smooth investment over the whole body, being thickened into a hard, horny tissue at the points most exposed to pressure, and developing various appendages, such as hairs and nails. Epithelium lines also the sensorial surfaces of the eye, ear, nose, and mouth, and thus serves as the medium through which all impressions from the external world—touch, smell, taste, sight, hearing—reach the delicate nerve endings, whence they are conveyed to the brain.

The ciliated epithelium which lines the air-passages serves to promote currents of the air in the bronchial tubes and to propel fluids and minute particles of solid matter out of the body. In the case of the Fallopian tube, the cilia assist the progress of the ovum toward the cavity of the uterus.

The epithelium of the various glands, and of the whole intestinal tract, has the power of *secretion*, *i.e.*, of producing certain materials by processes of metabolism in its protoplasm.

Epithelium is likewise concerned in the processes of transudation, diffusion, and absorption.

II. THE CONNECTIVE TISSUES.

This group of tissues forms the skeleton with its various connections—bones, cartilages, and ligaments—and also affords a supporting framework and investment to the various organs composed of nervous, muscular, and glandular tissue. Its chief function is the mechanical one of support, and for this purpose it is so intimately interwoven with nearly all the textures of the body that if all other tissues could be removed, and the connective tissues left, we should have a wonderfully exact model of almost every organ and tissue in the body.

General Structure of Connective Tissue. The connective tissue is made up of two chief elements, namely, *cells* and *intercellular* or *formed substance*.

Cells. The cells are usually of an oval shape, often with branched processes, which are united to form a network. They are most readily

observed in the cornea, in which they are arranged, layer above layer, parallel to the free surface. They lie in spaces in the intercellular or ground substance, which form by anastomosis a system of branching canals freely communicating, figure 37.

The flattened tendon corpuscles which are arranged in long lines or rows parallel to the fibers belong to this class of cells, figure 39.

These branched cells often contain pigment granules, giving them a dark appearance; they form one variety of pigment cell. Pigment cells of this

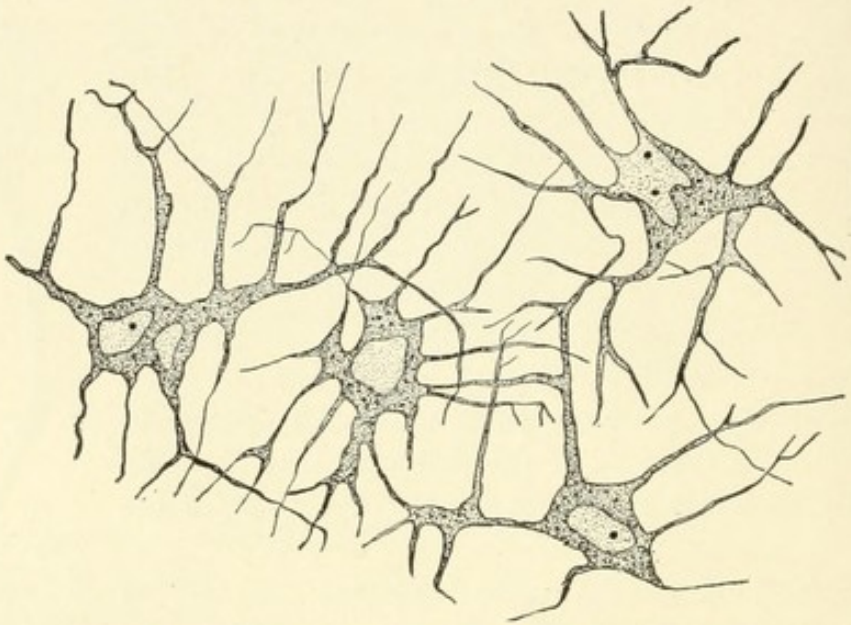


FIG. 37.—Horizontal Preparation of the Cornea of Frog, Stained in Gold Chloride; showing the network of branched corneal corpuscles. The ground substance is completely colorless. × 400. (Klein.)

kind are found in the outer layers of the choroid. In many of the lower animals, such as the frog, they are found widely distributed not only in the skin, but also in internal parts, the mesentery, sheaths of blood-vessels, etc. Under the action of light, electricity, and other stimuli, the pigment granules become massed in the body of the cell, leaving the processes quite hyaline; if the stimulus be removed, they will gradually be distributed again throughout the processes. Thus the skin in the frog is sometimes uniformly dusky, and sometimes quite light-colored, with isolated dark spots.

Intercellular Substance. This is *fibrillar*, as in the fibrous tissues and in certain varieties of cartilage; or *homogeneous*, as in typical mucoid tissue.

The fibers composing the former are of two kinds, white fibrous and yellow elastic tissue.

The chief varieties of connective tissues may be thus classified:

White fibrous.
Elastic.
Areolar.
Gelatinous.

Adenoid or retiform.
Adipose.
Neuroglia.
Cartilage.
1. Hyaline.
2. White fibrous.
3. Elastic.

Bone and dentine.

The White Fibrous Tissue. It is found typically in tendon; also in ligaments, in the periosteum and perichondrium, the dura mater, the pericardium, the sclerotic coat of the eye, the fibrous sheath of the testicle, in the fasciæ and aponeuroses of muscles, and in the sheaths of lymphatic glands.

Structure. To the naked eye, tendons and many of the fibrous membranes, when in a fresh state, present an appearance as of watered silk. This is due

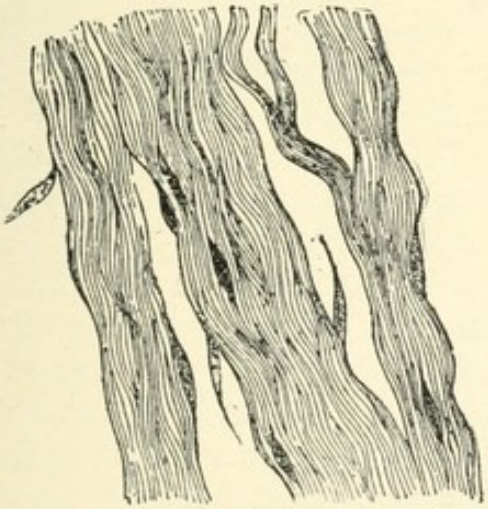


FIG. 38.

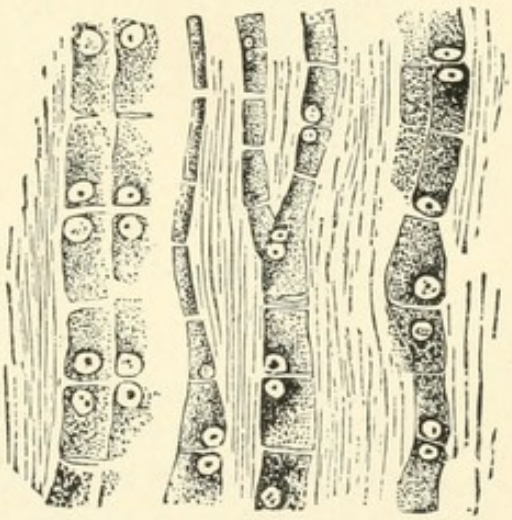


FIG. 39.

FIG. 38.—Mature White Fibrous Tissue of Tendon, Consisting Mainly of Fibers with a Few Scattered Fusiform Cells. (Stricker.)

FIG. 39.—Caudal Tendon of Young Rat, Showing the Arrangement, Form, and Structure of the Tendon Cells. × 300. (Klein.)

to the arrangement of the fibers in wavy parallel bundles. Under the microscope the tissue appears to consist of long, often parallel, bundles of fibers of different sizes. The cells in tendons, figure 39, are arranged in long chains in the ground substance separating the bundles of fibers, and are more or less regularly quadrilateral with large round nuclei containing nucleoli, generally placed so as to be contiguous in two cells. Each of these cells consists of a thick body from which processes pass in various directions into, and partially fill up the spaces between, the bundles of fibers. The rows of cells are separated from one another by lines of cement-substance.

Yellow Elastic Tissue. Yellow elastic tissue is found chiefly in the ligamentum nuchæ of the ox, horse, and other animals; the ligamenta subflava of man; the arteries, constituting the fenestrated coat of Henle;

the veins in the lungs and trachea; the stylo-hyoid, thyro-hyoid, and crico-thyroid ligaments; in the true vocal cords; and in areolar tissue.

Structure. Elastic tissue occurs in various forms, from a structureless, elastic membrane to a tissue whose chief constituents are bundles of fibers crossing each other at different angles; when seen in bundles elastic fibers are yellowish in color, but individual fibers are not so distinctly colored. The varieties of the tissue may be classified as follows:

FIG. 40.—Elastic Fibers from the Ligamenta Subflava. × 200. (Sharpey.)

a. Fine elastic fibrils, which branch and anastomose to form a network. This variety of elastic tissue occurs chiefly in the skin and mucous membranes, in subcutaneous and submucous tissue, in the lungs and true vocal cords.

b. Thick fibers, sometimes cylindrical, sometimes flattened, which branch, anastomose and form a network: these are seen most typically in the ligamenta subflava and also in the ligamentum nuchæ of such animals as the ox and horse, in which that ligament is largely developed, figure 40.

A certain number of connective-tissue cells are found in the ground substance between the elastic fibers which make up this variety of connective tissue, page 33.

Areolar Tissue. This variety of fibrous tissue has a very wide distribution and constitutes the subcutaneous, subserous, and submucous tissue. It is found in the mucous membranes, in the true skin, and in the outer sheaths of the blood-vessels. It forms sheaths for muscles, nerves, glands, and the internal organs, and, penetrating into their interior, supports and connects the finest parts.

Structure. To the naked eye it appears, when stretched out, as a fleecy, white, and soft meshwork of fine fibrils, with here and there wider films joining in it, the whole tissue being evidently elastic. The openness of the meshwork varies with the locality from which the specimen is taken. Under the microscope it is found to be made up of fine white fibers, which interlace in a most irregular manner, together with a variable number of elastic fibers. On the addition of acetic acid, the white fibers swell up, and become gelatinous in appearance; but as the elastic fibers resist the action of the acid, they may still be seen arranged in various directions, sometimes appearing to pass in a more or less circular or spiral manner round a small gelatinous mass of changed white fiber. The cells of areolar tissues are connective-tissue corpuscles.

Gelatinous Tissue. Gelatinous connective tissue forms the chief part of the bodies of such marine animals as the jelly-fish. It is found in

many parts of the human embryo. It may be best seen in the "Whartonian jelly" of the umbilical cord and in the enamel organs of developing teeth.

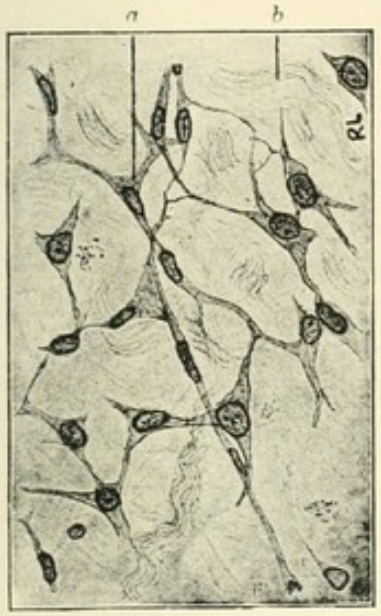


FIG. 41.

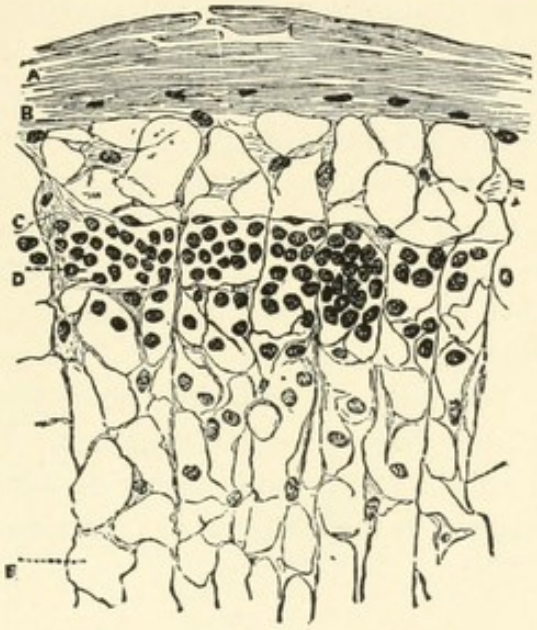


FIG. 42.

FIG. 41.—Mucous Connective Tissue from the Umbilical Cord. *a*, Cells; *b*, fibrils.

FIG. 42.—Part of a Section of a Lymphatic Gland, from which the Corpuscles have been for the most part Removed, showing the Adenoid Reticulum. (Klein and Noble Smith.)

Structure. It consists of cells, which in the jelly of the enamel organ are stellate, embedded in a soft jelly-like intercellular substance which forms the bulk of the tissue.

Adenoid or Lymphoid Tissue. *Distribution.* This variety of tissue makes up the stroma of the spleen and lymphatic glands, and is found also

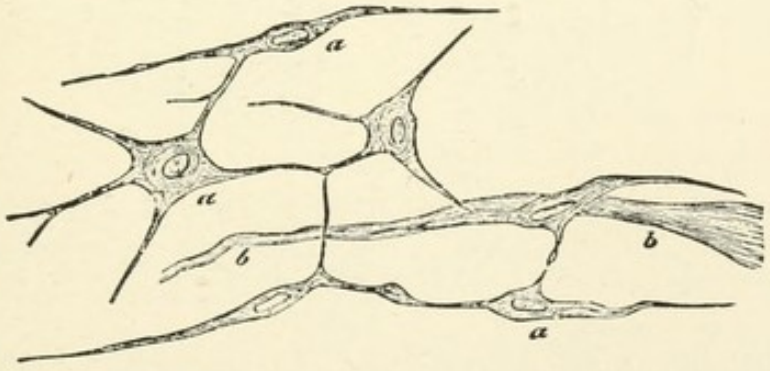


FIG. 43.—Portion of Submucous Tissue of Gravid Uterus of Sow. *a*, Branched cells, more or less spindle-shaped; *b*, bundles of connective tissue. (Klein.)

in the thymus, in the tonsils, and in the follicular glands of the tongue; in Peyer's patches, in the solitary glands of the intestines, and in the mucous membranes generally.

Structure. Adenoid or retiform tissue consists of a very delicate network of

minute fibrils, figure 46. The network of fibrils is concealed by being covered with flattened connective-tissue corpuscles, which may be readily dissolved in caustic potash, leaving the network bare. The network consists of white fibers, the interstices of which are filled with lymph-corpuscles. The cement-substance of adenoid tissue is very fluid.

Neuroglia. This form of connective tissue found in the nervous system is described on page 77.

Development of Fibrous Tissues. In the embryo the place of the fibrous tissues is at first occupied by a mass of roundish cells, derived chiefly from the mesoderm, but also from ectoderm and from entoderm. These develop either into a network of branched cells or into groups of fusiform cells, figure 43.

The cells are embedded in a semifluid albuminous substance derived probably from the cells themselves. Later this formed material is converted into fibrils under the influence of the cells. The process gives rise to fibers arranged in the one case in interlacing networks, *areolar tissue*, in the other

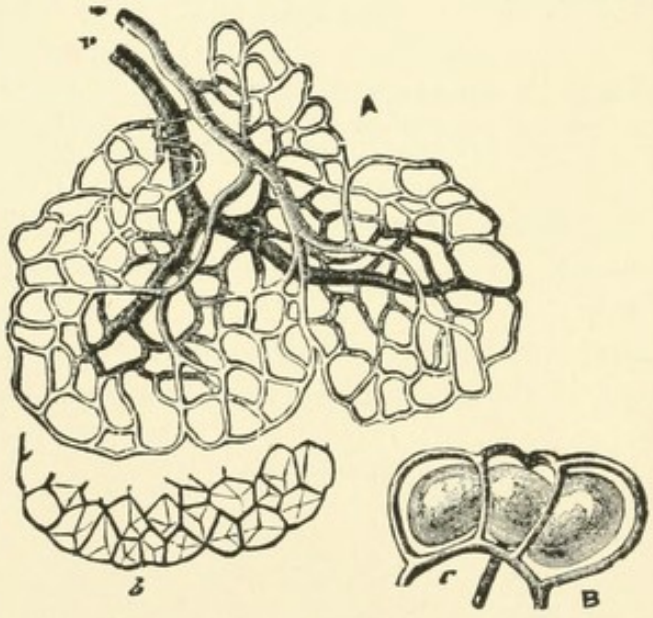


FIG. 44.—Blood-Vessels of Adipose Tissue. A, Minute flattened fat-lobule, in which the vessels only are represented. *a*, The terminal artery; *v*, the primitive vein; *b*, the fat-vesicles of one border of the lobule separately represented. × 100. B, Plan of the arrangement of the capillaries. *c*, on the exterior of the vesicles; more highly magnified. (Todd and Bowman.)

in parallel bundles, *white fibrous tissue.* In the mature forms of purely fibrous tissue not only the remnants of the cell-substance, but even the nuclei, may disappear. The embryonic tissue, from which *elastic* fibers are developed, is composed of fusiform cells, and a structureless intercellular substance. The fusiform cells dwindle in size and eventually disappear so completely that in mature elastic tissue hardly a trace of them is to be found: meanwhile the elastic fibers steadily increase in size.

Adipose Tissue. In almost all regions of the human body a larger or smaller quantity of adipose or fatty tissue is present. Adipose tissue is almost always found seated in areolar tissue, and forms in its meshes little masses of unequal size and irregular shape, to which the term *lobules* is commonly applied.

Structure. Adipose tissue consists essentially of cells which present dark, sharply defined edges when viewed with transmitted light; each consisting of a structureless and colorless membrane or bag formed of the remains of the original protoplasm of the cell, filled with fat. A nucleus

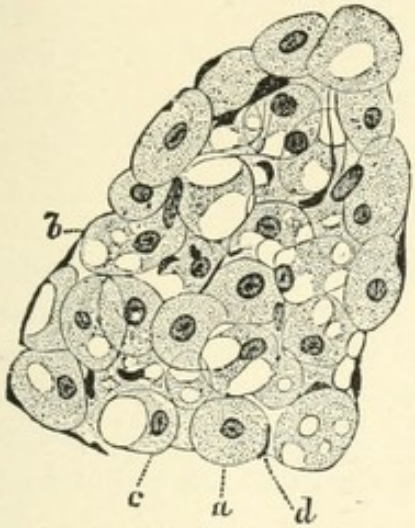


FIG. 45.—A Lobule of Developing Adipose Tissue from an Eight-Months' Fetus. *a*, Spherical or, from pressure, polyhedral cells with large central nucleus, surrounded by a finely reticulated substance staining uniformly with hematoxylin. *b*, Similar cells with spaces from which the fat has been removed by oil of cloves. *c*, Similar cells showing how the nucleus with enclosing protoplasm is being pressed toward periphery. *d*, Nucleus of endothelium of investing capillaries. (McCarthy.) Drawn by Treves.

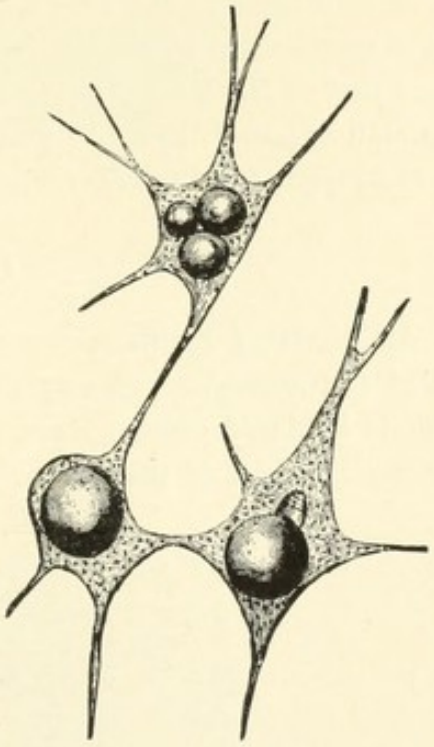


FIG. 46. — Branched Connective-Tissue Corpuscles, Developing into Fat-Cells. (Klein.)

is always present in some part or other of the cell protoplasm, but in the ordinary condition of the loaded cell it is not easily or always visible. This membrane and the nucleus can generally be brought into view by extracting the fat with ether and by staining the tissue.

The ultimate cells are held together by capillary blood-vessels, figure 44; while the little clusters thus formed are grouped into small masses, and held so, in most cases, by areolar tissue. The oily matter contained in the cells is composed chiefly of the compounds of fatty acids with glycerin, *olein*, *stearin*, and *palmitin*.

Development of Adipose Tissue. Fat cells are developed from connective-tissue corpuscles. In the infra-orbital connective tissue there are cells exhibiting every intermediate gradation between an ordinary branched connective-tissue corpuscle and mature fat cells. Their developmental appearance

is as follows: a few small drops of oil make their appearance in the protoplasm, and by their confluence a larger drop is produced, figure 45. This gradually increases in size at the expense of the original protoplasm of the cell, which becomes correspondingly diminished in quantity till in the mature cell it forms only a thin crescentic film with a nucleus closely pressed against the cell-wall. Under certain circumstances this process may be reversed.

A large number of blood-vessels are developed in adipose tissue, which subdivide until each lobule of fat contains a fine meshwork of capillaries ensheathing each individual fat-globule, figure 44.

Adipose tissue serves as a storehouse of combustible matter which may be reabsorbed into the blood when occasion requires, and, being used up in the metabolism of the tissues, may help to preserve the heat of the body. That part of the fat which is situated beneath the skin must, by its want of conducting power, assist in preventing undue waste of the heat of the body by escape from the surface.

CARTILAGE.

All kinds of cartilage are composed of *cells* embedded in a substance called the *matrix*. The apparent differences of structure met with in the various kinds of cartilage are more due to differences in the character of the matrix than of the cells. With the exception of the articular variety,

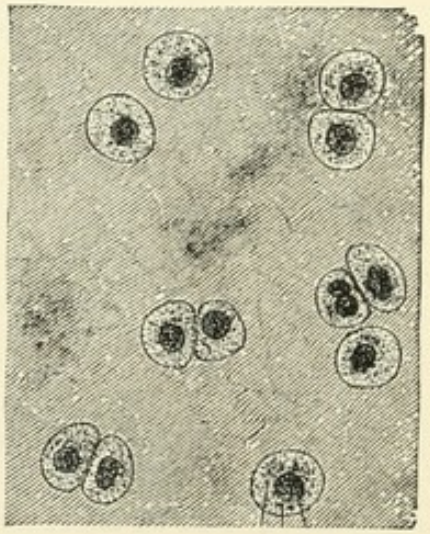


FIG. 47.—Hyaline Articular Cartilage (Human). The cell bodies entirely fill the spaces in the matrix. × 340 diams. (Schäfer.)

cartilage is invested by a thin but tough firm fibrous membrane called the *perichondrium*.

Cartilage exists in three different forms in the human body, viz., *hyaline cartilage*, *yellow elastic cartilage*, and *white fibro-cartilage*.

Hyaline Cartilage. This variety of cartilage is met with largely in

the human body where it invests the articular ends of bones, and forms the costal cartilages, the nasal cartilages, and those of the larynx with the ex-

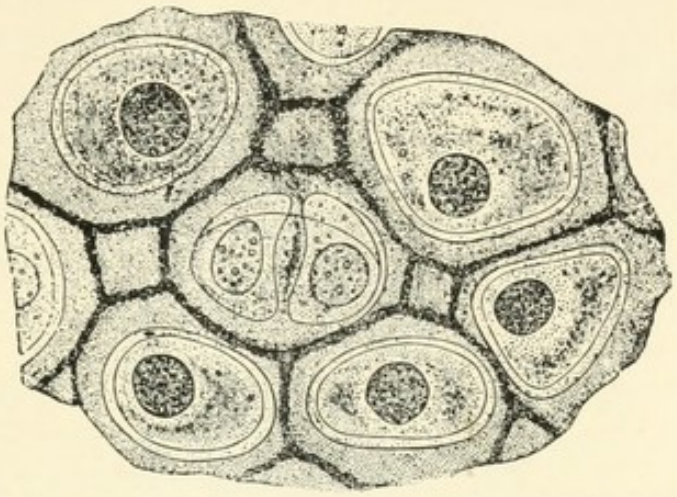


FIG. 48.—Fresh Cartilage from the Triton. (A. Rollett.)

ception of the epiglottis and cornicula laryngis, the cartilages of the trachea and bronchi.

Structure. Like other cartilages it is composed of cells embedded in a matrix. The cells are irregular in shape, generally grouped together in patches, figure 47. The patches are of various shapes and sizes and placed at unequal distances apart. They generally appear flattened near the free

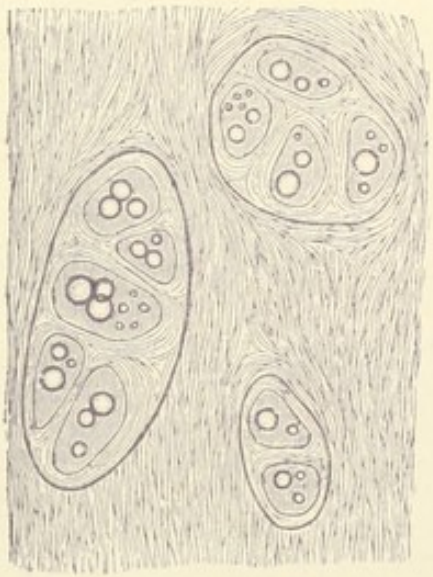


FIG. 49.—Costal Cartilage from an Adult Dog, showing the Fat-Globules in the Cartilage Cells. (Cadiat.)

surface of the mass of cartilage, and more or less perpendicular to the surface in the more deeply seated portions.

The intercellular substance of hyaline cartilage, when viewed fresh or after ordinary fixation, appears homogeneous. However, when subjected to special methods, the seemingly homogeneous intercellular substance can

be shown to be made up of fibers, comparable with those found in white fibrous tissue, embedded in the homogeneous matrix.

In the hyaline cartilage of the ribs the cells are mostly larger than in the articular variety and there is a tendency to the development of fibers

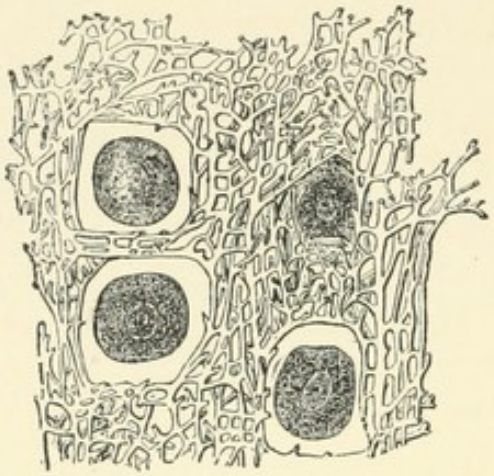


FIG. 50.—Yellow Elastic Cartilage of the Ear. Highly magnified. (Hertwig.)

in the matrix, figure 49. The costal cartilages also frequently become calcified in old age, as also do some of those of the larynx.

In the fetus cartilage is the material of which the bones are first constructed; the "model" of each bone being laid down, so to speak, in this

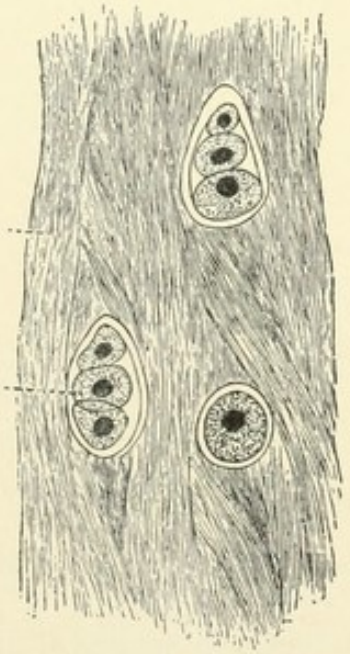


FIG. 51.—White Fibro-Cartilage. (Cadiat.)

substance. In such cases the cartilage is termed *temporary*. It closely resembles the ordinary hyaline cartilage but the cells are more uniformly distributed throughout the matrix.

Elastic and White Fibro-Cartilage. The first variety is found in the cartilage of the external ear; the latter in portions of the joints, the intervertebral cartilages, etc.

Structure. Elastic and white fibro-cartilage are composed of cells and a matrix; the latter being made up almost entirely of fibers closely resembling those of fibrous connective tissue.

Development of Cartilage. Cartilage is developed out of mesoblast cells with a very small quantity of intercellular substance. The cells multiply by fission within the cell-capsules.

BONE.

The characteristic of bone is that the matrix is solidified by a deposit of earthy salts, chiefly calcium phosphate, but some magnesium phosphate and calcium carbonate.

To the naked eye there appear two plans of structure in different bones, and in different parts of the same bone, namely, the *dense* or *compact*, and the *spongy* or *cancellous* tissue. In a longitudinal section of a long bone, as the humerus, the articular extremities are found capped on their surface by a thin shell of compact bone, while their interior is made up of the spongy or cancellous tissue. The *shaft* is formed almost entirely of a thick layer of the compact bone which surrounds a central canal, the *medullary* cavity, so called from its containing the *medulla*, or marrow. In the flat bones, the parietal bone or the scapula, a layer of cancellous structure lies between two layers of the compact tissue. In the short and irregular bones, as those of the *carpus* and *tarsus*, the cancellous tissue alone fills the interior, while a thin shell of compact bone forms the outside.

The Marrow. There are two distinct varieties of marrow—the *red* and the *yellow*.

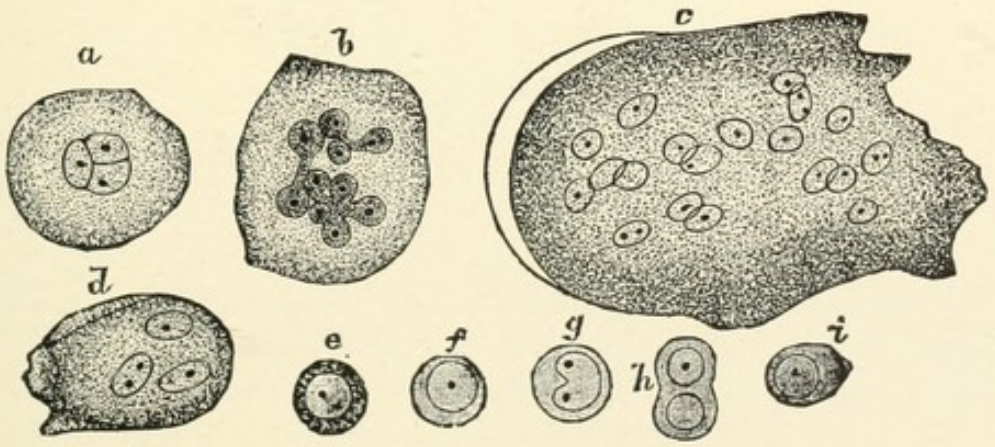


FIG. 52.—Cells of the Red Marrow of the Guinea-Pig, highly magnified. *a*, A large cell, the nucleus of which appears to be partly divided into three by constrictions; *b*, a cell, the nucleus of which shows an appearance of being constricted into a number of smaller nuclei; *c*, a so-called giant cell, or myeloplaxe, with many nuclei; *d*, a smaller myeloplaxe, with three nuclei; *e–i*, proper cells of the marrow. (Schäfer.)

Red marrow is that variety which occupies the spaces in the cancellous tissue; it is highly vascular, and thus maintains the nutrition of the spongy bone, the interstices of which it fills. It contains a few fat cells and a large number of marrow cells, many of which are undistinguishable from lymphoid corpuscles, and has for a basis a small amount of fibrous tissue. Among the cells are some nucleated cells containing hemoglobin like the blood-corpuscles. There are also a few large cells with many nuclei, termed *giant cells* or *myeloplaxes*, which are probably derived from the ordinary marrow cells, figure 52.

Yellow marrow fills the medullary cavity of long bones, and consists chiefly of fat cells with numerous blood-vessels. Many of its cells are in every respect similar to lymphoid corpuscles.

From these marrow cells, especially those of the red marrow, the red blood-corpuscles are derived.

The Periosteum and Nutrient Blood-Vessels. The surfaces of bones, except the part covered with articular cartilage, are clothed by a

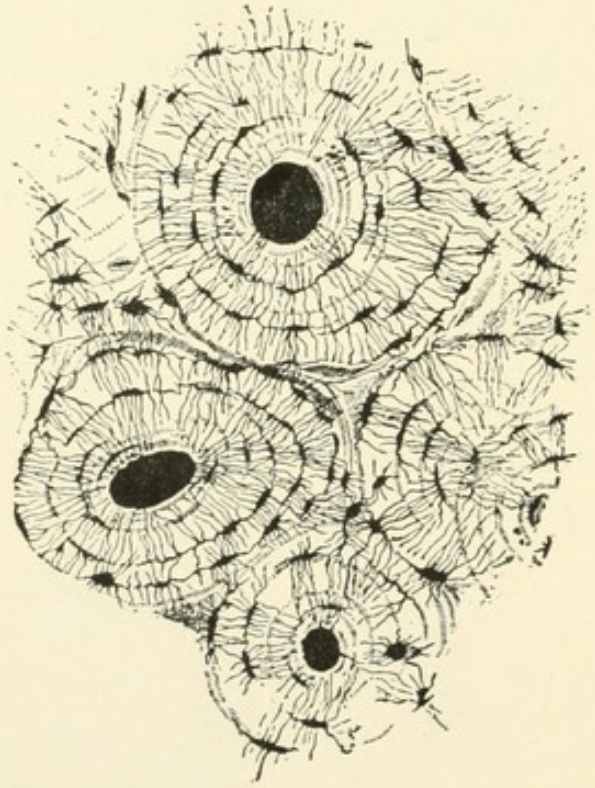


FIG. 53.—Transverse Section of Compact Bone (of humerus). Three of the *Haversian canals* are seen, with their concentric rings; also the *lacunæ*, with the *canaliculi* extending from them across the direction of the *lamellæ*. The Haversian apertures were filled with débris in grinding down the section, and therefore appear black in the figure, which represents the object as viewed with transmitted light. The Haversian systems are so closely packed in this section, that scarcely any *interstitial lamellæ* are visible. × 150. (Sharpey.)

tough, fibrous membrane, the *periosteum*, which is closely attached to the surface of the bone. Blood-vessels are distributed in this membrane, and minute branches from these periosteal vessels enter the Haversian canals

to supply blood to the solid part of the bone. The long bones are supplied also by a proper nutrient artery which, entering at some part of the shaft so as to reach the medullary canal, breaks up into branches for the supply of the marrow, from which again small vessels are distributed to the interior of the bone. Other small nutrient vessels pierce the articular extremities for the supply of the cancellous tissue.

Microscopic Structure of Bone. Notwithstanding the differences of arrangement just mentioned, the structure of all compact bone substance is found under the microscope to be essentially the same.

Examined with a rather high power its substance is found to contain a multitude of small irregular spaces, approximately fusiform in shape, called *lacunæ*, with very minute canals or *canaliculi*, as they are termed, leading

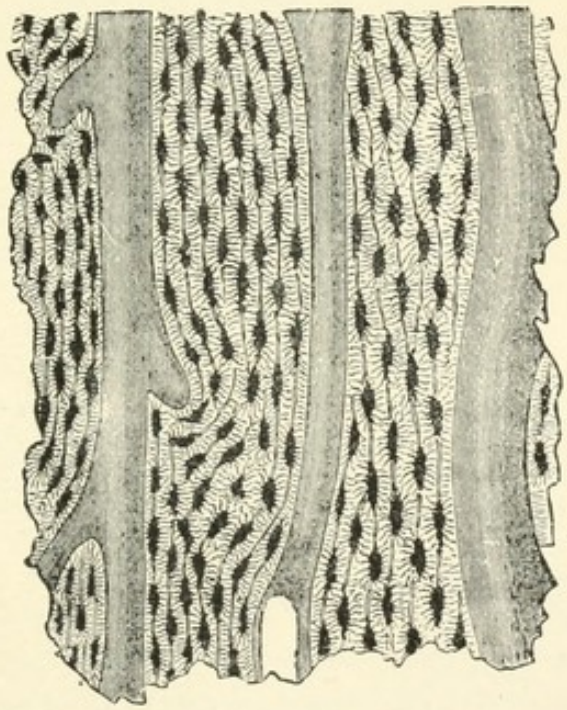


FIG. 54.—Longitudinal Section from the Human Ulna, Showing Haversian Canals, Lacunæ, and Canaliculi. (Rollett.)

from them, and anastomosing with similar prolongations from other lacunæ, figure 53. In very thin layers of bone, no other canals than these may be visible; but on making a transverse section of the compact tissue of a long bone, as the humerus or ulna, the arrangement shown in figure 53 can be seen. The bone seems mapped out into small circular districts, at or about the center of each of which is a hole, around which are concentric layers, the *lamellæ*, the *lacunæ* and *canaliculi* following the same concentric distribution around the center, with which indeed they communicate.

On making a longitudinal section, the central holes are shown to be simply the cut extremities of small canals which run lengthwise through the bone, anastomosing with each other by lateral branches, figure 54, and

are called *Haversian Canals*, after the name of the physician, Clopton Havers, who first accurately described them.

The Haversian Canals. The average diameter of the Haversian canals is 50 μ. They contain blood-vessels, and by means of them blood is conveyed to even the densest parts of the bone; the minute canaliculi and lacunæ absorbing nutrient matter from the Haversian blood-vessels and conveying it still more intimately to the very substance of the bone which they traverse. The blood-vessels enter the Haversian canals both from without from the periosteum, and from within from the medullary cavity or from the cancellous tissue. The arteries and veins usually occupy separate canals.

The *lacunæ* are occupied by branched cells, the *bone-cells* or *bone-corpuscles*, figure 55, which very closely resemble the ordinary branched connective-tissue corpuscles. The processes of the bone-cells extend into the canaliculi. Each cell controls the nutrition of the bone immediately surrounding it. Each lacunar corpuscle communicates with the others in its surrounding

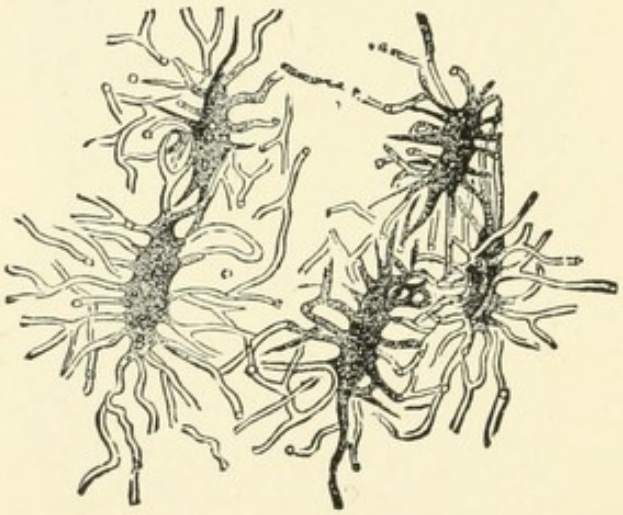


FIG. 55.—Bone-Corpuscles with their Processes as Seen in a thin Section of Human Bone. (Rollett.)

district, and with the blood-vessels of the Haversian canals by means of the ramifications just described.

It will be seen from the above description that bone bears a very close structural resemblance to what may be termed typical connective tissue. The bone corpuscles with their processes occupying the lacunæ and canaliculi correspond exactly to the cornea-corpuscles lying in the branched spaces.

The Lamellæ of Compact Bone. In the shaft of a long bone three distinct sets of lamellæ can be clearly recognized: *General* or fundamental lamellæ, which are just beneath the periosteum and parallel with it, and around the medullary cavity; *Special* or Haversian lamellæ, which are concentrically arranged around the Haversian canals to the number of six to eighteen around each; *Interstitial* lamellæ, which connect the systems of Haversian lamellæ,

filling the spaces between them, and consequently attaining their greatest development where the Haversian systems are few.

The ultimate structure of the lamellæ appears to be fibrous. A thin film peeled off the surface of a bone, from which the earthy matter has been removed by acid, is composed of a finely reticular structure, formed apparently of very slender fibers decussating obliquely, but coalescing at the points of intersection, as if here the fibers were fused rather than woven together.

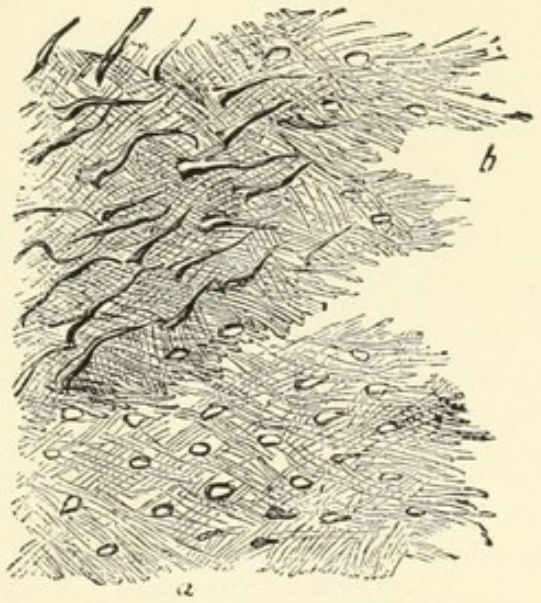


FIG. 56.—Lamellæ Torn Off from a Decalcified Human Parietal Bone at some Depth from the Surface. *a*, *a*, Lamellæ, showing reticular fibers; *b*, *b*, darker part, where several lamellæ are superposed; *c*, perforating fibers. Apertures through which perforating fibers had passed, are seen especially in the lower part, *a*, *a*, of the figure. (Allen Thomson.)

The reticular lamellæ are perforated by the *perforating fibers of Sharpey*, which bolt the neighboring lamellæ together, and may be drawn out when the latter are torn asunder, figure 56. These perforating fibers originate from ingrowing processes of the periosteum, and in the adult still retain their connection with it.

Development of Bone. From the point of view of their development, all bones may be subdivided into two classes:

Those which are ossified directly in *membrane* or fibrous tissue, *e.g.*, the bones forming the vault of the skull, parietal, frontal, and a certain portion of the occipital bones;

Those whose form, previous to ossification, is laid in down *hyaline cartilage*, *e.g.*, humerus, femur, etc.

The process of development, pure and simple, may be best studied in bones which are not preceded by cartilage, *i.e.*, *membrane-formed*. Without a knowledge of ossification in *membrane* it is difficult to understand the much more complex series of changes through which such a structure as the carti-

laginous femur of the fetus passes in its transformation into the bony femur of the adult (ossification in *cartilage*).

Ossification in Membrane. The membrane, afterward forming the periosteum, from which such a bone as the parietal is developed, consists of two layers, an external *fibrous*, and an internal *cellular* or *osteogenetic*.

The *external layer* consists of ordinary connective tissue, with branched corpuscles here and there between the bundles of fibers. The internal layer consists of a network of fine fibrils with nucleated cells and ground or cement substance between the fibrous bundles. It is more richly supplied with capillaries than the outer layer. The relatively large number of its cellular elements, together with the abundance of blood-vessels, clearly mark it as the portion of the periosteum which is immediately concerned in the formation of bone.

In such a bone as the parietal there is first an increase in vascularity, followed by the deposition of bony matter in radiating spicula, starting from a *center of ossification*. These primary bony spicula are *osteogenetic fibers*, composed of *osteogen*, in which calcareous granules are deposited. Calcareous granules are deposited also in the interfibrillar matrix. By the junction of the osteogenetic fibers and their resulting bony spicula a meshwork of bone is formed. The osteoblasts, being in part retained within the bone trabeculæ thus produced, form bone-corpuscles. Lime salts are deposited in the circumferential part of each osteoblast, and thus a ring of osteoblasts gives rise to a ring of bone with the remaining uncalcified portions of the osteoblasts embedded in it as bone-corpuscles. At the same time the plate increases at the periphery by the extension of the bony spicula and by deposits taking place from the osteogenetic layer of the periosteum. The bulk of the primitive spongy bone is gradually converted into compact bony tissue of the Haversian systems.

Ossification in Cartilage. Under this heading, taking the femur as a typical example, we may consider the process by which the solid cartilaginous rod which represents the bone in the fetus is converted into the hollow cylinder of compact bone with expanded ends formed of cancellous tissue in the adult long bone.

The fetal cartilage is sheathed in a membrane termed the *perichondrium*, which resembles the periosteum described above. Thus, the differences between the fetal perichondrium and the periosteum of the adult are such as usually exist between the embryonic and mature forms of connective tissue.

There are several steps in the transformation of the fetal cartilage to the adult bone, due to the fact that there is first an impregnation of the cartilage with lime salts, followed later by the resorption of this entire material with formation of the embryonic spongy bone, which is later replaced by the permanent bone. The complicated phenomenon takes place in steps or stages as follows:

Stage of Proliferation and Calcification. The cartilage cells in and near the center of ossification become enlarged, proliferate, and arrange themselves in rows in the long axis of the fetal cartilage, figure 57. Lime salts are next deposited in fine granules in the hyaline matrix of the cartilage, and this gradually becomes transformed into calcified trabeculæ, figure 57. The enlarging cartilage cells become more transparent, and finally disintegrate, the spaces occupied by them forming the primordial marrow cavities. During

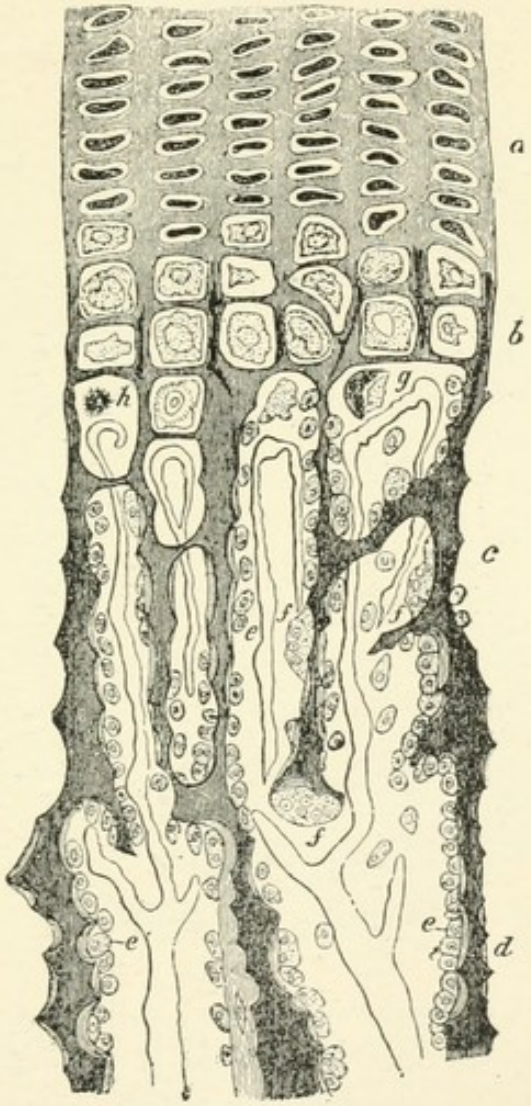


FIG. 57.—Developing Bone of Femur of the Rabbit. (Schäfer, from Klein.) × 350. *a*, Cartilage cells; *b*, cartilage cells enlarged in the region of calcifying matrix; *c*, *d*, trabeculæ of calcifying cartilage covered with *e*, osteoblasts; *f*, osteoclasts eroding the trabeculæ; *g*, *h*, disappearing cartilage cells. The osteoblasts are seen to be depositing layers of bony substance. Loops of blood-vessels extend to the limit of the region in which the bone is forming.

this stage the perichondrium has become the periosteum, and is beginning to deposit bone on the outside of the cartilage.

Stage of Vascularization of the Cartilage. Processes from the osteogenetic layer of the periosteum containing blood-vessels break through the bone into the primordial marrow cavities and form the primary marrow,

beginning at the *centers of ossification*, and spreading chiefly up and down the shaft.

Stage of Substitution of Embryonic Spongy Bone for Calcified Cartilage. The cells of the primary marrow arrange themselves as a continuous epithelium-like layer on the calcified trabeculæ and deposit a layer of bone,

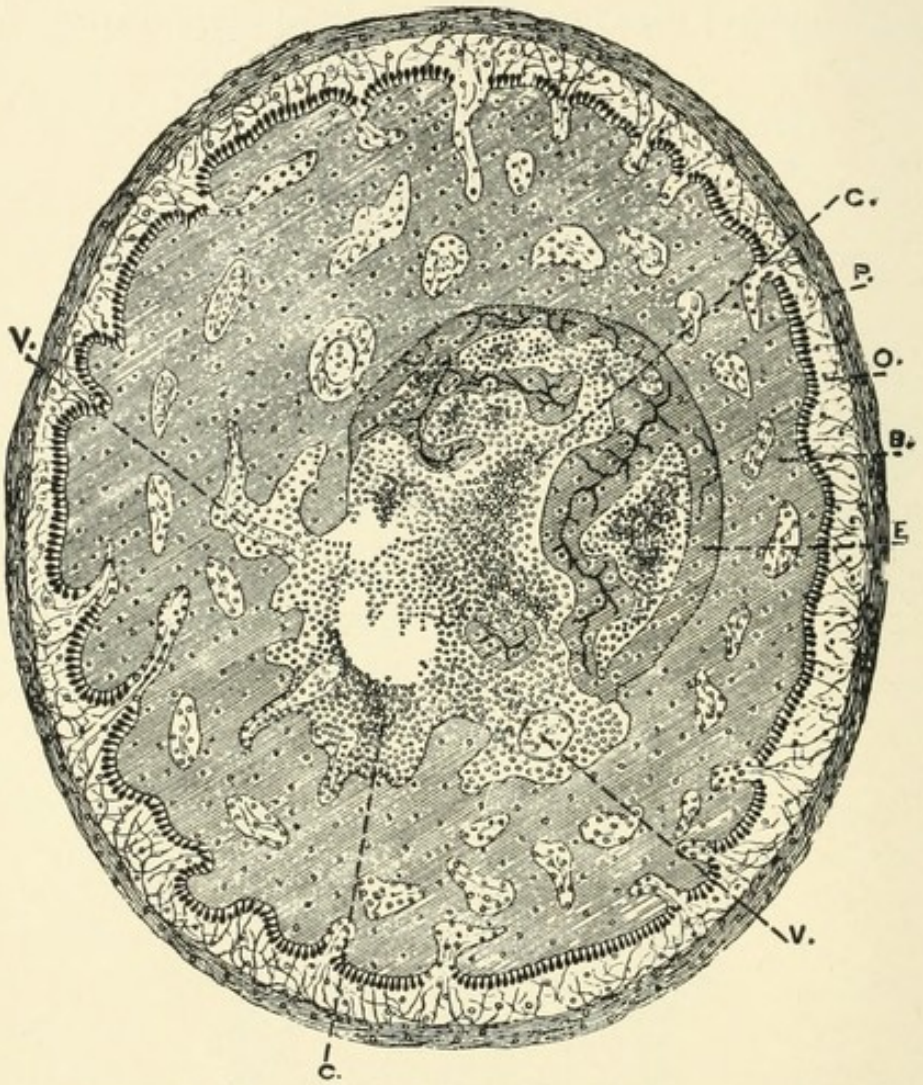


FIG. 58.—Transverse Section through the Tibia of a Fetal Kitten, semidiagrammatic. × 60. P, Periosteum. O, Osteogenetic layer of the periosteum, showing the osteoblasts arranged side by side, represented as pear-shaped black dots on the surface of the newly formed bone. B, The periosteal bone deposited in successive layers beneath the periosteum and ensheathing E, the spongy endochondral bone; represented as more deeply shaded. Within the trabeculæ of endochondral spongy bone are seen the remains of the calcified cartilage trabeculæ represented as dark wavy lines. C, The medulla, with V, V, veins. In the lower half of the figure the endochondral spongy bone has been completely absorbed. (Klein and Noble Smith.)

and ensheath them. The encased trabeculæ are gradually absorbed by the *osteoclasts* of Kölliker.

These stages are precisely similar to what goes on in the growing shaft of a bone which is increasing in length by the advance of the process of ossification into the intermediary cartilage between the diaphysis and epiphysis. In this case the cartilage cells become flattened and, multiplying by division,

are grouped into regular columns at right angles to the plane of calcification while the process of calcification extends into the hyaline matrix between them.

The embryonic spongy bone, formed as above described, is simply a temporary tissue occupying the place of the fetal rod of cartilage; the preceding stages show the successive changes *at the center* of the shaft. Periosteal bone is at the same time deposited in successive layers beneath the periosteum *at the circumference* of the shaft, exactly as described in the section on ossification in membrane, and thus a casing of periosteal bone is formed around the embryonic endochondral spongy bone. The embryonic spongy

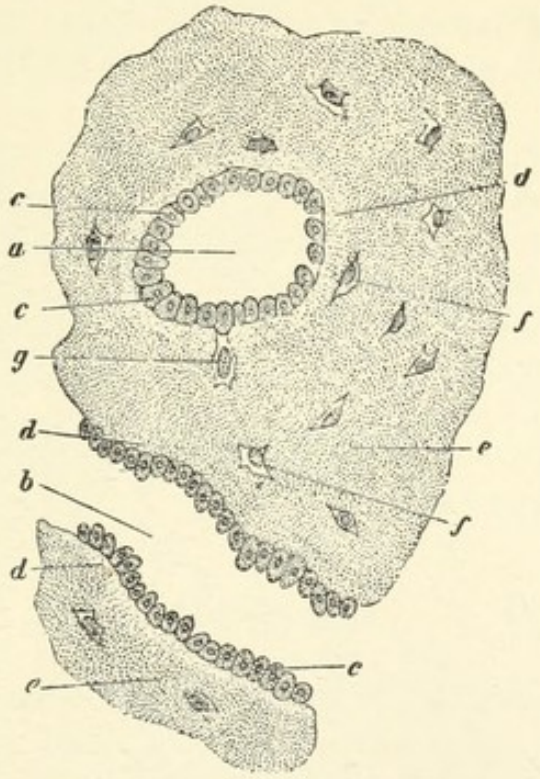


FIG. 59.—Transverse Section of Femur of a Human Embryo about Eleven Weeks Old. *a*, Rudimentary Haversian canal in cross-section; *b*, in longitudinal section; *c*, osteoblasts; *d*, newly formed osseous substance of a lighter color; *e*, that of greater age; *f*, lacunæ with their cells; *g*, a cell still united to an osteoblast. (Frey.)

bone is absorbed, through the agency of the *osteoclasts*, until the trabeculæ are replaced by one great cavity, the medullary cavity of the shaft.

Stage of Formation of Compact Bone. The transformation of spongy periosteal bone into compact bone is effected in a manner exactly similar to that which has been described in connection with ossification in membrane, page 46. The irregularities in the walls of the spongy periosteal bone are absorbed by the osteoclasts, while the osteoblasts which line them are developed in concentric layers, each layer in turn becoming ossified till the comparatively large space in the center is reduced to a well-formed Haversian canal, figure 59. When once formed, bony tissue grows to some

extent *interstitially*, as is evidenced by the fact that the lacunæ are rather further apart in full-formed than in young bone.

It will be seen that the common terms *ossification in cartilage* and *ossification in membrane* are apt to mislead, since they seem to imply two processes radically distinct. The process of ossification, however, is in all cases one and the same, all true bony tissue being formed from membrane, perichondrium or periosteum; but in the development of such a bone as the femur, lime salts are first of all deposited in the cartilage; this calcified cartilage, however, is gradually and entirely reabsorbed, replaced by bone formed from the periosteum. Thus calcification of the cartilaginous matrix precedes the real formation of bone. We must, therefore, clearly distinguish between *calcification* and *ossification*. The former is simply the infiltration of an animal tissue with lime salts, while ossification is the formation of true bone.

Growth of Bone. Bones increase *in length* by the advance of the process of ossification into the cartilage intermediate between the diaphysis and epiphysis. The increase in length indeed is due entirely to growth at the two ends of the *shaft*. Increase in *thickness* in the shaft of a long bone occurs by the deposition of successive layers beneath the periosteum. If a thin metal plate be inserted beneath the periosteum of a growing bone it will soon be covered by osseous deposit, but if it be put between the fibrous and osteogenetic layers it will never become enveloped in bone, for all the bone is formed beneath the latter.

THE TEETH.

During the course of his life, man, in common with most other mammals, is provided with two sets of teeth; the first set, called the *temporary* or *milk-teeth* of infancy, are shed and replaced by the second or *permanent* set.

Temporary Teeth.

MIDDLE LINE OF JAW.

Molars.	Canine.	Incisors.	Incisors.	Canine.	Molars.	
2	1	2	2	1	2	= 10
2	1	2	2	1	2	= 10

= 20

The figures indicate in months the age at which each tooth appears:

LOWER CENTRAL INCISORS.	UPPER INCISORS.	FIRST MOLAR AND LOWER LATERAL INCISORS.	CANINES.	SECOND MOLARS.
6 to 9	8 to 12	12 to 15	18 to 24	24 to 30

Permanent Teeth.

MIDDLE LINE OF JAW.

True Molars.	Bicuspids or Premolars.	Canine.	Incisors.	Incisors.	Canine.	Bicuspids or Premolars.	True Molars.
3	2	1	2	2	1	2	3
3	2	1	2	2	1	2	3

The age at which each permanent tooth is cut is indicated in this table in years:

FIRST MOLARS.	INCISORS.		BICUSPIDS OR PRE-MOLARS.		CANINES.	SECOND MOLARS.	THIRD MOLARS OR WISDOMS.
	Centrals.	Laterals.	First.	Second.			
6	7	8	9	10	12 to 14	12 to 15	17 to 25

Structure. A tooth is generally described as possessing a *crown*, *neck*, and *root* or *roots*. The *crown* is the portion which projects beyond the level of the gum. The *neck* is that constricted portion just below the crown which is embraced by the free edges of the gum, and the *root* includes all below this.

On making longitudinal and transverse sections through its center, figure 61, A, B, a tooth is found to be principally composed of a hard superficial

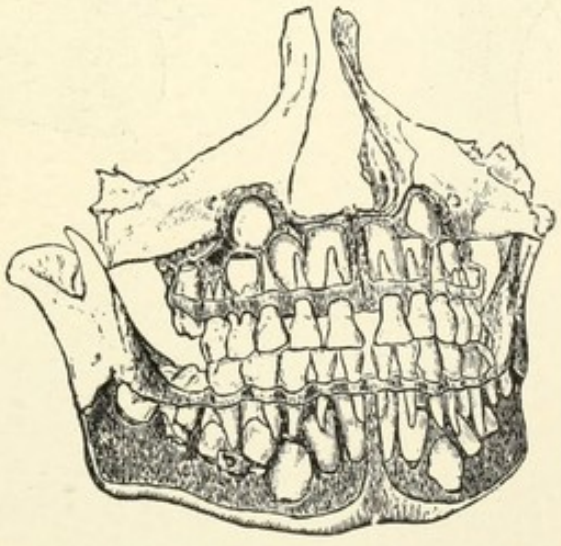


FIG. 60.—Normal Well-formed Jaws, from which the Alveolar Plate has been in great part Removed, so as to expose the Developing Permanent Teeth in their Crypts in the Jaws. (Tomes.)

material, *dentine* or ivory, which is hollowed out into a central cavity which resembles in general shape the outline of the tooth, and is called the *pulp*-cavity.

The *tooth pulp* is composed of fibrous connective tissue, blood-vessels, nerves, and large numbers of cells of varying shapes, and on the surface in

close connection with the dentine a specialized layer of cells called *odontoblasts*, which are elongated columnar cells with a large nucleus at the tapering ends farthest from the *dentine*. The cells are all embedded in a mucoid gelatinous matrix.

The blood-vessels and nerves enter the pulp through a small opening at the apical extremity of each root.

A layer of very hard calcareous matter, the *enamel*, caps the dentine of the crown; beneath the level of the gum is a layer of true bone, called the *cement* or *crusta petrosa*. The enamel and cement are very thin at the neck of the tooth where they come in contact, the cement overlapping the enamel. The enamel becomes thicker toward the crown, and the cement toward the lower end or apex of the root.

Dentine or Ivory.—Dentine closely resembles bone in chemical composition. It contains, however, rather less animal matter.

Structure. Dentine is finely channelled by a multitude of delicate tubes, which by their inner ends communicate with the pulp-cavity, and by their

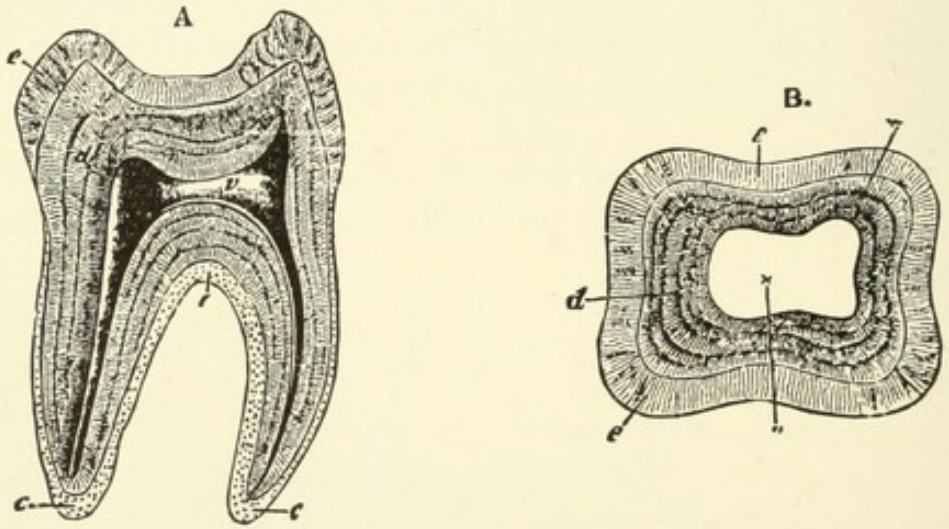


FIG. 61.—A.—A Longitudinal Section of a Human Molar Tooth. *c*, Cement; *d*, dentine; *e*, enamel; *v*, pulp cavity (Owen). B.— Transverse section. The letters indicate the same as in *A*.

outer extremities come into contact with the under part of the enamel and cement, and sometimes even penetrate them for a greater or less distance, figures 63, 64. The matrix in which these tubes lie is composed of "a reticulum of fine fibers of connective tissue modified by calcification, and, where that process is complete, entirely hidden by the densely deposited lime salts" (Mummery).

The tubules of the dentine contain fine prolongations from the tooth-pulp, which give the dentine a certain faint sensitiveness under ordinary circumstances and, without doubt, have to do also with its nutrition. They are probably processes of the dentine-cells or *odontoblasts* lining the pulp-cavity. The relation of these processes to the tubules in which they lie is

precisely similar to that of the processes of the bone-corpuscles to the canaliculi of bone. The outer portion of the dentine, underlying the cement and the enamel, figure 63, *b*, *c*, contains cells like bone-corpuscles.

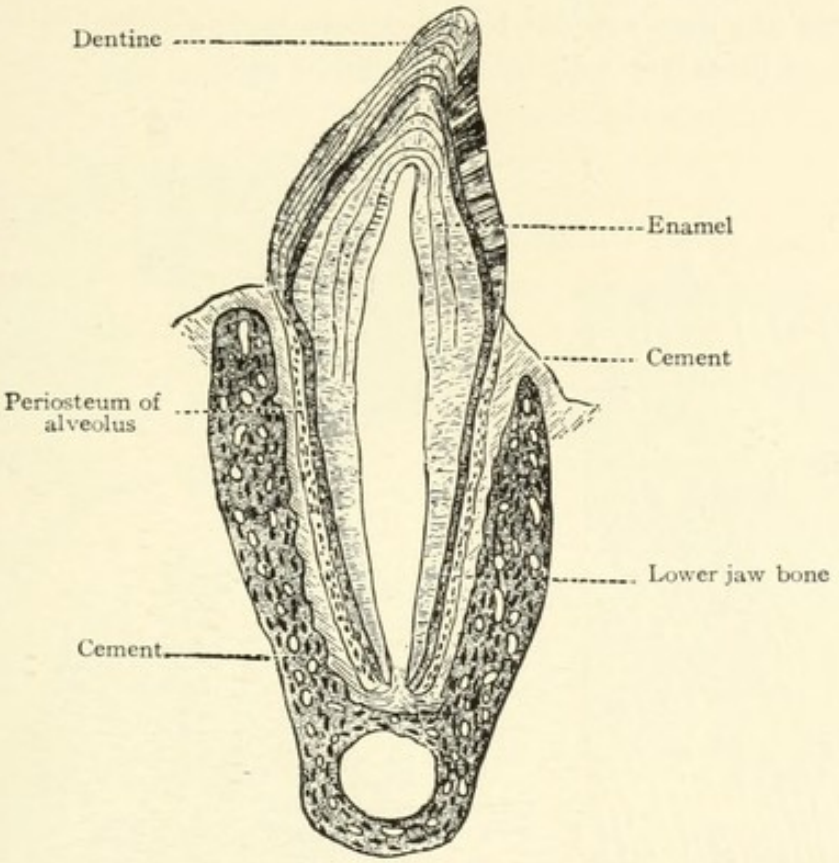


FIG. 62.—Premolar Tooth and Surrounding Bone of Cat.

Enamel. The *enamel*, which is by far the hardest portion of a tooth, is composed chemically of the same elements that enter into the composition of dentine and bone, but the animal matter amounts only to

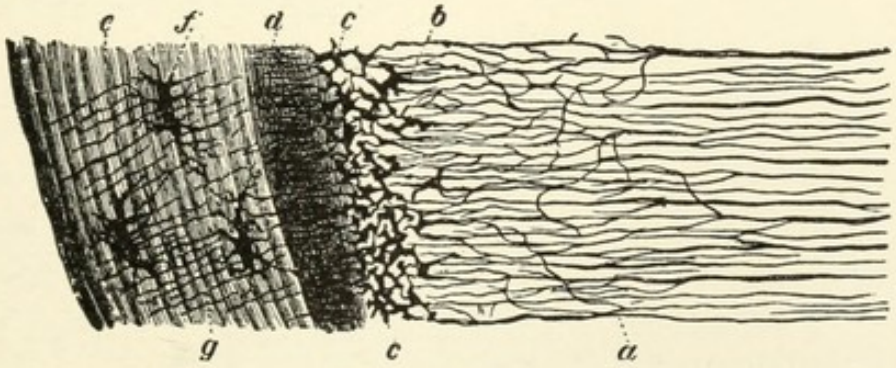


FIG. 63.—Section of a Portion of the Dentine and Cement from the Middle of the Root of an Incisor Tooth. *a*, Dental tubuli ramifying and terminating, some of them in the interglobular spaces *b* and *c*, which somewhat resemble bone lacunæ; *d*, inner layer of the cement with numerous closely set canaliculi; *e*, outer layer of cement; *f*, lacunæ; *g*, canaliculi. × 350. (Kölliker.)

about 2 or 3 per cent. It contains a larger proportion of inorganic matter and is harder than any other tissue in the body.

Structure. Enamel is composed of fine hexagonal fibers, figures 64, 65. These are set on end vertical to the surface of the dentine, and fit into corresponding depressions in the same.

Like the dentine tubules, they are disposed in wavy and parallel curves. The fibers are thus marked by transverse lines. They are mostly solid, but some of them may contain a very minute canal.

FIG. 64.

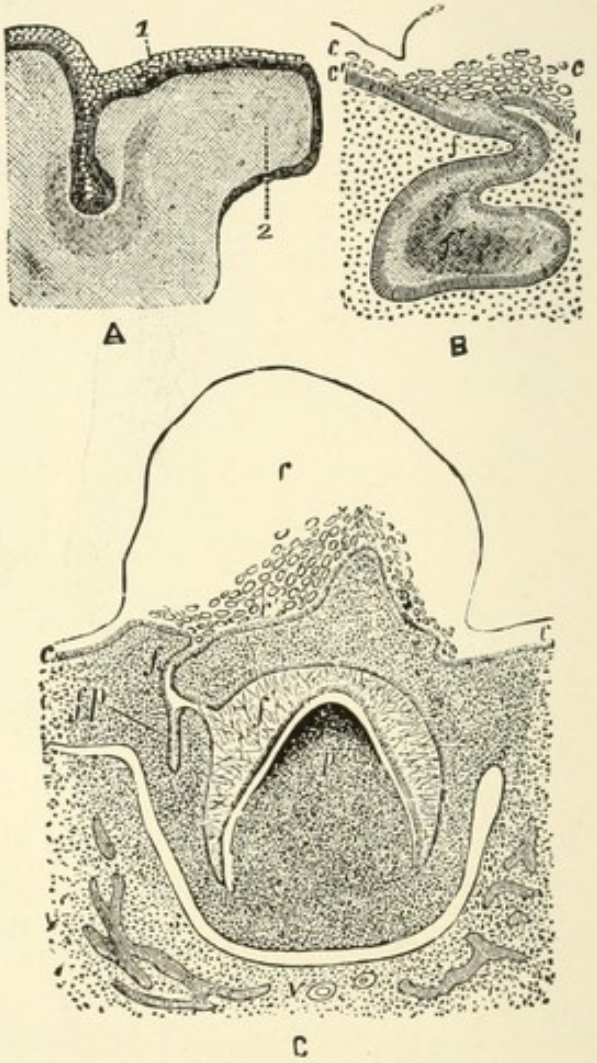


FIG. 65.

FIG. 64.—Thin Section of the Enamel and a Part of the Dentine. *a*, Cuticular pellicle of the enamel (Nasmyth's membrane); *b*, enamel fibers, or columns with fissures between them and cross striæ; *c*, larger cavities in the enamel, communicating with the extremities of some of the dentinal tubuli (*d*). × 350. (Kölliker.)

FIG. 65.—Section of the Upper Jaw of a Fetal Sheep. A.—1, Common enamel germ dipping down into the mucous membrane; 2, palatine process of jaw; 3, rete Malpighi. (Waldeyer.) B.—Section similar to A, but passing through one of the special enamel germs here becoming flask-shaped; *c*, *c'*, epithelium of mouth; *f*, neck; *f'*, body of special enamel germ. (Rose.) C.—A later stage; *c*, outline of epithelium of gum; *f*, neck of enamel germ; *f'*, enamel organ; *p*, papilla; *s*, dental sac forming; *fp*, the enamel germ of permanent tooth; *m*, bone of jaw; *v*, vessels cut across. (Kölliker.) Copied from Quain's "Anatomy."

The enamel prisms are connected together by a trace of hyaline cement-substance.

Development. The first step in the development of the teeth consists in a downward growth, figure 65, A, 1, from the deeper layer of stratified

epithelium of the mouth, which first becomes thickened in the neighborhood of the maxillæ or jaws, now also in the course of formation. This epidermal papilla grows downward into a recess of the imperfectly developed tissue of the embryonic jaw. It forms the *primary enamel organ* or *enamel germ*, and its position is indicated by a slight groove in the mucous membrane of the jaw. The next step consists in the elongation and the inclination outward of the deeper part, figure 65, B, *f'*, of the enamel germ, followed by an increased development at certain points corresponding to the situations of the future milk-teeth. The enamel germ becomes divided at its deeper portion, or extended by further growth, into a number of special enamel germs corresponding to each of the milk-teeth, and connected to the common germ by a narrow neck. Each tooth is thus placed in its own special recess in the embryonic jaw, figure 65, C, *f'*.

As these changes proceed, there grows up from the underlying tissue into each enamel germ, figure 65, C, *p*, a distinct vascular *papilla*, dental

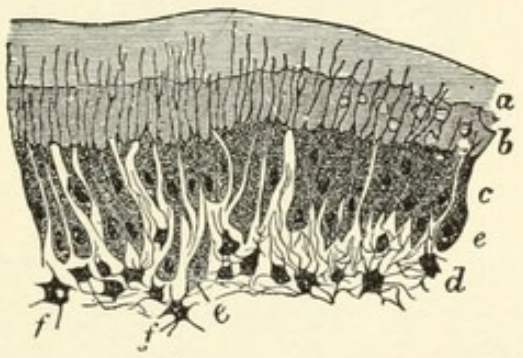


FIG. 66.—Part of Section of Developing Tooth of a Young Rat, showing the Mode of Deposition of the Dentine. Highly magnified. *a*, Outer layer of fully formed dentine; *b*, uncalcified matrix with one or two nodules of calcareous matter near the calcified parts; *c*, odontoblasts sending processes into the dentine; *d*, pulp; *e*, fusiform or wedge-shape cells found between odontoblasts; *f*, stellate cells of pulp in fibrous connective tissue. The section is stained in carmine, which colors the uncalcified matrix but not the calcified part. (E. A. Schäfer.)

papilla, and upon it the *enamel germ* becomes molded, and presents the appearance of a cap of two layers of epithelium separated by an interval, figure 65, C, *f'*. While part of the sub-epithelial tissue is elevated to form the dental papillæ, the part which bounds the embryonic teeth forms the dental sacs, figure 65, C, *s;* and the rudiment of the jaw sends up processes forming partitions between the teeth. The papilla, which is really part of the dental sac, is composed of nucleated cells arranged in a meshwork, in the outer layer of which are the columnar cells called *odontoblasts*. The *odontoblasts* form the dentine, while the remainder of the papilla forms the pulp. The method of the formation of the dentine from the odontoblasts is said to be as follows: The cells form elongated processes at their outer surfaces which are directly converted into the tubules of dentine, figure 66, *c*, and into the contained fibrils.

Each papilla early takes the shape of the crown of the tooth to which it corresponds, but as the dentine increases in thickness the papilla diminishes until when the tooth is cut only a small amount remains as the pulp. It is supplied by vessels and nerves which enter at the end of the root. The roots are not completely formed at the time of the eruption of the teeth.

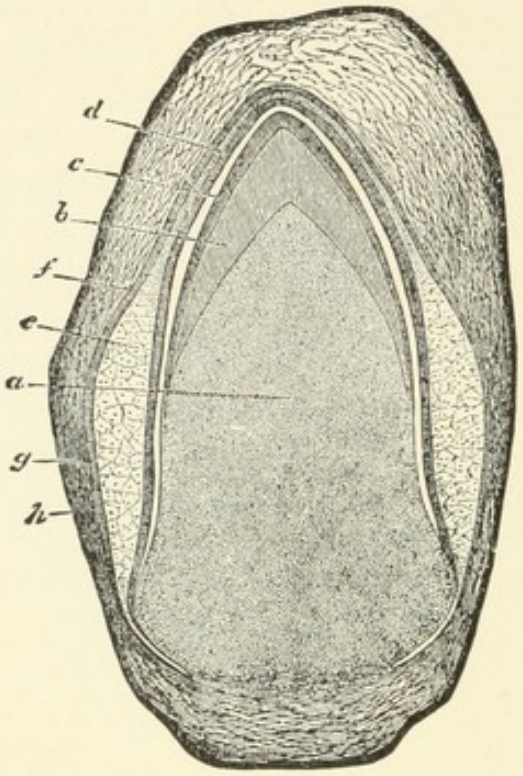


FIG. 67.—Vertical Transverse Section of the Dental Sac, Pulp, etc., of a Kitten. *a*, Dental papilla or pulp; *b*, the cap of dentine formed upon the summit; *c*, its covering of enamel; *d*, inner layer of epithelium of the enamel organ; *e*, gelatinous tissue; *f*, outer epithelial layer of the enamel organ; *g*, inner layer, and *h*, outer layer of dental sac. × 14. (Thiersch.)

The *enamel cap* is formed by the enamel cells, by the deposit of a keratin-like substance, which subsequently undergoes calcification. Other layers are formed in the same manner meanwhile.

The *temporary* or *milk-teeth* are speedily replaced by the growth of the permanent teeth.

The development of the temporary teeth commences about the sixth week of intra-uterine life, after the laying down of the bony structure of the jaws. Their permanent successors begin to form about the sixteenth week of intra-uterine life.

III. MUSCULAR TISSUE.

There are two chief kinds of muscular tissue, differing both in minute structure as well as in mode of action, viz., (1) the *smooth* or *non-striated*, and (2) the *striated*.

SMOOTH OR NON-STRIATED MUSCLE.

Non-striated muscle forms the proper muscular coats of the digestive canal from the middle of the esophagus to the internal sphincter ani; of the ureters and urinary bladder; of the trachea and bronchi; of the ducts of glands; of the gall-bladder; of the vesiculæ seminales; of the uterus and Fallopian tubes; of the blood-vessels and lymphatics; and of the iris and some other parts of the eye. This form of tissue also enters largely into the

FIG. 68.—Isolated Smooth Muscle Cells from Human Small Intestine. × 400. Rod-shaped nucleus surrounded by area of finely granular protoplasm; longitudinal striations of cytoplasm.

composition of the *tunica dartos* of the scrotum. Unstriped muscular tissue occurs largely also in the true skin generally, being especially abundant in the interspaces between the bases of the papillæ, and, when it contracts, the papillæ are made unusually prominent, giving rise to the peculiar roughness of the skin termed *cutis anserina*, or goose flesh. It also occurs in all parts

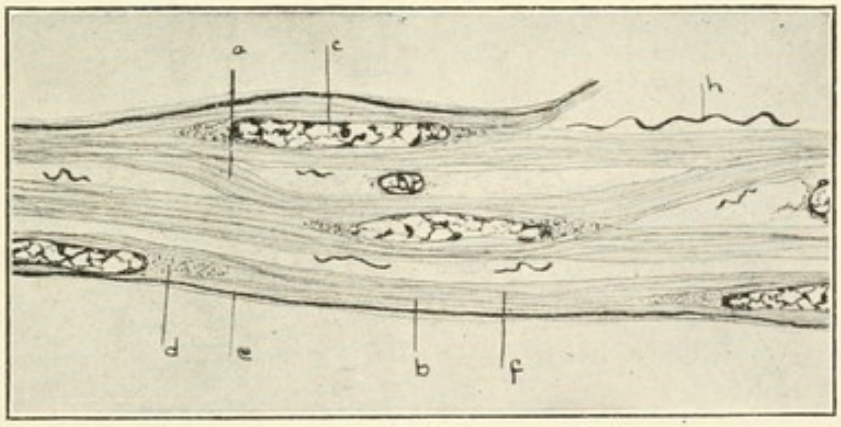


FIG. 69.—Smooth Muscle from Intestine of Pig, Showing Syncytial Structure. *a*, Protoplasmic process connecting two muscle fibers; *b*, end-to-end union of two muscle fibers, showing the continuity of protoplasm and myofibrils; *c*, nucleus of muscle fiber; *d*, granular protoplasm at the end of muscle nucleus; *e*, coarse myofibril; *f*, Fine myofibril; *g*, connective-tissue cell with connective-tissue fibrils surrounding it; *h*, elastic fiber. (New figure by Caroline McGill.)

where hairs occur, in the form of flattened roundish bundles which lie alongside the hair-follicles and sebaceous glands.

Structure. Unstriated muscle fibers are elongated, spindle-shaped, mononucleated cells, 7 to 8 μ in diameter by 40 to 200 μ in length, figures 68 and 69. The protoplasm of each cell, the contractile substance, is marked by longitudinal striations representing fibrils which have been described as contractile. The nucleus is an oblong mass placed near the

center of the cell. It is covered by a nuclear membrane which encloses a network of anastomosing fibrils.

Development. In the pig the smooth muscle of the alimentary canal originates in the syncytium of the mesodermal cells which surround the entoderm. The cells soon begin to grow into the adult spindle-shape form and the fibrils make their appearance. Even in the adult muscle the syncytial connections are retained according to Miss McGill.

Striated Muscle.

Striated or striped muscle constitutes the whole of the muscular apparatus of the skeleton, of the walls of the abdomen, the limbs, etc.—the whole

FIG. 70.—Transverse Section through Muscular Fibers of Human Tongue. The deeply stained nuclei are situated at the inside of the sarcolemma. Each muscle fiber shows "Cohnheim's fields," that is, the sarcous elements in transverse section separated by clear (apparently linear) interstitial substance. × 450. (Klein and Noble Smith.)

FIG. 71.

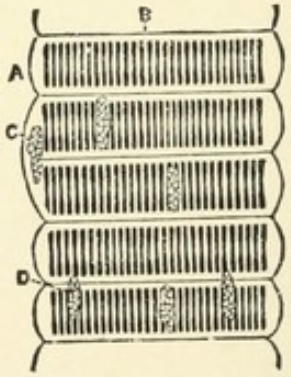


FIG. 72.

FIG. 71.—Muscle Fiber Torn Across; the sarcolemma still connects the two parts of the fiber. (Todd and Bowman.)

FIG. 72.—Part of a Striped Muscle Fiber of a Water Beetle prepared with Absolute Alcohol. *A*, Sarcolemma; *B*, Krause's membrane. The sarcolemma shows regular bulgings. Above and below Krause's membrane are seen the transparent "lateral discs." The chief mass of a muscular compartment is occupied by the contractile disc composed of sarcous elements. The substance of the individual sarcous elements has collected more at the extremity than in the center; hence this latter is more transparent. The optical effect is that the contractile disc appears to possess a "median disc" (Disc of Hensen). Several nuclei, *C* and *D*, are shown, and in them a minute network. × 300. (Klein and Noble Smith.)

of those muscles which are under the control of the will and hence termed *voluntary;* also the muscle of the heart.

For the sake of description, striated muscular tissue may be divided into two classes, (a) *skeletal*, which comprises the whole of the striated muscles of the body except (b) the *heart*.

Skeletal Muscle. The muscle fibers of the skeletal muscles are usually grouped in small parallel bundles, *fasciculi*. The fasciculi extend through the muscle, converging to their tendinous insertions. Connective-tissue sheaths, *endomysium*, surround the fasciculi and support the blood-vessels, while a stronger sheath, the *perimysium*, encases the entire muscle.

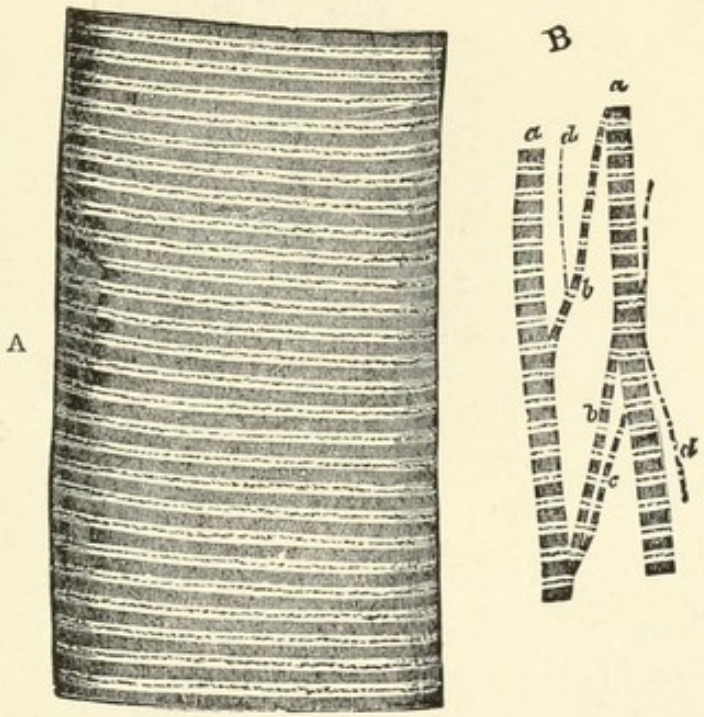


FIG. 73.—*A*, Portion of a Medium-sized Human Muscle Fiber. *B*, Separated bundles of fibril equally magnified; *a*, *a*, larger, and *b*, *b*, smaller collections; *c*, still smaller; *d*, *d*, the smallest which could be detached, possibly representing a single series of sarcous element. × 800. (Sharpey.)

The unit of muscular structure is the fiber. Each muscle fiber is a long cylinder with fusiform ends. The fibers vary in diameter from 10 to 100 μ, while the length may reach as much as 40 mm. Each fiber is enclosed in a distinct sheath, the *sarcolemma*. The *sarcolemma* is a transparent structureless sheath of great resistance which surrounds each fiber, figure 71.

The substance of the fiber enclosed by the sarcolemma, the contractile substance, contains a number of oval nuclei distributed along the length of the fiber and lying just under or through the sarcolemma. Each nucleus is accompanied by a small mass of granular protoplasm at its poles. The main mass of the fiber is characterized by transverse light and dark bands, figure 73, from which the name *striated muscle* arises.

Longitudinal striation is also apparent under certain modes of treatment, figure 81. The muscle fibers can be split longitudinally into fibrils, called *sarcostyles*, figures 73 and 74, each of which exhibits the characteristic

striation of the whole fiber. Under certain treatment the sarcostyles break transversely into smaller discs by cleavage at the line of Krause's membrane.

The sarcostyle is, therefore, composed of a number of smaller elements joined end to end. These are the *sarcous elements* of Bowman. The sar-

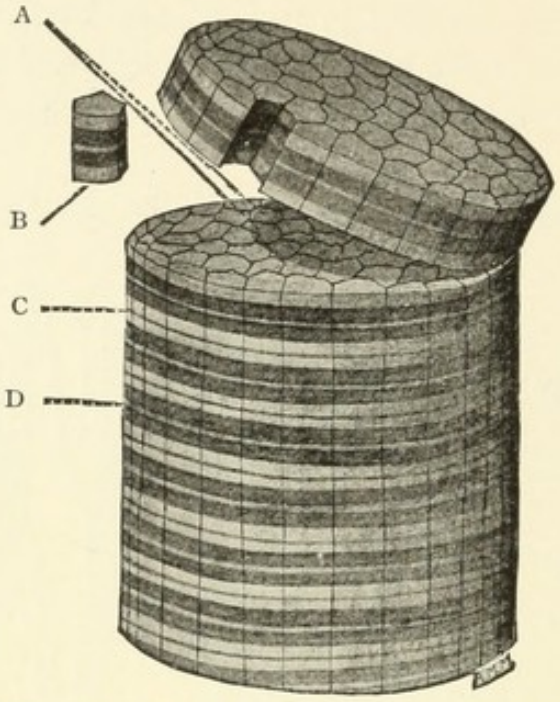


FIG. 74.—Diagram of Segment of Muscle Fiber, showing Sarcostyle *A*, Sarcous element *B*, Krause's line *C*, Hensen's line *D*.

cous element has a highly refractive denser middle piece surrounded by a less refractive more fluid material. The polarizing microscope reveals the fact that the middle piece which corresponds in position to the dark trans-

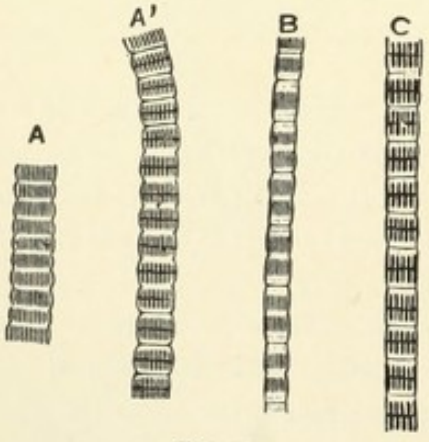


FIG. 75.

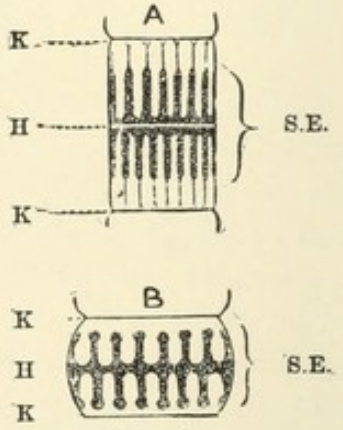


FIG. 76.

FIG. 75.—Sarcostyles from the Wing-Muscles of a Wasp. *A*, *A'*, Sarcostyles showing degrees of retraction, *B*, a sarcostyle extended with the sarcous elements separated into two parts, *C*, sarcostyles moderately extended (semidiagrammatic). (E. A. Schäfer.)

FIG. 76.—Diagram of a Sarcomere in a Moderately Extended Condition, *B*. *K*, *K*, Krause's membranes; *H*, plane of Henson; *S*, *E*, poriferous sarcous element. (E. A. Schäfer.)

verse band is doubly refractive, isotropic, while the surrounding material, the light band, is singly refractive, anisotropic.

In transverse section, figure 70, the area of the muscle substance is mapped out into small polygonal areas by a network of clear lines called *Cohnheim's areas*. The lines represent the substance between the sarcostyles. This substance probably represents the less differentiated contractile substance, called *sarcoplasm*. In figure 81 the interfibrillar sarcoplasm is indicated by the longitudinal and transverse lines.

Heart Muscle. The muscle substance of the heart is composed of mononucleated masses of protoplasm, cardiac muscle cells, in which the substance of the cell presents the transversely striated appearance characteristic of the voluntary muscle just described. But the heart muscle is physiologically much more like an involuntary muscle. The cells are rather small, two to four times as long as thick, and the nucleus is usually situated near the middle of

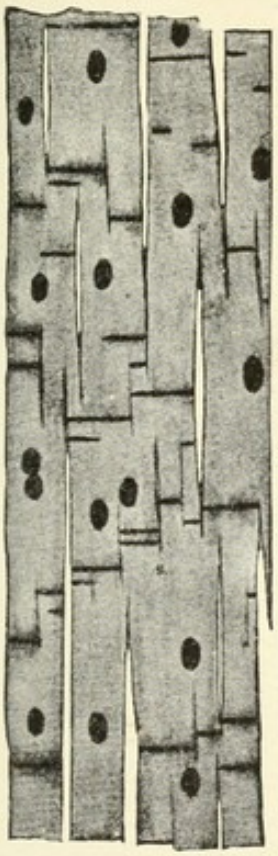


Fig. 77.

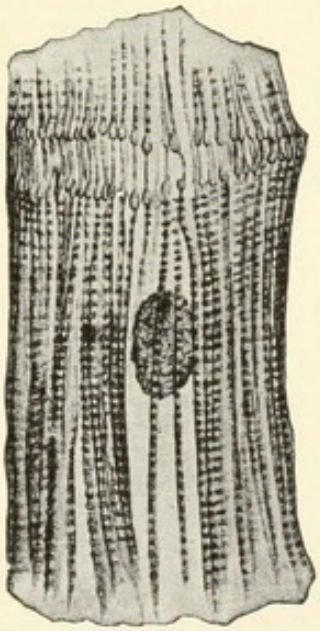


Fig. 78.

Fig. 77.—A Section of Cardiac Muscle, Diagrammatic. (From E. A. Schäfer, after Heidenhain.)

Fig. 78.—Intercellular Continuity of Muscle Fibrils in Cardiac Muscle. (From E. A. Schäfer after Przewosky.)

the cell, figure 79. There is no sarcolemma; on the other hand, the cells present branched and irregular outlines, but adjacent cells interlock in close-fitting contact.

Certain observers have described fibrils as extending across the so-called cell boundary and noted that not all such boundaries enclose nuclei. These observations suggest that cardiac muscle belongs to the group of tissues possessing a syncytium. However, the section of cardiac tissue may very possibly cut many cells without enclosing a nucleus. The continuity of

fibrils is an important observation from the physiological point of view; see Circulation Chapter.

In certain parts of the heart, the cardiac tissue is not completely differentiated and retains in the adult somewhat embryonic characters; for ex-

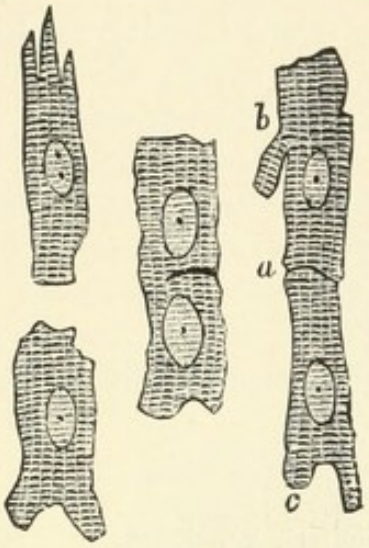


Fig. 79.

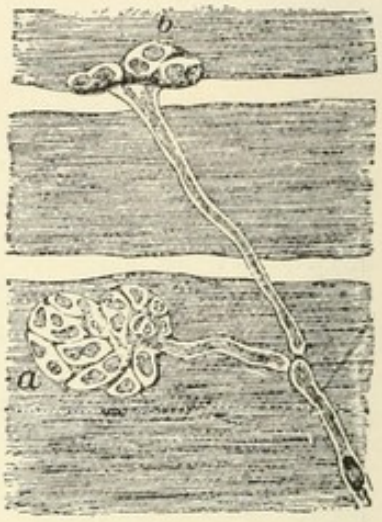


Fig. 80.

Fig. 79.—Muscular Fiber Cells from the Heart. (E. A. Schäfer.)

Fig. 80.—From a Preparation of the Nerve Termination in the Muscular Fibers of a Snake. *a*, End plate seen only broad-surfaced: *b*, end plate seen as narrow surface. (Lingard and Klein.)

ample, the bundle of His running in the septum from the auricles to the ventricles and the cells containing Purkinje's fibers lying immediately under the endocardium.

Blood and Nerve Supply. The muscles are freely supplied with blood-vessels; the capillaries form a network with oblong meshes around the fibers. Nerves also are supplied freely to muscles; the striated voluntary muscles receiving them from the cerebro-spinal nerves, and the cardiac muscle from both the cerebro-spinal and the sympathetic nerves.

In *striped* muscle the nerves end in *motor end-plates*. The nerve fibers are medullated; and when a branch passes to a muscle fiber, its primitive sheath becomes continuous with the sarcolemma, and the axis-cylinder forms a network of its fibrils on the surface of the muscle fiber. This network lies embedded in a flattened granular mass containing nuclei of several kinds; this is the *motor end-plate*, figures 80 and 81. There is considerable variation in the exact form of the nerve end-plate in the muscle. In batrachia the nerve fiber ends in a brush of branching nerve fibrils which are accompanied here and there by attached oval nuclei.

Development. The striated muscle of the voluntary variety is usually developed from the mesoderm. The embryonic cells increase enormously in size, the nuclei multiply by fission and distribute themselves beneath the sarcolemma. There is a differentiation of the cell protoplasm

which takes place by the formation of sarcostyles. This begins nearest the surface of the cells and proceeds toward the center of the mass.

The sarcolemma is apparently produced from embryonic connective tissue.

The *cardiac* muscle cells are at first spindle-shaped embryonic cells which elongate more and more. In further differentiation their protoplasm

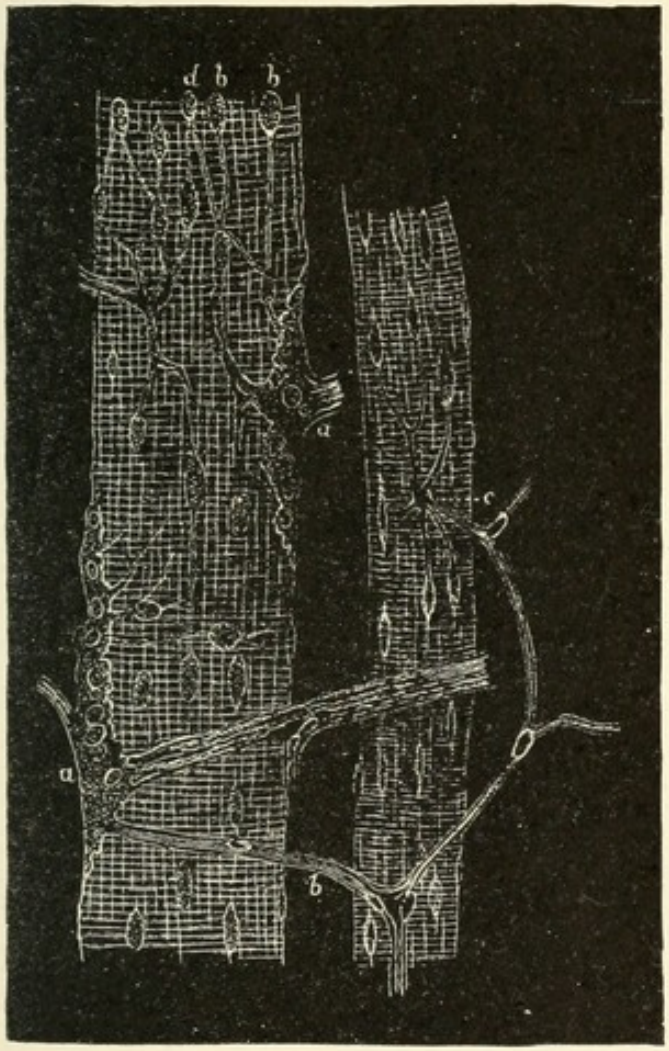


Fig. 81.

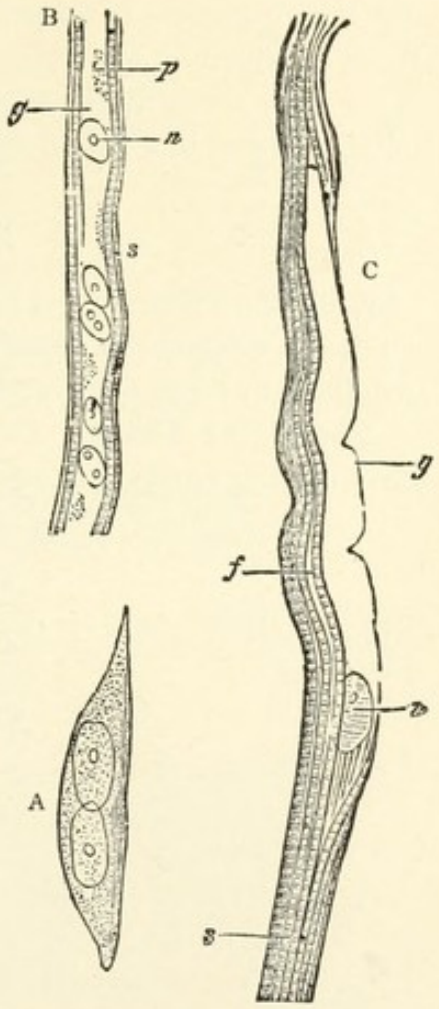


Fig. 82.

Fig. 81.—Two Striped Muscle Fibers of the Hyoglossus of Frog. *a*, Nerve end-plate; *b*, nerve fibers leaving the end-plate; *c*, nerve-fibers terminating after dividing into branches; *d*, a nucleus in which two nerve-fibers anastomose. × 600. (Arndt.)

Fig. 82.—Developing Striated Muscular Fibers, Showing Different Stages of Development and Different Positions of the Unstriated Protoplasm. A.—Elongated cell with two nuclei; the longitudinal striation is beginning to show on the right side. From a fetal sheep. (Wilson Fox.) B.—Developing muscular fiber, showing both longitudinal and transverse striations at the periphery, and a central unstriated cylinder of protoplasm containing several nuclei. From a human fetus near the third month. (Ranvier.) *n*, Nucleus (there is usually a mass of glycogen near each nucleus); *p*, central unstriated protoplasm; *s*, peripheral striated substance. C.—Developing muscular fiber, showing a lateral position of the unstriated protoplasm. From a three-months' human fetus. (Ranvier.) *n*, Nucleus; *p*, unstriated protoplasm at one side of the fiber; *s*, striated sarcous substance with longitudinal and transverse striations.

exhibits faint striations which pervade the cell as it grows in the great increase in size. The rhythmic contractions begin long before the striations appear.

IV. NERVOUS TISSUE.

Nervous tissue has usually been described as being composed of two distinct substances, nerve-fibers and nerve-cells. The modern view of the nature of nerve tissue is, however, that the nerve-cell and the nerve fibers are to be considered together as one unit, called the *neurone*. The neurone is embedded in and supported by a substance called *neuroglia*. This neurone consists of a *cell body*, a number of branching processes termed *dendrites*, and a long process running out from it, the *neuraxone*, or *axone*, which becomes eventually a *nerve fiber*. The nerve-cell and the nerve fiber are parts of the same anatomical unit, and the nervous centers are made up of those units, arranged in different ways throughout the nervous system, figure 81, *A*.

NERVE FIBERS.

While the nerve fiber is really to be considered as a process of the nerve-cell, it is convenient to describe it separately. Nerve fibers are of two kinds, *medullated* or *white fibers*, and *non-medullated* or *gray fibers*.

Medullated Fibers. Each medullated nerve fiber is made up of the following parts: An external sheath, called the *primitive sheath*, *neuri-*

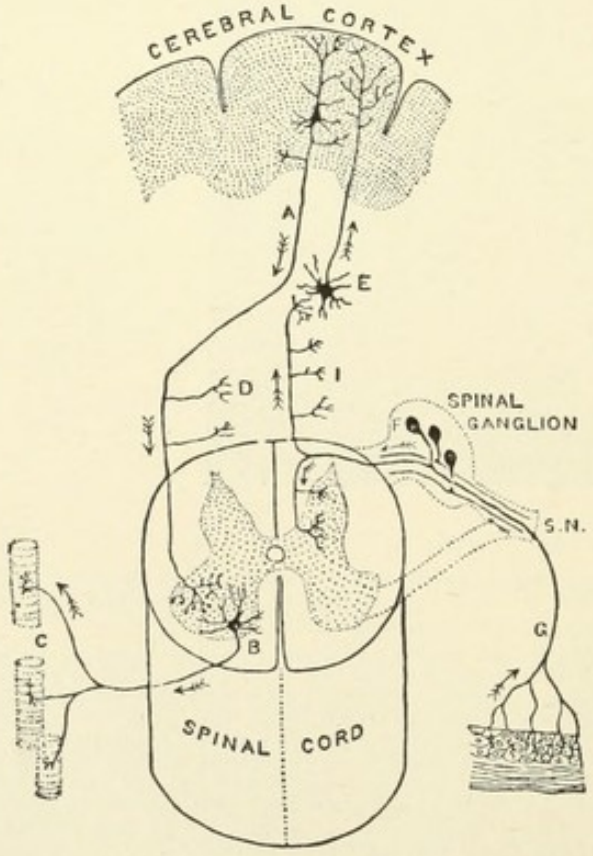


FIG. 83.—Diagram Showing the Arrangement of the Neurons or Nerve Units in the Architecture of the Nervous System. (Raymón y Cajàl.) *A*, Pyramidal neurone of cerebral cortex; *B*, anterior-horn motor cell of spinal cord; *D*, collateral branches of *A*; *E*, medullary neurone with ascending axone: *F*, spinal-ganglion neurones; *G*, sensory axones of *F*; *I*, collaterals of *F* in the cord.

lemma, or nucleated sheath of Schwann; an intermediate, known as the *medullary* or *myelin sheath*, or white substance of Schwann; and a central thread, the *axis-cylinder*, or axial fiber.

The Primitive Sheath. This is a pellucid membrane forming the outer investment of the nerve fiber. The sheath is constricted at intervals of a millimeter or less, the nodes of Ranvier. Each internodal segment bears a single nucleus surrounded by a variable amount of protoplasm. This membrane is described as having its origin in the mesoblastic cells, and the nuclei are the indications of the cellular nature of each nodal segment.

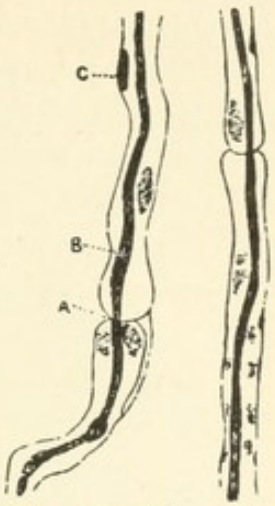


FIG. 84.—Two Nerve Fibers of the Sciatic Nerve. *A*, Node of Ranvier. *B*, axis-cylinder; *C*, sheath of Schwann, with nuclei. × 300. (Klein and Noble Smith.)

The Medullary or Myelin Sheath. This is the part to which the peculiar opaque white aspect of medullated nerves is due. The thickness of this layer of a nerve fiber varies considerably. It is a semifluid, fatty substance of high refractive power. It possesses a fine reticulum (Stilling, Klein), in

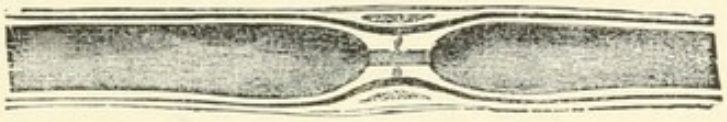


FIG. 85.—A Node of Ranvier in a Meduliated Nerve Fiber, viewed from above. The medullary sheath is interrupted, and the primitive sheath thickened. Copied from Axel Key and Retzius. × 750. (Klein and Noble Smith.)

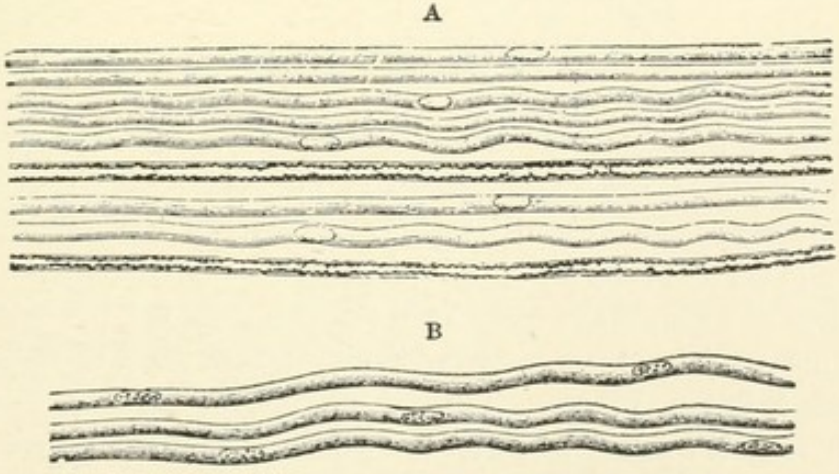


FIG. 86.—Gray, Pale, or Gelatinous Nerve Fibers. *A*, From a branch of the olfactory nerve of the sheep; two dark-bordered or white fibers from the fifth pair are associated with the pale olfactory fibers. *B*, from the sympathetic nerve. × 450. (Max Schultze.)

the meshes of which is embedded the fatty material. It stains well with osmic acid.

The Axis-Cylinder. The central thread of a medullated nerve fiber is the axis-cylinder. It is the prolongation of a nerve-cell and extends un-

interrupted for the full length of the fiber. It consists of a large number of primitive *fibrillæ*, as shown in the cornea, where the axis-cylinders of nerves break up into minute fibrils which form terminal networks. From various considerations, such as its invariable presence and unbroken continuity in all nerves, there can be little doubt that the axis-cylinder is the essential con-

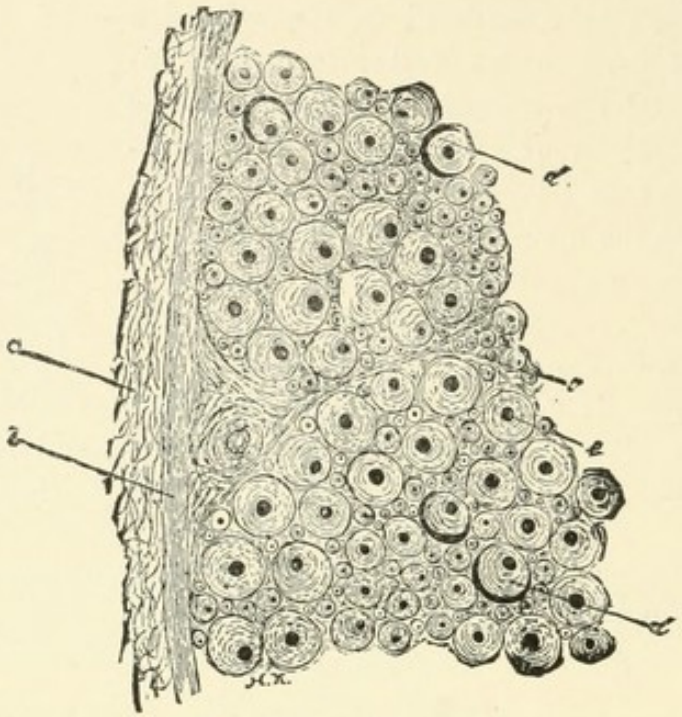


FIG. 87.—Transverse Section of a Portion of the Sciatic Nerve of the Rabbit, Hardened in Chromic Acid and Stained with Picro-carmine, to show medullated fibers in end view. × 275. *a*, Perifascicular connective tissue; *b*, lamellar sheath; *c*, axis-cylinder.

ducting part of the fiber, the other parts having the subsidiary function of support and possibly of insulation.

The size of the nerve fibers varies, figure 87. The largest fibers are found within the trunks and branches of the spinal nerves, in which the majority measure from 14 μ to 19 μ in diameter. In the so-called visceral or autonomic nerves of the brain and spinal cord medullated nerves are found, the diameter of which varies from 1.8 μ to 3.6 μ. In the hypoglossal nerve they are intermediate in size, and generally measure 7.2 μ to 10.8 μ.

Non-medullated Fibers. The fibers of the second kind, figure 86, which are also called *fibers of Remak*, constitute the principal part of the trunk and branches of the *sympathetic nerves*, the whole of the olfactory nerve, and are mingled in various proportions in the cerebro-spinal nerves. They differ from the preceding chiefly in not possessing the outer layer of medullary substance; their contents being composed exclusively of the axis-cylinder.

The non-medullated nerves are only about one-third to one-half as large as the medullated nerves, they do not exhibit the double contour, and they

are grayer than the medullated nerves. The non-medullated fibers frequently branch.

It is worthy of note that in the fetus, at an early period of development, all nerve fibers are non-medullated.

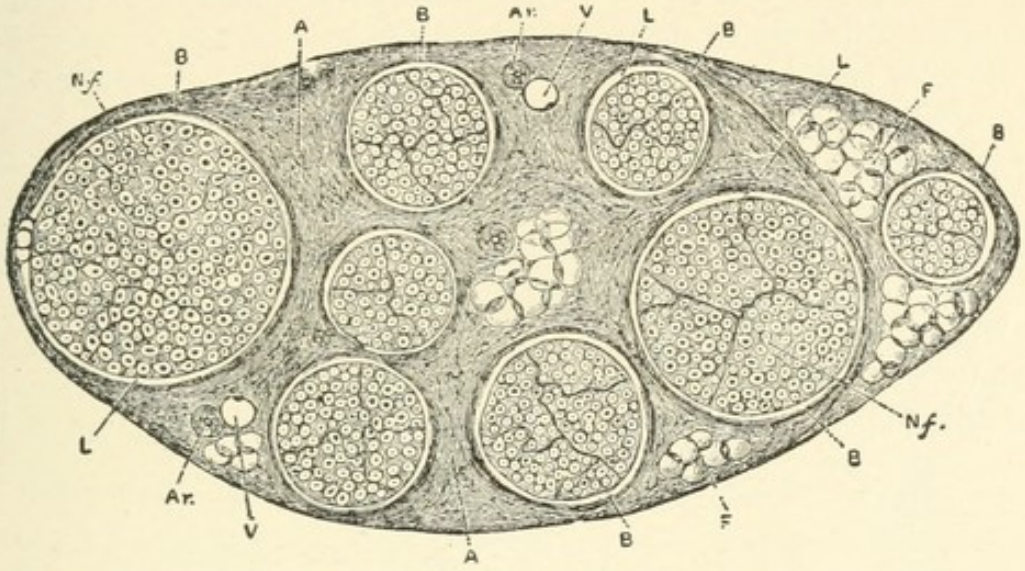


FIG. 88.—Transverse Section of the Sciatic Nerve of a Cat, about × 100. It consists of bundles (*Funiculi*) of nerve fibers ensheathed in a fibrous supporting capsule, *epineurium*, *A*; each bundle has a special sheath (not sufficiently marked out from the *epneurium* in the figure) or *perineurium*, *B*, the nerve fibers, *N. f.*; *L*, lymph spaces; *Ar*, artery; *V*, vein; *F*, fat. Somewhat diagrammatic. (V. D. Harris.)

Nerve Trunks. Each nerve trunk is composed of a variable number of different-sized bundles, *funiculi*, of nerve fibers which have a special

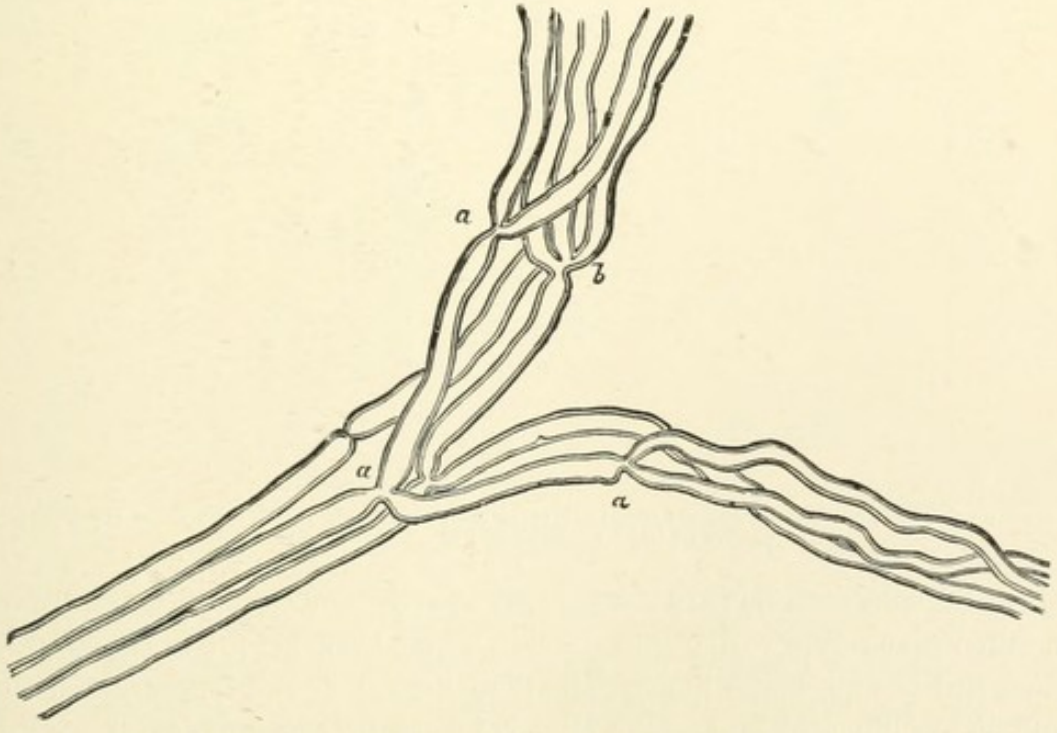


FIG. 89.—Small Branch of a Motor Nerve of the Frog, near its Termination, Showing Divisions of the Fibers. *a*, into two; *b*, into three. × 350. (Kölliker.)

sheath, *perineurium*. The funiculi are enclosed in a firm fibrous sheath, *epineurium;* this sheath also sends in processes of connective tissue which connect the bundles together. In the funiculi between the fibers is a delicate supporting tissue, the *endoneurium*. There are numerous lymph-spaces both beneath the connective tissue investing individual nerve fibers and also beneath that which surrounds the funiculi.

Bundles of fibers run together in the nerve trunk, but they merely lie in approximation to each other, they do not unite. Even when nerves anastomose, there is no union of fibers, but only an interchange of fibers between the anastomosing bundles. Although each nerve fiber is thus single through most of its course, yet, as it approaches the region in which it terminates, it may break up into several subdivisions before its final ending.

Nerve Collaterals. It has been discovered through the researches of Golgi, and confirmed by the further studies of Cajal and other anatomists, that each individual nerve fiber in the central nervous system gives off in its

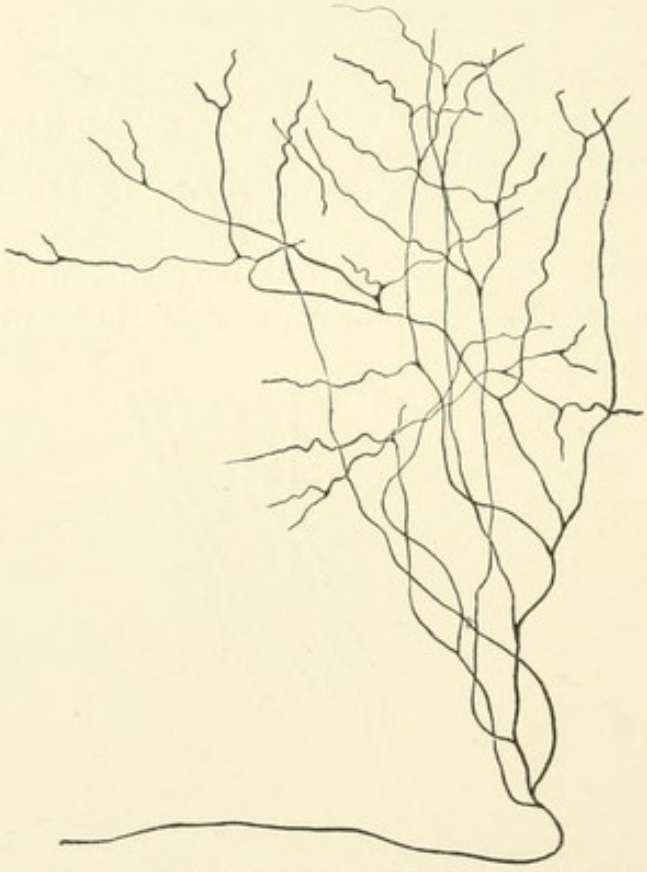


FIG. 90.—Terminal Ramifications of a Collateral Branch Belonging to a Fiber of the Posterior Column in the Lumbar Cord of an Embryo Calf.

course branches which pass out from it at right angles for a short distance, and then may run in various directions. These branches are called *collaterals*. They end in fine, brush-like terminations known as *end-brushes*, or in little bulbous swellings which come in close contact with some nerve cell, figure 90.

In the nerve-centers, that is, in the brain and spinal cord, the different

nerve fibers end just as the collaterals do, by splitting up into fine branches which form the *end-brushes*. Collaterals of the nerve fibers and end-brushes are chiefly found in the nervous centers. The nerve fibers of the peripheral nerves end in the muscles, glands, or special sensory organs, such as the eye and ear, each by its own special type of ending. Here, however, some analogy to the end-brush can also be discovered. As the peripheral nerve fibers approach their terminations, they lose their medullary sheath, and consist then merely of an axis-cylinder and primitive sheath. They may even lose the latter, and only the axis-cylinder be left. Finally, the axis-cylinder breaks up into its elementary fibrillæ, to end in various ways to be described later.

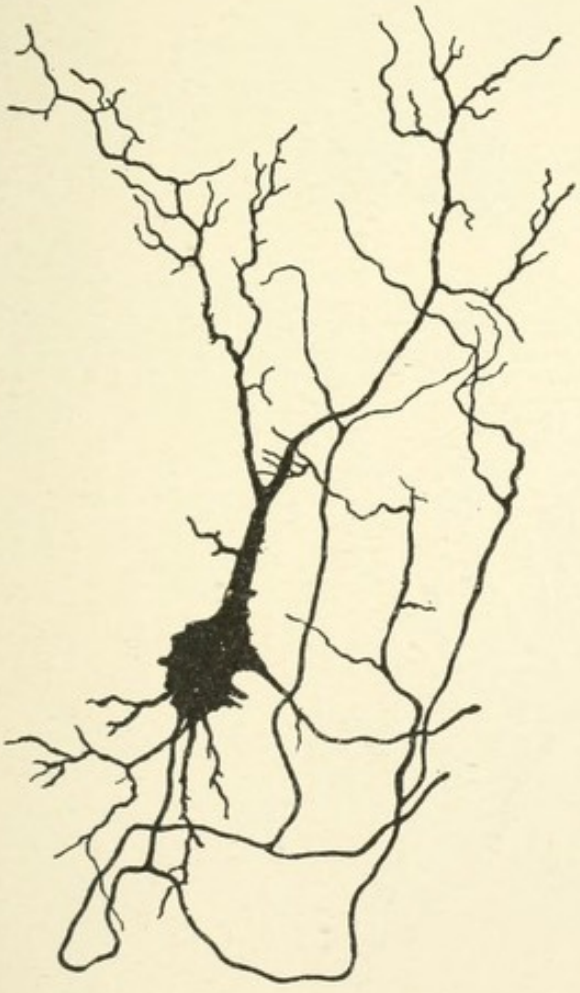


FIG. 91.

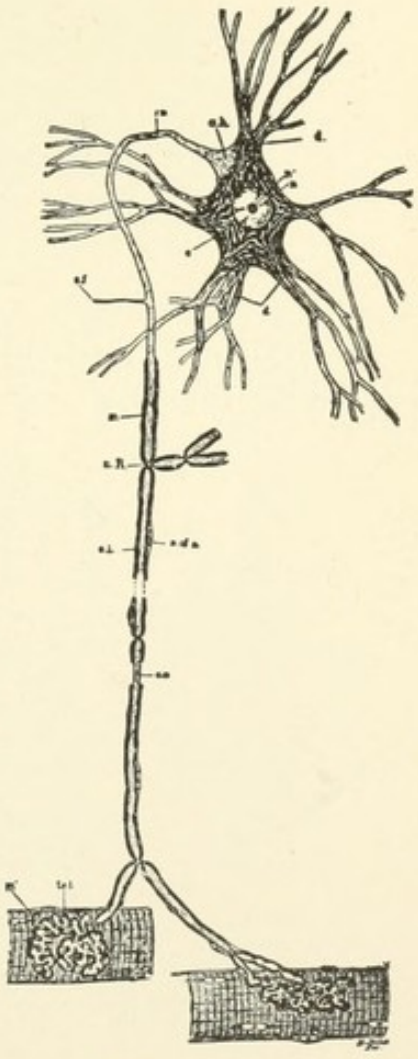


FIG. 92.

FIG. 91.—Nerve Cell with Short Axis-Cylinder from the Posterior Horn of the Lumbar Cord of an Embryo Calf, measuring 0.55 cm. (After Van Gehuchten.)

FIG. 92.—Scheme of Lower Motor Neurone. The cell body, protoplasmic processes, axone, collaterals, and terminal arborizations in muscle are all seen to be parts of a single cell and together constitute the *neurone*. (Barker.) *c*, Cytoplasm of cell body containing chromophilic bodies, neurofibrils, and perifibrillar substance; *n*, nucleus; *n'*, nucleolus; *d*, dendrites; *ah*, axone hill free from chromophilic bodies; *ax*, axone; *sf*, side fibril (collateral); *m*, medullary sheath; *nR*, node of Ranvier where side branch is given off; *sl*, neurilemma and incisures of Schmidt; *m*, striated muscle fiber; *tel*, motor end plate.

THE NERVE CELL BODY.

The nerve-cell body is the nodal and important part of the neurone, and from it are given off the dendrites and axis-cylinder process or axone. It consists of a mass of protoplasm, of varying shape and size, containing within

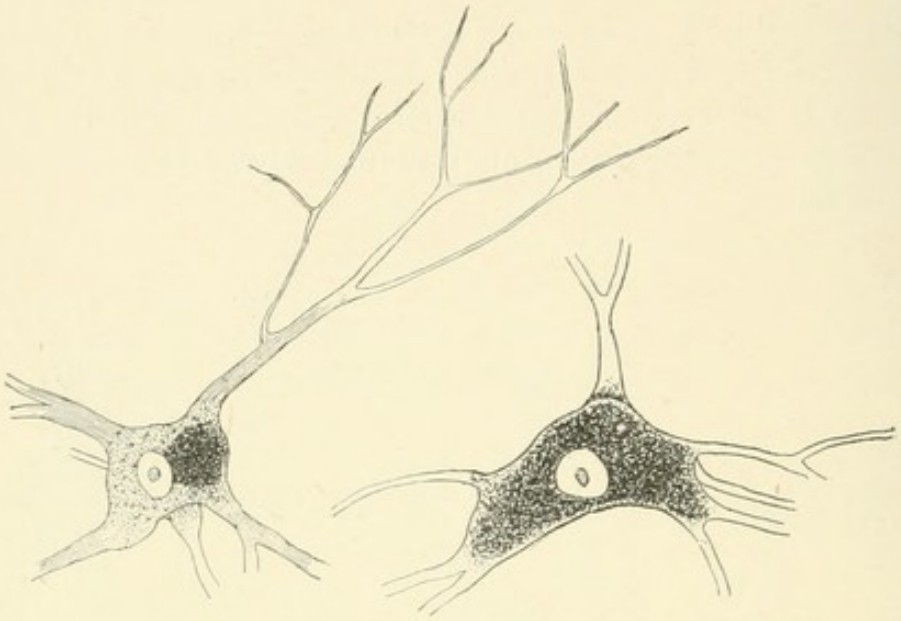


FIG. 93.—Large Nerve Cells with Processes, from the Ventral Cornua of the Cord of Man. ×350. On the cell at the right two short processes of the cell body are present, one or the other of which may have been an axis-cylinder process (Deiters). A similar process appears also on the cell at the left.

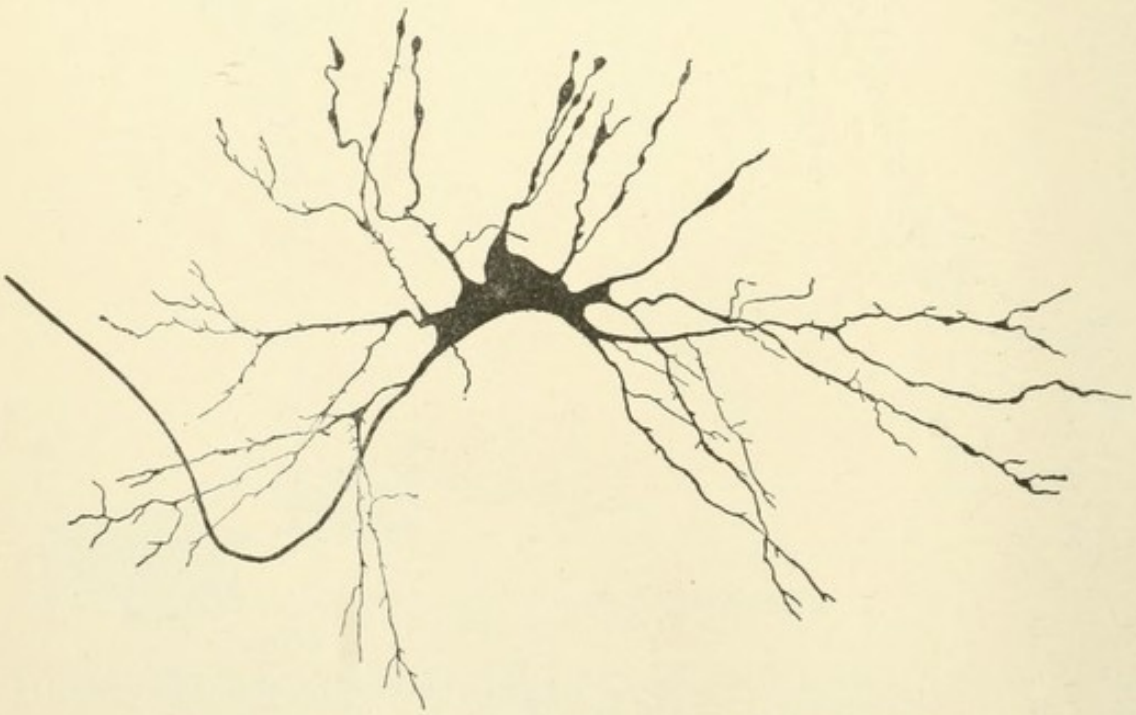


FIG. 94.—Multipolar Nerve Cell of the Cord of an Embryo Calf.

it a nucleus and nucleolus. All nerve cells give off one or more processes which branch out in various directions, dividing and subdividing like the

branches of a tree, but never anastomosing with each other or with other cells. These branches are what have already been referred to as the *dendrites* of

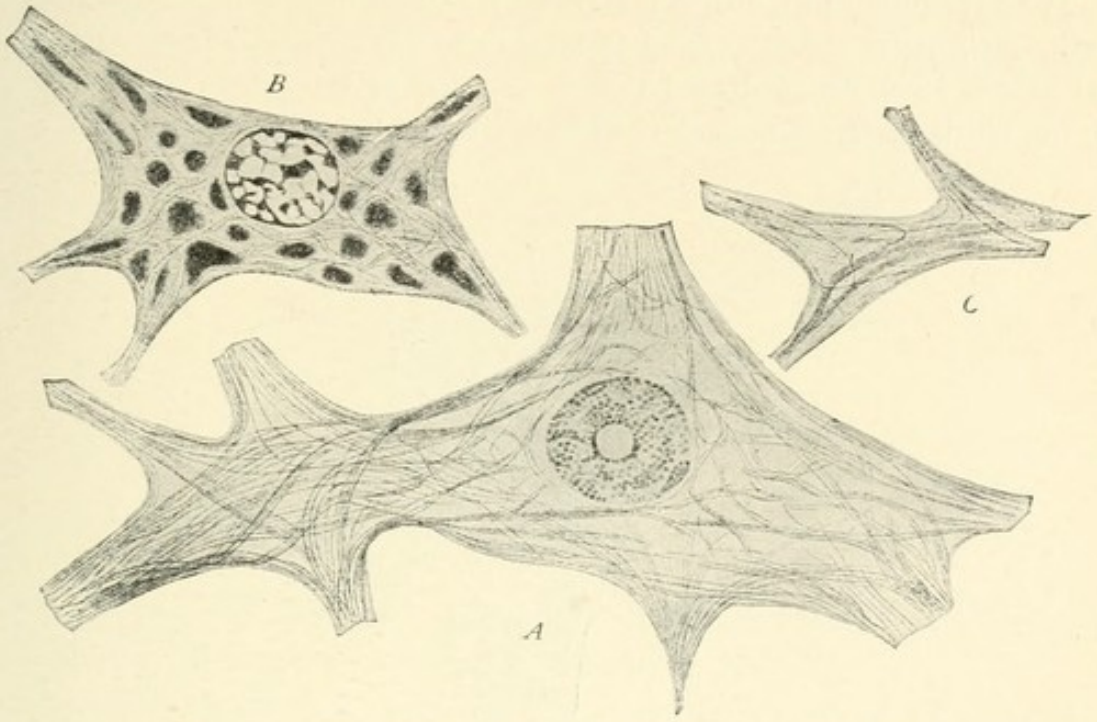


FIG. 95.—Ganglion Cells, Showing Neurofibrils. *A*, Anterior-horn cells of human; *B*, cell from the facial nucleus of rabbit; *C*, dendrite of anterior-horn cell of human. (Bethe.)

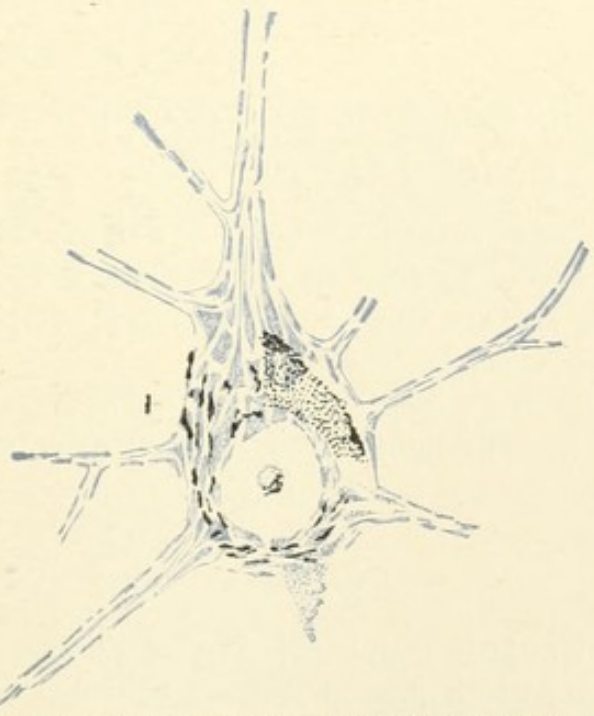


FIG. 96.—Cell of the Anterior Horn of the Human Spinal Cord, Stained by Nissl's Method, showing *chromophiles*. (After Edinger.)

the cell. They were formerly called the protoplasmic processes, figures 91, 93. It is thus seen that the neurone or nerve unit consists of a number of subdivisions, namely, the cell body, with its nucleus and nucleolus, the

dendrites or protoplasmic processes, and the axone or axis-cylinder process, which forms what is known as a *nerve fiber*.

The protoplasm of the cells is shown by various dyes to consist of *neurofibrils*, *perifibrillar substance*, and in most cells *chromophilic bodies*. Apáthy and others have demonstrated that a network of interlacing and anastomosing fibrils traverses both the cell body and its branches, figure 95.

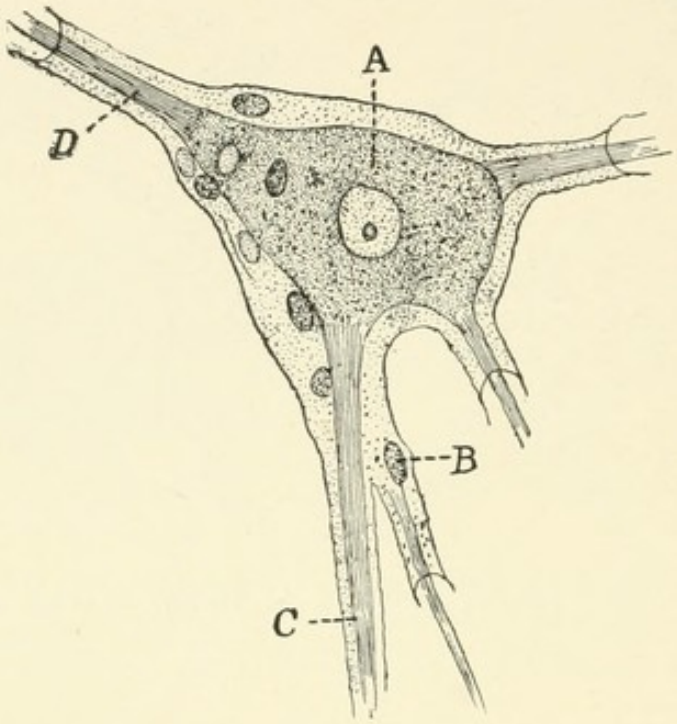


FIG. 97.—An Isolated Sympathetic Ganglion Cell of Man, Showing Sheath with Nucleated Cell Lining, *B*. *A*, Ganglion cell, with nucleus and nucleolus; *C*, branched process or dendrite, *D*, unbranched process or axone. (Key and Retzius.) × 750.

The perifibrillar substance is a fluid or semifluid substance in which the fibrils are embedded. By treating nerve-cells with special stains granular bodies of varying size are found embedded in the cytoplasm. These bodies are the chromophilic bodies, figure 96.

Ganglion cells are generally enclosed in a transparent membranous capsule similar in appearance to the external nucleated sheath of nerve-fibers; within this capsule is a layer of small flattened cells.

Nerve Terminations.

Nerve fibers terminate peripherally in four different ways: 1, by the terminal subdivisions which pass in between epithelial cells, and are known as inter-epithelial arborizations; 2, by motor-plates which lie in the muscles; 3, by special end-organs, connected with the senses of sight, hearing, smell, and taste; and, 4, by various forms of tactile corpuscles.

The Inter-epithelial Arborizations. This forms a most common mode of termination of the sensory nerves of the body. The nerve fibers

to the surface of the skin or mucous membrane lose their neurilemma and myelin sheath, the bare axis-cylinder divides and subdivides into minute ramifications among the epithelial cells of the skin and mucous membrane. In the various glands of the body this form of termination also prevails.

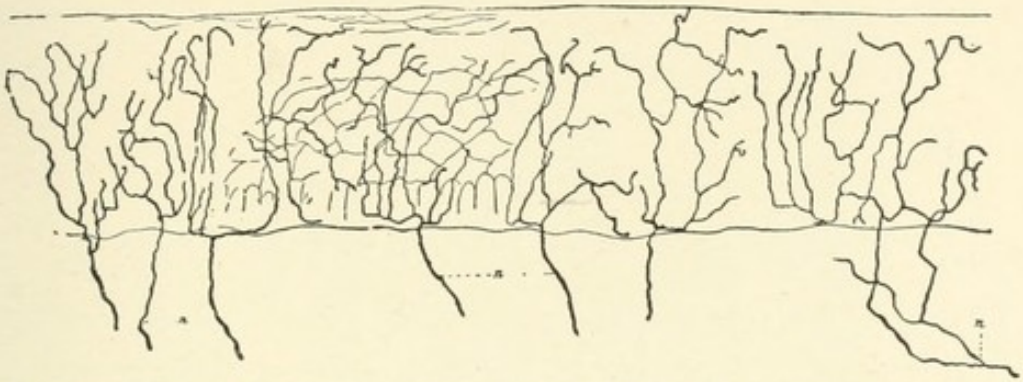


FIG. 98.—Sensory-Nerve Terminations in Stratified Pavement Epithelium. Golgi's rapid method. (After G. Retzius.)

The hair-bulbs, the teeth, and the tendons of the body are supplied by this same process of terminal arborization, figures 98, 99.

The motor nerves to the muscles end in what are known as *muscle-plates*, the details of whose structure have been already described.

The special sensory end-organs will be described later in the chapter on the Special Senses.

A fourth form of termination consists of corpuscles that are more or less encapsulated, and these are known as the *corpuscles of Pacini, the tactile*

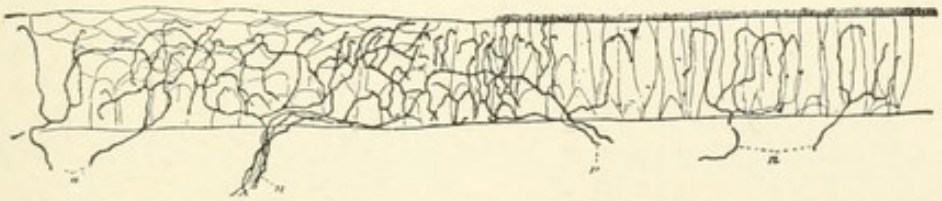


FIG. 99.—Sensory-Nerve Termination in the Epithelium of the Mucosa of the Inferior Vocal Cord and in the Ciliated Epithelium of the Subglottic Region of the Larynx of a Cat Four Weeks Old. (After G. Retzius.) Golgi's rapid method. *n*, Nerve-fibers rising from the connective-tissue layer into the epithelial layer, where they terminate in ramified and free arborizations.

corpuscles of Meissner, the tactile corpuscles of Krause, the tactile menisques, and the corpuscles of Golgi.

The Pacinian Corpuscles. These nerve endings, named after their discoverer Pacini, are elongated oval bodies situated on some of the cerebro-spinal and sympathetic nerves. They occur on the cutaneous nerves of the hands and feet, the branches of the large sympathetic plexus about the abdominal aorta, the nerves of the mesentery, and have been observed also in the pancreas, lymphatic glands, and thyroid glands, figure 100. Each corpuscle is attached by a narrow pedicle to the nerve on which it is situated, and is formed of several concentric layers of fine membrane, each

layer being lined by endothelium, figure 100. A single nerve fiber passes through its pedicle, traverses the several concentric layers, enters a central cavity, and terminates in a knob-like enlargement or in a bifurcation.

The physiological import of these bodies is still obscure.

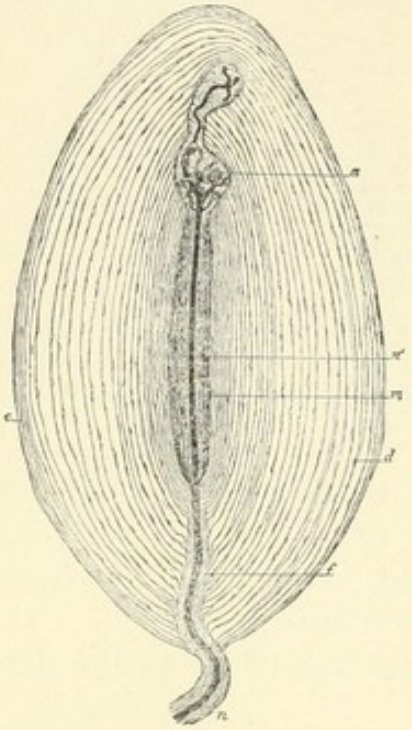


FIG. 100.

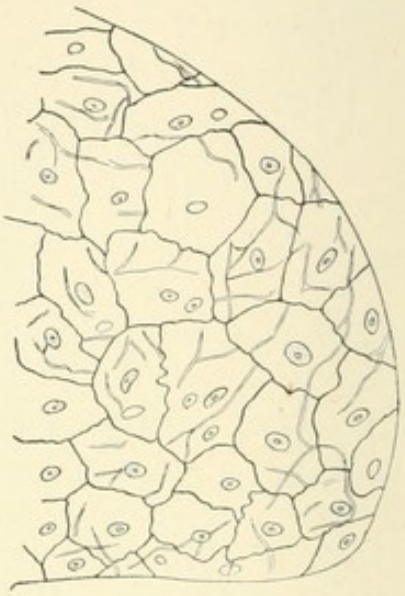


FIG. 101.

FIG. 100.—Pacinian Corpuscle of the Cat's Mesentery. The stalk consists of a nerve fiber, *n*, with its thick outer sheath. The peripheral capsules of the Pacinian corpuscle are continuous with the outer sheath of the stalk. The intermediary part becomes much narrower near the entrance of the axis-cylinder into the clear central mass. A hook-shaped termination with the end-bulb, *a*, is seen in the upper part. (Ranvier.)

FIG. 101.—Summit of a Pacinian Corpuscle of the Human Finger, showing the Endothelial Membranes Lining the Capsules. × 220. (Klein and Noble Smith.)

The Tactile Corpuscles of Meissner. They are found in the papillæ of the skin of the fingers and toes, or among its epithelium. When simple they are small, slightly flattened transparent bodies composed of nucleated cells enclosed in a capsule. When compound, the capsule contains several small cells. The nerve fiber penetrates the corpuscles, loses its myelin sheath, and divides and subdivides to form a series of arborizations. The terminal arborizations occupy the central part of the corpuscle, and are surrounded by a great number of marginal cells. The touch or tactile corpuscles of Meissner have been regarded at one time as epithelial, at another time as nervous, but they are to-day proved to be mesodermic cells, and differentiated for the special purpose of the sense of touch (Dejerine).

The Corpuscles of Krause or End-Bulbs. These exist in great numbers in the conjunctiva, the glans penis, clitoris, lips, skin, and in tendon of man. They resemble the corpuscles of Pacini, but have much fewer concentric layers to the corpuscle, and contain a relatively voluminous central

mass composed of polyhedral cells. In man these corpuscles are spherical in shape, and receive many nerve fibers which wind through the corpuscles and end in the free extremities, figure 103.

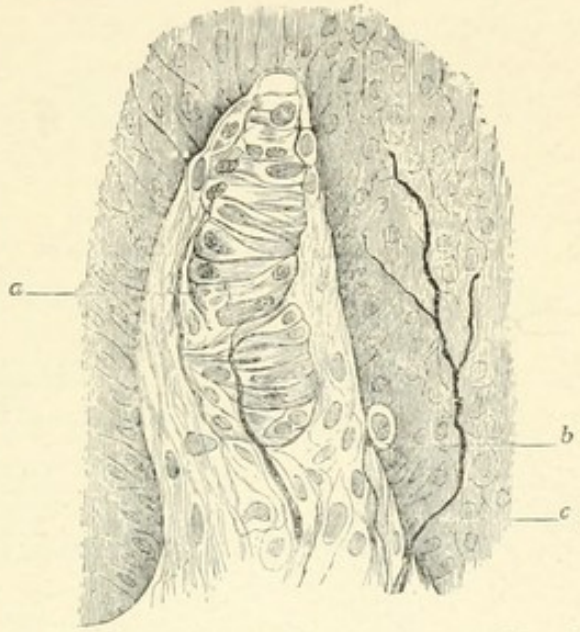


FIG. 102.—Tactile Corpuscle of Meissner, Tactile Cell and Free Nerve Ending. (Merkel-Henle.) *a*, Corpuscle proper, outside of which is seen the connective-tissue capsule; *b*, fiber ending on tactile cell; *c*, fiber ending freely among the epithelial cells.

Tactile Menisques. In different regions of the skin of man, one meets, in the superficial layers and in the Malpighian layers, nerves which, after having lost their myelin sheath, divide and subdivide to form

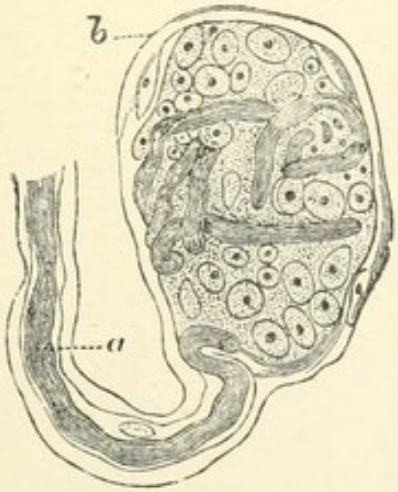


FIG. 103.

FIG. 104.

FIG. 103.—End-Bulb of Krause. *a*, Medullated nerve fiber; *b*, capsule of corpuscle.

FIG. 104.—A Termination of a Medullated Nerve Fiber in Tendon, lower half with Convoluted Medullated Nerve Fiber. (Golgi.)

extremely beautiful arborizations. The branches of these arborizations are the *tactile menisques*. These menisques, which simulate the form of a leaf, represent a mode of terminal nervous arborization (Ranvier).

The Corpuscles of Golgi. These are small terminal plaques placed at the union of tendons and muscles, but belonging more properly to the

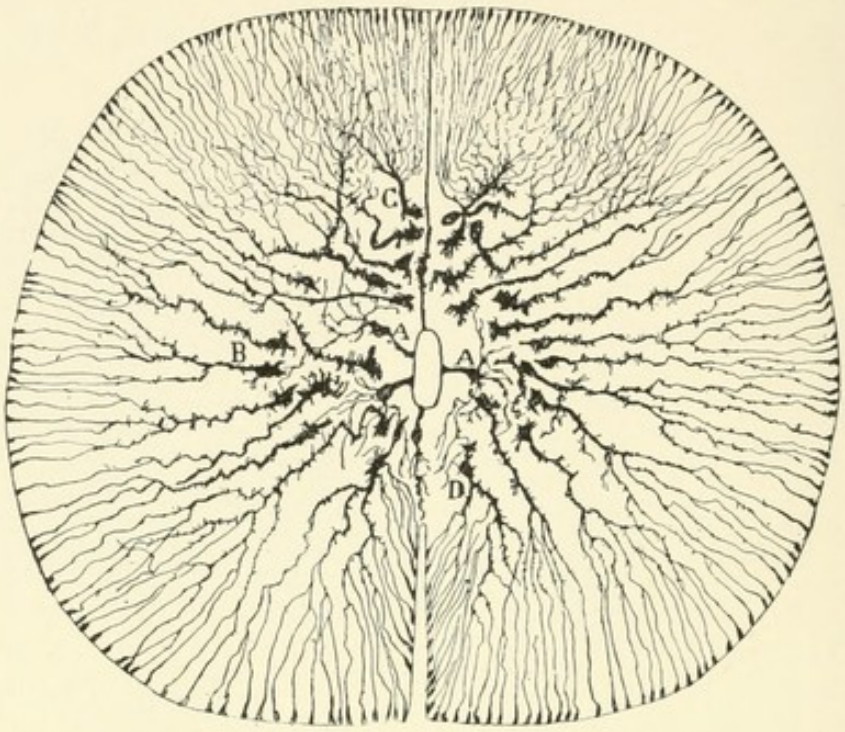


FIG. 105.—Neuroglia Cells in the Cord of an Adult Frog. (After Cl. Sala.) *A*, Ependyma cells with their peripheral extremities atrophied and ramified; *B*, *C*, *D*, neuroglia cells in different degrees of emigration and separation from the ependymal canal; their central extremity is atrophied and much contracted; their peripheral extremity, on the other hand, is greatly extended; the ramifications of the latter, terminating in conical buttons, *I*, end under the pia mater.

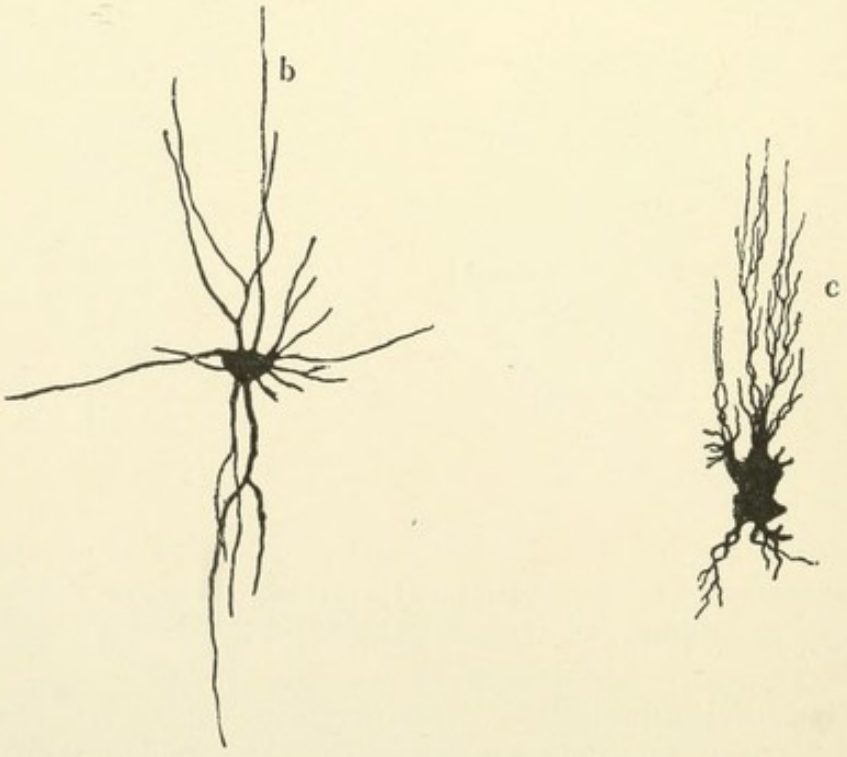


FIG. 106.—Different Types of Neuroglia Cells. (After Van Gehuchten.) *b*, Neuroglia cells of the white substance, and *c*, of the gray substance of the cord of an embryo calf.

tendon. They are fusiform in shape and are flattened upon the surface of the tendon close to its insertion into the muscular fibers. They are composed of a granular substance, enveloped in several concentric hyaline membranes which contain some nuclei. The nerve fiber passes into this little corpuscle, splitting itself up into fine terminals. The corpuscles of Golgi are believed to be related to the muscular sense, figure 104.

THE NEUROGLIA.

The neuroglia, while not a nervous tissue, is closely mingled with it and forms an important constituent of the nervous system. It consists of cells giving off a fine network of richly branching fibers. Neuroglia is a form of connective tissue, and it is in its functions strictly comparable to the connective tissue which supports the special structures of other organs, like the lungs and kidneys, figure 106. In the adult animal the neuroglia-tissue is composed of cells from which are given off immense numbers of fine processes. These extend out in every direction, and intertwine among the nerve-fibers and nerve-cells, figure 105. The neuroglia cell differs in size and shape very much in different parts of the nervous system in accordance with the arrangement of the nervous structures about it. The cell is composed of granular protoplasm, and lying in it is a large nucleus, within which is a nucleolus. The body of the cell is small in proportion to the nucleus.

CHAPTER III

THE CHEMICAL COMPOSITION OF THE BODY

Of the eighty chemical elements which have been isolated, no less than seventeen combine in varying quantities to form the chemical basis of the animal body. The substances which contribute the largest share are the non-metallic elements, *Oxygen*, *Carbon*, *Hydrogen*, and *Nitrogen*—oxygen and carbon making up altogether about 85 per cent of the whole. The most abundant of the metallic elements are *Calcium*, *Sodium*, and *Potassium.**

These elements do not exist in the animal body in the free state, but are combined into complex chemical compounds. Of course we cannot analyze the living protoplasm and isolate its compounds.

The first step in the act of separating the composition products of protoplasm produces changes which destroy the chemical and physical relations of these products which maintain the state of life. Dead protoplasm, however, yields a number of substances which must be very directly derived from the living protoplasm. On the other hand, certain products can be isolated from the animal body which are evidently not a part of the protoplasm itself, but products of protoplasmic activity. Some of these, like fat, glycogen, etc., are constructive products, others are disintegration products of protoplasmic activity.

A large number of the animal compounds, particularly those of the nitrogenous group, are characterized by their *complexity*. Many elements enter into their composition, and many atoms of the same element occur in each molecule. This latter fact no doubt explains the reason of their *instability*.

Of the numerous compounds that have been isolated from the animal body, only a very few of the most important will be discussed in this chapter.

*The following table represents the relative proportion of the various elements in the body. (Marshall.)

Oxygen	72.0	Fluorine	0.08
Carbon	13.5	*Potassium*	0.026
Hydrogen	9.1	Iron	0.01
Nitrogen	2.5	Magnesium	0.0012
Calcium	1.3	Silicon	0.0002
Phosphorus	1.15	(Traces of copper, lead, and aluminum)	
Sulphur	0.1476		
Sodium	0.1		
Chlorine	0.085		100

THE NITROGENOUS BODIES.

Nitrogenous bodies take the chief part in forming the solid tissues of the body, and are found also to a considerable extent in the circulating fluids (blood, lymph, chyle), the secretions and excretions. They often contain, in addition to carbon, hydrogen, nitrogen, and oxygen, the elements sulphur and phosphorus; but although the composition of most of them is approximately known, no general rational formula can at present be given for the proteids.

Proteids. The nitrogenous substances constitute the most important and complex compounds of the body. According to their chemical composition and reactions they are divided into three main classes, viz., 1, simple proteids; 2, compound proteids; and 3, albuminoids.

The proteids are the chief of the nitrogenous organic compounds and exist in both plants and animals, one or more of them entering as an essential part into the formation of all living tissue. They exist abundantly in the lymph, chyle, and blood. Very little is known with any certainty about their exact chemical composition. Their formulæ are unknown, the chemists who have attempted to construct the structural formulæ differing very greatly among themselves. In fact the very term proteid is an extremely arbitrary one. It simply means a body which, according to Hoppe-Seyler, contains in its molecule the elements carbon, hydrogen, nitrogen, oxygen, and sulphur, in certain arbitrary but varying amounts, thus—**Carbon,** from 51.5 to 54.5; **Hydrogen,** from 6.9 to 7.3; **Nitrogen,** from 15.2 to 17; **Oxygen,** from 20.9 to 23.5; **Sulphur,** from 0.3 to 2. Some proteids contain from 0.8 to 4.5 per cent of phosphorus; a small amount of iron is usually associated with proteids, but it is not certain whether or not it is an integral part of the molecule. Chittenden defines a proteid as a substance which contains carbon, hydrogen, oxygen, nitrogen, and sulphur, the nitrogen being in a form which serves the physiological needs of the body; and yields, on decomposition, a row of crystalline amido-acids and crystalline nitrogenous bases; nearly all contain 52 per cent of carbon and 16 per cent of nitrogen.

Properties of Proteids. Proteids are for the most part amorphous and non-crystallizable. Certain of the vegetable proteids have been crystallized, and according to Hofmeister, egg albumin is also capable of crystallization. They possess as a rule no power (or scarcely any) of passing through animal membranes. They are soluble, but undergo alteration in composition in strong acids and alkalies; some are soluble in water, others in neutral saline solutions, some in dilute acids and alkalies, none in alcohol or ether. Their solutions exercise a left-handed rotation on polarized light.

The hope that it may be possible in the immediate future to synthesize proteids is not very great, because of the extraordinary variety of compounds obtained by the decomposition of proteids by various chemical methods,

the compounds differing according to the method employed. In the body it seems clear that living proteid is built up by the food supplied to it, which necessarily contains proteid derived from either a vegetable or an animal source; how this process takes place we are yet unable to say. Recently Taylor has been able to synthesize proteid, protamin, by the reversible action of trypsin on the amido-acids which were previously obtained by the digestion of protamin. The reaction is indicated by the equation:

$$\text{Protein} + \text{Water} \rightleftarrows \text{Amido-acids.}$$

Robertson has demonstrated a similar reversible reaction of pepsin on paranuclein derived from the digestion of casein. These experiments lend a new stimulus to the efforts to build up proteids in the chemical laboratory along the lines of catalytic action of enzymes.

In the course of later chapters in this book we shall endeavor to trace the steps of the breaking up of proteid in the body, but we may anticipate by mentioning that it is now generally believed that the chief ultimate products of this decomposition are *urea*, a body the formula of which is $CO(NH_2)_2$, *carbon dioxide* and *water*, while the intermediate substances or by-products are chiefly ammonia compounds. When proteid material is decomposed by putrefaction, by the action of chemical reagents, acids, alkalies, or by heat, various bodies are produced, of which amido-acids (acids in which one or more of the hydrogen atoms of the radical of the acid are replaced by amidogen, NH_2) and bodies belonging to the aromatic or benzene series predominate. Hence it comes that various theories of the way in which proteids are built up have arisen. The one which has appeared to have received the greatest support is that of Latham. This observer has suggested that proteid may be considered as made up of a series of *cyan-alcohols* (bodies obtained by the union of any aldehyde with hydrocyanic acid) with a benzene nucleus. Taking ordinary ethyl alcohol, CH_3CH_2OH, as the type, the aldehyde of which is CH_3CHO, the corresponding cyan-alcohol would be $CH_3CHCNOH$.

CLASSES OF PROTEIDS.

Simple Proteids.

Native Albumins.

Albumins; serum albumins, egg albumins, lactalbumin.

Globulins; serum globulin, myosinogen, cytoglobulin, etc.

Derived Albumins.

Albuminates; acid and alkali albumins.

Coagulated proteids; heat coagulated and enzyme coagulated proteid.

Proteose, Peptones, Polypeptids; all derived as cleavage-products of enzyme action on other proteids.

Histons; contain 35 to 42 per cent of their nitrogen as basi · nitrogen.

Protamins; contain 63 to 88 per cent of their nitrogen as basic nitrogen.

Compound Proteids.

Hemoglobin; decomposes into a proteid and a chromogen.

Nucleoproteid; decomposes into a proteid and nucleic acid.

Glycoproteid; decomposes into a proteid and a reducing substance, mucin.

Albuminoid substances; mucin, keratin, albumoid, collagen, elastin, etc.

The Albumins. Of native albumins there are several varieties: egg albumin; serum albumin; lact albumin, etc.

When in solution in water it is a transparent, frothy, yellowish fluid, neutral or slightly alkaline in reaction. It gives all of the general proteid reactions. On digestion it yields 8 per cent of argenin, 22.6 per cent of leucin, and 2 per cent of tyrosin.

At a temperature not exceeding 40° C. it is dried up into a yellowish, transparent, glassy mass, soluble in water. At a temperature of 70° C. it is *coagulated* into a new substance, *coagulated proteid*, which is quite insoluble in water. It is coagulated also by the prolonged action of alcohol; by strong mineral acids, especially by nitric acid; also by tannic acid, or carbolic acid; and by ethers. The coagulum is soluble in caustic soda.

With strong nitric acid the albumin is precipitated at the point of contact with the acid in the form of a fine white or yellow ring.

Serum Albumin is contained in blood serum, lymph, serous and synovial fluids, and in the tissues generally; it may be prepared from serum after removal of paraglobulin, by a saturation with sodium sulphate. It appears in the urine in the pathological condition known as albuminuria.

It gives similar reactions to egg albumin, but differs from it in not being coagulated by ether. It also differs from egg albumin in not being easily precipitated by hydrochloric acid, and in the precipitate being easily soluble in excess of that acid. Serum albumin, either in the coagulated or precipitated form, is more soluble in excess of strong acid than egg albumin.

Globulins. Globulins are found in egg; in blood, lymph, and other body fluids; and in most protoplasm.

The globulins give the general proteid tests; are insoluble in water; are soluble in dilute saline solutions; are soluble in acids and alkalies forming the corresponding derived albumin.

Most of them are precipitated from their solutions by saturation with solid sodium chloride, magnesium sulphate, or other neutral salt. They are coagulated, but at different temperatures, on heating.

A globulin is obtained from the crystalline lens by rubbing it up with

powdered glass, extracting with dilute saline solution, and by passing through the extract a stream of carbon dioxide. It differs from other globulins in not being precipitated by saturation with sodium chloride.

The globulin, myosin, may be prepared from muscle by removing all fat, tendon, etc., and washing repeatedly in water until the washing contains no trace of proteids, mincing it, and then treating with 10 per cent solution of sodium chloride, or similar solution of ammonium chloride or magnesium sulphate. The salt solution will dissolve a large portion into a viscid fluid, which filters with difficulty. If the viscid filtrate be dropped little by little into a large quantity of distilled water, a white flocculent precipitate of myosin will occur.

Myosin is soluble in 10 per cent saline solution; it is coagulated at 60° C. into coagulated proteid; it is soluble without change in very dilute acids; it is precipitated by picric acid, the precipitate being redissolved on boiling; it may give a blue color with ozonic ether and tincture of guaiacum.

Serum globulin is contained in plasma and in serum, in serous and synovial fluids, and may be precipitated by saturating plasma after removal of fibrinogen, or by saturating serum with solid sodium chloride or magnesium sulphate. Globulin separates as a bulky flocculent substance which can be removed by filtration. It may also be prepared by diluting blood-serum with ten volumes of water, and passing carbonic-acid gas rapidly through it. The fine precipitate may be collected on a filter, and washed with water containing carbonic-acid gas. It is very soluble in dilute saline solutions, 5 to 8 per cent, from which it is precipitated by carbonic-acid gas or by dilute acids. Its solution is coagulated at 72° C. Dilute acids and alkalies convert it into acid or alkali albumin.

Fibrinogen is contained in blood plasma, from which it may be prepared by the addition of sodium chloride to the extent of 13 per cent. It may also be prepared from hydrocele fluid or from other serous transudation by a similar method. Its general reactions are similar to those of paraglobulin. But its solution is coagulated at 55°–56° C. Its characteristic property consists in the facility with which it forms the insoluble proteid fibrin.

Edestin is a globulin which is found in many edible vegetables, grain, etc. A solution may be prepared by adding hempseed to a 10 per cent solution of sodium chloride and heating to 50° C.

Albuminates. There are two principal substances belonging to this class: *a*, acid albumin; *b*, alkali albumin.

Acid Albumin. Acid albumin is made by adding small quantities of dilute acid (of which the best is hydrochloric, 0.4 to 1 per cent) to either egg or serum albumin diluted with five to ten times its bulk of water, and keeping the solution at a temperature not higher than 50° C. for not less than half an hour. It may also be made by dissolving coagulated native albumin in strong acid, or by dissolving any of the globulins in acids. Solid acid

albuminate may be formed by adding strong acid drop by drop to a strong solution of proteid matter (*e.g.*, undiluted egg albumin) until solidification occurs.

It is not coagulated on heating, but on *exactly* neutralizing the solution a flocculent precipitate is produced; if it is then heated to 70° C. it will coagulate and cannot then be distinguished from any other form of coagulated proteids. This may be shown by adding to the acid albumin solution a little aqueous solution of litmus and then adding, drop by drop, a weak solution of caustic potash from a buret until the red color disappears. The precipitate is the derived albumin. It is soluble in dilute acid, dilute alkalies, and dilute solutions of alkaline carbonates. The solution of acid albumin gives the proteid tests. The substance itself is coagulated by strong acids, *e.g.*, nitric acid, and by strong alcohol; it is insoluble in distilled water, and in neutral saline solutions; it is precipitated from its solutions by saturation with sodium chloride. On boiling in lime-water it is partially coagulated, and a further precipitation takes place on addition to the boiled solution of calcium chloride, magnesium sulphate, or sodium chloride.

Alkali Albumin. If solutions of native albumin, or coagulated albumin, or other proteid be treated with dilute or strong fixed alkali, alkali albumin is produced. Solid alkali albumin (Lieberkühn's jelly) may also be prepared by adding caustic soda or potash, drop by drop, to undiluted egg albumin, until the whole forms a jelly. This jelly is soluble in an excess of the alkali or in dilute alkalies on boiling. A solution of alkali albumin gives the tests corresponding to those of acid albumin. It is not coagulated on heating except after neutralization, as in the case of acid albumin. It is thrown down on neutralizing its solution, except in the presence of alkaline phosphates, in which case the solution must be distinctly acid before a precipitate falls.

To differentiate between acid and alkali albumin, the following method may be adopted: Alkali albumin is *not* precipitated on *exact* neutralization if sodium phosphate has been previously added. Acid albumin is precipitated on exact neutralization, whether or not sodium phosphate has been previously added.

Coagulated Proteids. These are formed by the action of heat or of ferments upon other proteids; the temperature necessary to produce coagulation varying in the manner previously indicated. They may also be produced by the prolonged action of alcohol upon proteids; the process is one of dehydration. They are soluble in strong acids or alkalies; slightly so in dilute; are soluble in digestive fluids (gastric and pancreatic), and are insoluble in water or saline solutions (except fibrin).

Fibrin is formed by the action of fibrin ferment on fibrinogen and can be obtained as a soft, white, fibrous, and very elastic substance by whipping blood with a bundle of twigs and washing the adhering mass in a stream of

water unto all the blood-coloring matter is removed. It is soluble to a certain extent in strong sodium-chloride solutions.

Proteoses. These are intermediate substances of the digestion of other proteids, the ultimate product of which is peptone or lower cleavage products. They are produced by the action of the gastric and pancreatic juices and also, slowly, by boiling with dilute acids. The term is a general one, the proteose of albumin being albumose, that of globulin being globulose, etc. They are divided into primary and secondary groups representing the stages of progression from proteids to peptones, so that there may be a primary and a secondary albumose, etc. As digestion is a process of hydration with cleavage, the successive stages present progressively simpler substances. Each group reacts to fewer reagents than the preceding one; *e.g.*, none of the proteoses can be coagulated by boiling. Nitric acid will precipitate the primary proteoses but not the secondary ones.

Peptones. Peptone is formed by the action of the digestive ferments, *pepsin* or *trypsin*, on other proteids, and on gelatin. It is a still simpler form of substance than the proteoses and reacts to still fewer reagents. Peptones will be considered in connection with the physiology of digestion, as will also be the intermediate compounds.

Histons. Histons are decomposition products but present well-defined proteid reactions. They are strongly basic and have a large content of hexon bases. Histons are soluble in water; are precipitated by weak ammonia; are soluble in acids; do not coagulate by heat in water solutions unless salts are present. They are not changed by and may be recovered from the salt heat coagulation. They do not contain phosphorus. They give the biuret reaction, but do not give Millon's reaction.

Protamin. This substance is of special interest in that it is the simplest of the proteids. It is a cleavage product which exists in nature in fish sperm as a nucleic acid compound. It gives the biuret but not Millon's reaction, is not coagulated by heat. It yields amido-acids as cleavage-products. These cleavage-products have been recently resynthesized by Taylor by the action of trypsin.

Compound Proteids. The compound proteids are compounds of a simple proteid with some other molecule. According to their chemical composition and characteristics they are divided into several classes, viz.: *Chromoproteids.* This is a combination of a proteid substance with some form of pigment. For example, hemoglobin is a combination of a globulin with hematin, an iron-containing radicle. Hemoglobin is described more fully in the chapter on the Blood. *Nucleoproteids.* Nucleoproteids are a combination of a proteid substance with a nucleic acid; they are divided into two groups according to the character of the acid. The true nucleoproteids contain true nucleic acid; the para-nucleoproteids or pseudo-nucleoproteids contain para-nucleic acid. Both acids, and therefore both groups,

contain phosphorus; but the true nucleoproteids yield nuclein (xanthin) bases while the para-nucleoproteids do not. The nucleoproteids are found in the nucleus and protoplasm of every cell. The para-nucleoproteids are found in milk, as caseinogen, and in the yolk of egg, as vitellin. *Glycoproteids.* Glycoproteid is a combination of a proteid substance with a carbohydrate radicle. Examples are mucin, which is found in mucous secretions; and mucoids, which are found in certain tissues, cartilages, etc.

Mucin. Mucin is a compound of a globulin with a carbohydrate radicle, and is the characteristic component of mucus; it is contained also in fetal connective tissue, in tendons, and in salivary glands. It can be obtained from mucus by diluting with water, filtering, treating the insoluble portion with weak caustic alkali, and reprecipitating with acetic acid. The mucins derived from different sources probably have different compositions.

Mucin has a ropy consistency. It can be coagulated; is insoluble in water, salt-solution, and very dilute muriatic acid; is soluble in alkalies and concentrated sulphuric acid. It gives the proteid reaction with Millon's reagent and with nitric acid. Neither mercuric chloride nor tannic acid gives a precipitate. It does not dialyze. When treated with sulphuric acid and then neutralized with solid potassium hydrate, it will give both the biuret test, denoting the presence of proteid matter, and also Fehling's test, showing the presence of a sugar.

Nucleins. The substance known as *nuclein* and found in all cells is really a compound proteid and consists of a series of bodies made up of proteid and nucleic acid in varying proportions; there is almost no limit to the possible variations. At one end of the series is *nucleic acid* ($C_{39}H_{52}N_9P_3O_{17}$, according to Kossel), a body containing the maximum (9 to 11 per cent) of phosphorus but without any proteid, and found as such only in spermatozoa; in the middle are the *nucleins* proper; and at the other end are the *nucleoproteids*, containing the minimum of phosphorus. As phosphorus is the characteristic component of nucleic acid, its amount will measure the amount of the acid present in any molecule.

The chemical differences in the action of cytoplasm and karyoplasm toward solvents are due also to the proportion of nucleic acid and proteid which they contain. These differences are qualitative and not quantitative. All of the nucleoproteids in the cell body are true ones in that they yield nuclein bases.

Caseinogen. Caseinogen, the chief proteid of milk, yields paranuclein on digestion. It bears the same relation to casein that fibrinogen does to fibrin. When acted on by rennin it splits into two parts of which one, the smaller, is peptone-like in character. The other, and larger part, is known as soluble casein and does not solidify in the absence of calcium salts. As calcium is always present in milk, it there unites with it and forms insoluble calcium casein; strictly speaking, therefore, the curd of milk is

the calcium compound of soluble casein. Caseinogen may be prepared by adding dilute hydrochloric acid to milk until the mixture is distinctly acid, when a flocculent precipitate of caseinogen will be thrown down and may be separated by filtration. The fat which is carried down with this precipitate may be removed by washing with alcohol and then with ether.

Caseinogen may also be prepared by adding to milk an excess of crystallized magnesium sulphate or sodium chloride, either of which salts causes it to separate out. Caseinogen gives the biuret and Millon's reactions. It is soluble in distilled water, dilute or strong alkalies, and sulphuric acid, but insoluble in sodium chloride and 0.2 per cent of hydrochloric acid.

Vitellin. Vitellin is prepared from yolk of egg by washing with ether until all the yellow matter has been removed. The residue is then dissolved in 10 per cent saline solution, filtered, and poured into a large quantity of distilled water. The precipitate which falls is impure vitellin. It gives the same tests as myosin, but is not precipitated on saturation with sodium chloride; it coagulates at about 75° C.

Albuminoids. The albuminoids belong to the simple tissues of the body which are derived from the epiblast and are characterized by a lack of any degree of activity, either physiological or chemical. They are nitrogenous bodies derived from proteid matter in the cells, and give crystalline amido-acids and nitrogenous bases on decomposition, but differ from true proteids in not having their nitrogen in a form fit for the physiological needs of the body. In other words, they are not true nitrogen-supplying foods, though gelatin has a certain indirect value as it protects the body proteids from work in many ways. The albuminoids are soluble in dilute acids or alkalies; they may be distinguished from albumin or globulin by being insoluble in water or salt solution respectively. Typical albuminoids are *gelatin*, *elastin*, *chondrin*, *keratin*, etc.

Gelatin. Gelatin is contained in the form of *collagen*, its anhydride, in bone, *ossein*, teeth, fibrous connective tissues, tendons, ligaments, etc. It may be obtained by prolonged action of boiling water or of dilute acetic acid.

The percentage composition is O 25.24 per cent, H 6.56 per cent, N 17.81 per cent, C 50 per cent, SO 25 per cent. It contains more nitrogen and less carbon and sulphur than proteids. It is amorphous, and transparent when dried. It does not dialyze; it is insoluble in cold water, but swells up to about six times its volume; it dissolves readily on the addition of very dilute acids or alkalies. It is soluble in hot water, and forms a jelly on cooling, even when only 1 per cent of gelatin is present. It is also soluble in hot salt solution. Prolonged boiling in dilute acids or in water destroys the power of forming a jelly on cooling. On decomposition it gives 2 per cent of leucin and 2.6 per cent of argenin, but no tyrosin, and a large amount of glycocoll (amido-acetic acid or glycin), a crystalline substance.

A fairly strong solution of gelatin, 2 per cent to 4 per cent, gives the *xanthoproteic test*, but with no previous precipitate by nitric acid; the *biuret test*, the *Millon's test*, but with no precipitate. It is precipitated with tannic acid, with alcohol and picric acid. It is not precipitated with acetic acid, hydrochloric acid, mercuric chloride, nor with potassium ferrocyanide, and acetic acid.

Elastin is found in elastic connective tissue, in the ligamenta subflava, ligamentum nuchæ, etc. It is insoluble in all ordinary reagents, but swells up both in cold and hot water. It is slowly soluble in strong caustic soda, when heated. It is precipitated by tannic acid and does not gelatinize. It gives the proteid reactions with strong nitric acid and ammonia, and imperfectly with Millon's reagent. On decomposition it gives 4.5 per cent of leucin, a small amount of argenin, and a mere trace of tyrosin. It is prepared by boiling with water, then treating with artificial gastric and pancreatic juices, then boiling again in water, and then extracting with acids, alcohol, and ethers; the remainder is elastin.

Chondrin is found in the condition of chondrigen in cartilage. It is obtained from chondrigen by boiling. It is soluble in hot water, and in solutions of neutral salts, *e.g.*, sulphate of sodium, in dilute mineral acids, caustic potash, and soda. It is insoluble in cold water, alcohol, and ether. It is precipitated from its solutions by dilute mineral acids (excess redissolves it), by alum, by lead acetate, by silver nitrate, and by chlorine water. On boiling with strong hydrochloric acid, it yields grape-sugar and certain nitrogenous substances. Prolonged boiling in dilute acids, or in water, destroys its power of forming a jelly on cooling.

Keratin is obtained from hair, horns, finger-nails, etc. Its composition is very similar to that of ordinary albumin and is approximately C 49.5, H 6.5, N 16.8, S 4, O 23.2; the keratins obtained from the various substances are distinct and differ slightly though closely related. Sulphur is the characteristic body found in keratin and occurs as a sulphur-containing radicle. A large amount of mercaptan sulphur can usually be obtained. On decomposition, keratin yields argenin 2.26 per cent, leucin 10 per cent, and tyrosin 4 per cent.

Keratin is insoluble in water, salt, sodium carbonate, and dilute hydrochloric acid. It is slowly soluble when warmed in caustic potash or sulphuric acid. It gives Millon's and the xanthoproteic reactions.

Neurokeratin is a form of keratin which is found in the white substance of Schwann around the axis-cylinders of nerves. It yields argenin 5 per cent, leucin 10 per cent, and tyrosin 3.5 per cent.

Products of Proteid Decomposition. The products of proteid decomposition under the influence of oxidizing and hydrolyzing agents are of the greatest significance in indicating the character and composition of the proteid molecule. Cleavage-products of widely varying degrees of com-

plexity are obtained. But, running through the cleavage compounds are certain nuclei or constitution complexes, which in all probability are found in the proteid itself, in fact form the basic structure of the molecule. The following account is taken from the excellent discussion by Witthaus ("The Medical Student's Manual of Chemistry"):

"Active oxidizing agents attack the proteid molecule profoundly, yielding products which are for the most part far removed from the original substance, and which are themselves products of decomposition of the 'atomic complexes' above referred to; acids and aldehydes of the fatty, oxalic, and benzoic series and their nitrils, including hydrocyanic acid, ketones, amido-acids, carbon dioxid, and ammonia. With HNO_3 various nitro derivatives are obtained, and with Cl, Br, and I halid derivatives. By oxidation with $K_2Mn_2O_8$ an acid, oxyprotosulfonic, containing the sulfonic group, is formed, and by continued oxidation peroxyprotonic acid. In oxidation with $BaMn_2O_8$ guanidin is one of the products.

"Fusion with caustic alkalies also causes deep decomposition, the products being ammonia, mercaptan, fatty acids, amido fatty acids, tyrosin, indol, and skatol.

"By boiling with dilute mineral acids, or with $HCl + SnCl_2$, the proteids are hydrolyzed with formation of hydrogen sulfid, ethyl sulfid and ammonia as simple products, and amido-acids, hexon bases, pyrrolidin and oxypyrrolidin carboxylic acids, and melanoidins, the last-named being also products of decomposition of the melanins, substances to which the hair and other dark portions of the body owe their color. The amido-acids, including serin, tyrosin, and cystin, produced in this and other hydrolytic decompositions probably exist in the proteids as polypeptids, formed by the union of several amido-acid complexes.

"Considering the nitrogen which is split off, in more or less complex combination, on hydrolysis of proteids by boiling with dilute acids, it appears to have existed in the parent proteid in five forms of combination, corresponding to five classes of decomposition products: 1, Easily separable, so-called amino-nitrogen, given off as NH_3; 2, Urea-forming nitrogen, in the guanidin remainder of argenin; 3, Basic nitrogen, or diamido-nitrogen, contained in basic nitrogen compounds, precipitable by phosphotungstic acid; 4, Monamido-nitrogen, in monamido-acids; 5, Humus nitrogen, in humus-like melanoidins, dark-colored, amorphous, nitrogenous remainders.

"The quantitative distribution of nitrogen in these five groups differs in different proteids: 1. Is entirely absent in protamins; 1 to 2 per cent in gelatin; 5 to 10 per cent in other animal proteids; 13 to 20 per cent in vegetable proteids. 2, In protamins 22 to 44 per cent; in histons 12 to 13 per cent; in gelatin 8 per cent; in other proteids 2 to 5 per cent. 3, In protamins 63 to 88 per cent; in histons 35 to 42 per cent; in other animal proteids 15 to 25 per cent; in vegetable proteids 5 to 37 per cent. 4, The greater

part of the nitrogen, 55 to 76 per cent, in proteids other than protamins is in this form. 5, Varies within wide limits.

"The sulfur, the amount of which varies greatly in different proteids, is given off on hydrolysis as cystin, cysteïn, *a*-thiolactic acid, mercaptans, and ethyl sulfid.

"The nitrogen-containing products of hydrolysis of proteids may be thus classified:

I. Aliphatic. A. Containing no sulfur:
   1, Guanidin remainder. $H_2N.C : NH_1$ (+ornithin=argenin);
   2, Monobasic monamido acids: glycocoll, alanin, amido-valerianic acid, leucin, serin;
   3, Dibasic monamido-acids: aspartic and glutamic;
   4, Monobasic diamido-acids: ornithin, lysin;
   B. Containing nitrogen and sulfur: Cystin, cysteïn;

II. Carbocyclic: phenylamidopropionic acid, tyrosin;

III. Heterocyclic: A. Pyrrol derivatives: pyrrolidin and oxypyrrolidin carboxylic acids;
   B. Glyoxalin derivatives (?): histidin;
   C. Indole derivatives: indol, skatol, tryptophane."

The amido-acids, although belonging to the different series, are, according to Fischer's views, supposed to be combined into more and more complex groupings. In the simplest combinations two or more molecules of the same or of different amido-acids combine with the elimination of water. This is the reverse of the hydrolytic process and results in Fischer's peptids. Protamin, the simplest of the proteids, yields a relatively simple series of amido-acids and according to Taylor's work, already referred to, is evidently a polypeptid of comparatively complex structure.

"All proteids except the protamins and some of the peptones contain sulfur. One fraction of this, referred to as 'loosely combined' sulfur, is given off as hydrogen sulfid by boiling with alkaline solutions. It is this fraction which causes the formation of a brown or black color, or even a black precipitate, when a proteid is heated with a solution of caustic alkali in the presence of lead acetate, in the 'sulfur test' for the proteids. The second fraction is not separable in this manner, but only, as a sulfate, by fusion with saltpeter and sodium carbonate, or, as a sulfid, by fusion with caustic potash. The ratio of loosely combined sulfur to total sulfur varies notably in different proteids, from $\frac{2}{3}$ in serum to $\frac{2}{5}$ in hemoglobin. It would appear from this constant difference in separability of different portions of sulfur from proteids that the molecules of these substances must contain at least two atoms of sulfur in different forms of combination. This conclusion, is, however, invalidated by the fact that both cystin and cysteïn only give off one-half of their sulfur, and that very slowly, by boiling with alka-

line solutions, yet the two atoms of sulfur in cystin are symmetrically combined, and the molecule of cysteïn contains but one sulfur atom.

"Many proteids, not only the glycoproteids, but also true albumins, as egg albumin, serum albumin, serum globulin, the nucleoproteids, etc., react with Molisch's reagent, and, on hydrolysis, split off a carbohydrate group, which is an amido-sugar, usually glucosamin, $CHO.CHNH_2(CHOH)_3CH_2OH$, probably existing in the proteid as a polysaccharid complex. Some of the nucleoproteids yield a pentose group, others lævulinic acid. Other proteids, as casein, myosin, and fibrinogen, yield no carbohydrate.

"The decomposition of proteids by the proteolytic enzymes, pepsin, trypsin, and papaïn, consists of a series of hydrolyses, and results first in the formation of albumoses and peptones, and later by trypsin, particularly of polypeptids, amido acids, hexon bases, tryptophane, amins, diamins, and ammonia. These changes occur in the processes of digestion."

The Pigments, etc. A number of pigments make their appearance in the body; for example, *bilirubin*, $C_{16}H_{18}N_2O_3$, is the common bile pigment. Its crystals are bluish-red in color and are probably derived from hematin of the blood. *Biliverdin*, $C_{16}H_{18}N_2O_4$, is an oxidation product of bilirubin.

Urochrome and *Urobilin* occur in bile and in urine; the latter is probably identical with *stercobilin*, which is found in the feces. *Uroerythrin* is one of the coloring matters of the urine. It is orange red and contains iron.

Melanin is a dark brown or black pigment which occurs especially in epidermal tissues, where it is associated with keratin. It is found in the lungs, bronchial glands, hair, choroid, skin, etc.; also in the urine and in melanotic diseases, *e.g.*, sarcoma. It is a transformation product of proteids, from which it can be derived by boiling proteid with sulphuric acid.

Lipochromes are pigments, usually yellow or yellowish-red, which are associated with fat, being almost always present in adipose tissue. Little is known about them, but they are thought to consist only of C, H, and O.

OILS AND FATS.

The animal oils and fats are for the most part mixtures of *tri-palmitin*, $C_3H_5(O.C_{16}H_{31}O)_3$, *tri-stearin*, $C_3H_5(O.C_{18}H_{35}O)_3$, and *tri-olein*, $C_3H_5(O.C_{18}N_{33}O)_3$, in different proportions. They are formed by the union of three molecules of fatty acid with one molecule of the triatomic alcohol, *glycerin*, $C_3H_5(OH)_3$, and are ethereal salts or esters of that alcohol. Palmitic acid is $C_{15}H_{31}COOH$, stearic acid is $C_{17}H_{35}COOH$; oleic acid is $C_{17}H_{33}COOH$. Human fat consists of a mixture of *tri-palmitin*, *tri-stearin*, and *tri-olein*, of which the two former contribute three-quarters of the whole. Olein is the only liquid constituent. The fat of milk (and butter) is tributyrin; butyric acid is $C_4H_8O_2$.

Fats are insoluble in water and in cold alcohol; soluble in hot alcohol, ether, and chloroform. Colorless and tasteless; easily decomposed or saponified by alkalies or superheated steam into glycerin and the fatty acids.

Certain of the **monatomic Fatty Acids** are found in the body, viz., *Formic* CH_2O_2, *acetic* $C_2H_4O_2$, and *propionic* $C_3H_6O_3$, present in sweat, but normally in no other human secretion. They have been found elsewhere in diseased conditions. *Butyric acid*, $C_4H_8O_2$, is found in milk and in sweat. Various others of these acids have been obtained from blood, muscular juice, feces, and urine.

Of the diatomic fatty acids, one acid, *Lactic acid*, $C_3H_6O_3$, exists in a free state in muscle-plasma, and is increased in quantity by muscular contraction, but is never contained in healthy blood.

Soaps. The fatty acids in combination with soda or potash, or similar bases, form *soaps* which are soluble in water, while the fats are not soluble.

CARBOHYDRATES.

The carbohydrates are bodies composed of C, H, and O, as aldehydes and ketols. They are classified as *monosaccharides*, dextrose, galactose, etc. These are the simplest molecules of the hexoses. They are sweet, odorless, soluble in water, and oxidize readily, hence their reducing power. They form crystalline osazones. They rotate polarized light. Their formula is $C_6H_{12}O_6$. *Disaccharides*, maltose, saccharose, lactose, etc. They are formed by the union of two simpler molecules and the elimination of a molecule of water. They have the formula $C_{12}H_{22}O_{11}$. And *polysaccharides*, glycogen, starch, dextrin, gum, etc. They are much less soluble, can be hydrolyzed into the simpler forms, and have the formula $(C_6H_{10}O_5)_n$.

Monosaccharides are especially soluble and polysaccharides are especially insoluble; monosaccharides and disaccharides do not give colored solutions with iodine, while polysaccharides do; monosaccharides and (except saccharose) disaccharides reduce Fehling's solution, while polysaccharides do not.

Of these the most important are:

Starch. It is contained in nearly all plants, and in many seeds, roots, stems, and some fruits. It is a soft white powder composed of granules having an organized structure, consisting of granulose (soluble in water) contained in a coat of *cellulose* (insoluble in water); the shape and size of the granules vary according to the source whence the starch has been obtained. It is not crystalline and will not dialyze. It is insoluble in cold water, in alcohol, and in ether; it is soluble after boiling for some time, and may be filtered, in consequence of the swelling up of the granulose, which bursts the cellulose coat, and, becoming free, is entirely dissolved in water. This solution is a solution of soluble starch or amydin. It gives a blue color-

ation with iodine, which disappears on heating and returns on cooling. It is converted into maltose by diastase, and by boiling with dilute acids into dextrose.

Glycogen. Glycogen is a polysaccharide contained in the liver, and also present in all muscles, but especially in those of very young animals, in the placenta, in colorless corpuscles, and in embryonic tissues. It is sometimes called animal starch and gives many reactions proper to starch itself. It is freely soluble in water, and its solution looks opalescent; it gives a port-wine coloration with iodine, which disappears on heating and returns on cooling. It is precipitated by basic lead acetate and is insoluble in absolute alcohol and in ether. It exists in the liver during life, but very soon after death is changed into sugar. It may be prepared by grinding muscle with sand till a pasty mass is formed, boiling the mass in water for twenty minutes, filtering, and then precipitating the glycogen from the filtrate by adding a little more than an equal quantity of 95 per cent alcohol. It is converted into sugar by diastase ferments, or into dextrose by boiling with dilute acids.

Dextrin. This substance is made in commerce by heating dry potato-starch to a temperature of 400°. It is also produced in the process of the conversion of starch into sugar by diastase, and by the salivary and pancreatic ferments. A yellowish amorphous powder, soluble in water, but insoluble in absolute alcohol and in ether. It corresponds almost exactly in tests with glycogen; but one variety (achroo-dextrin) does not give the port-wine coloration with iodine.

Cane-Sugar, or **Saccharose.** It is contained in the juices of many plants and fruits, and is extracted from the sugar-cane, from beet-root, or from the maple. It is crystalline and is precipitated from concentrated solutions by absolute alcohol. It has no power of reducing copper salts on boiling. It is dextro-rotatory. It is not subject to alcoholic fermentation, until by inversion it is converted into glucose, it chars on addition of sulphuric acid, and on heating with potassium or sodium hydrate.

Lactose. Lactose is the chief carbohydrate of milk. It is less soluble in water than glucose; it is not sweet, and is gritty to the taste; but it is insoluble in absolute alcohol. In digestion it yields a molecule of dextrose and a molecule of galactose. It undergoes alcoholic fermentation with extreme difficulty; gives the tests similar to glucose, but less readily. It is dextro-rotatory + 59°.

Maltose. This sugar is produced by the action of the saliva and pancreatic juice on starch. It is also formed by the action of malt upon starch by the action of the ferment diastase. It is converted into dextrose by dilute sulphuric acid. It is dextro-rotatory; ferments with yeast; reduces copper salts; and crystallizes in fine needles.

Dextrose, or **Glucose.** Dextrose occurs widely diffused in the

vegetable kingdom, in diabetic urine, in the blood, etc. It is usually obtained from grape-juice, honey, beet-root, or carrots. As prepared, it really is a mixture of two isomeric bodies, *Dextrose* or grape-sugar, which turns a ray of polarized light to the right (+ 56°), and *Lævulose* or fruit-sugar, which turns the ray to the left.

It is easily soluble in water and in alcohol; not so sweet as cane-sugar; the relation of its sweetness to that of cane-sugar is as 3 to 5. It is not so easily charred by strong sulphuric acid as cane-sugar. It is not entirely soluble in alcohol. It undergoes alcoholic fermentation with yeast.

Dextrose is the characteristic carbohydrate of the blood. It has the power of reducing the salts of silver, bismuth, mercury, and copper, either to the form of the metal in the first three cases, or to the form of the suboxide in the case with cuprous salts. Upon this property the chief tests for the sugar, *e.g.*, Trommer's and Böttcher's, depend. It undergoes alcoholic fermentation with yeast, and lactic-acid fermentation with bacteria lactis. It forms caramel when strongly heated, and is also charred with strong acids.

Lævulose is one of the products of the decomposition of cane-sugar by means of dilute mineral acids, or by means of the ferment *invertin* in the alimentary canal. It reacts to the same test as glucose, but is non-crystallizable, and is lævo-rotatory. It is soluble in water and in alcohol. Its compound with lime is solid, whereas that with dextrose is not.

Galactose. This monosaccharid is formed from lactose by the action of dilute mineral acids, or inverting ferments; it may also be obtained from cerebrin. It undergoes alcoholic fermentation, and reduces copper salts to the suboxide.

Inosite. Inosite occurs in the heart and voluntary muscles, as well as in beans and other plants. It crystallizes in the form of large colorless monoclinic tables, which are soluble in water, but insoluble in alcohol or ether. It has the formula of glucose, but is not a sugar. Inosite may be detected by evaporating the solution containing it nearly to dryness, and by then adding a small drop of solution of mercuric nitrate, and afterward evaporating carefully to dryness, a yellowish-white residue is obtained; on further cautiously heating, the yellow changes to a deep rose-color, which disappears on cooling, but reappears on heating. If the inosite be almost pure, its solution may be evaporated nearly to dryness. After the addition of nitric acid, the residue mixed with a little ammonia and calcium chloride, and again evaporated, yields a rose-red coloration.

INORGANIC PRINCIPLES.

Salts. The inorganic principles of the human body are numerous. They are derived, for the most part, directly from food and drink, and pass through the system unaltered. But some salts are decomposed on their

way, as chloride of sodium, of which only four-fifths of the quantity ingested are excreted in the same form. Some are newly formed within the body—as, for example, a part of the sulphates and carbonates.

Much of the inorganic saline matter found in the body is a necessary constituent of its structure, as necessary in its way as albumin or any other organic principle. Another part is important in regulating or modifying various physical processes, as absorption, solution, and the like. A part must be reckoned only as matter which is, so to speak, accidentally present, whether derived from the food or the tissues, and which will, at the first opportunity, be excreted from the body. The principal salts present in the body are:

Sodium and *Potassium Chlorides.* These salts are present in nearly all parts of the body. The former seems to be especially necessary, judging from the instinctive craving for it on the part of animals in whose food it is deficient, and from the diseased condition which is consequent on its withdrawal. The quantity of sodium chloride in the blood is greater than that of all its other saline ingredients taken together, but it is present chiefly in the fluids of the body. In the tissues, the muscles for example, the quantity of sodium chloride is less than that of the chloride of potassium, which forms a constant ingredient of protoplasm.

Calcium Fluoride. It is present in minute amount in the bones and teeth, and traces have been found in the blood and some other fluids.

Calcium, Potassium, Sodium, and Magnesium Phosphates. These phosphates are found in nearly every tissue and fluid. In some tissues—the bones and teeth—the phosphate of calcium exists in very large amount. The phosphate of calcium is intimately incorporated with the organic basis or matrix, but it can be removed by acids without destroying the general shape of the bone. After the removal of its inorganic salts, a bone is left soft, tough, and flexible.

Potassium and sodium phosphates, with the carbonates, maintain the alkalinity of the blood.

Calcium Carbonate. It occurs in bones and teeth, but in much smaller quantity than the phosphate. It is found also in some other parts. The small concretions of the internal ear (otoliths) are composed of crystalline calcium carbonate, and form the only example of inorganic crystalline matter existing as such in the body.

Potassium and Sodium Carbonates and Sulphates. These are found in the blood and most of the secretions and tissues.

Silicon. A very minute quantity of silica exists in the urine and in the blood. Traces of it have been found also in bones, hair, and some other parts.

Iron. The especial place of iron is in hemoglobin, the coloring-matter of the blood, of which a full account will be given with the chemistry of the blood. Iron is found, in very small quantities, in the ashes of bones, mus-

cles, and many tissues, and in lymph and chyle, albumin of serum, fibrin, bile, milk, and other fluids. A salt of iron, probably a phosphate, exists in the hair, black pigment, and other deeply colored epithelial or horny substances.

Water. Water forms a large proportion, more than two-thirds, of the weight of the whole body. Its relative amount in some of the principal solids and fluids of the body is shown in the following table (from Robin and Verdeil):

Quantity of Water in Per Cent.

Teeth	10.0	Bile	88.0
Bones	13.0	Milk	88.7
Cartilage	55.0	Pancreatic juice	90.0
Muscles	75.0	Urine	93.6
Ligament	76.8	Lymph	96.0
Brain	78.9	Gastric juice	97.5
Blood	79.5	Perspiration	98.6
Synovia	80.5	Saliva	99.5

In all the fluids and tissues of the body—blood, lymph, muscle, gland, etc.—water acts the part of a general solvent, and by its means alone circulation of nutrient matter is possible. It is the medium also in which all fluid and solid aliments are dissolved before absorption, as well as the means by which all, except gaseous, excretory products are removed. All the various processes of secretion, transudation, and nutrition depend of necessity on its presence for their performance.

The greater part, by far, of the water present in the body is taken into it as such from without, in the food and drink. A small amount, however, is the result of the chemical union of hydrogen with oxygen in the oxidations of the body.

The loss of water from the body is intimately connected with excretion from the lungs, skin, and kidneys, and, to a less extent, from the alimentary canal. The loss from these various organs may be thus apportioned (quoted by Dalton from various observers):

From the Alimentary canal (feces)	4	per cent
" Lungs	20	"
" Skin (perspiration)	30	"
" Kidneys (urine)	46	"
	100	

LABORATORY EXPERIMENTS ON THE CHEMISTRY OF THE BODY.

Proteid General Reactions. Certain tests depending on the presence of one or more of the constituent groups in the proteid molecule, while not conclusive each in itself, when taken together serve for proteid

identification. Dilute some white of egg with ten volumes of water, filter off the precipitated globulin, and use the egg albumin in the following tests:

1. **Color Reactions of Proteids.** *a. Xanthoproteic.* Add concentrated nitric acid to 2 c.c. of the egg albumin in a test tube, a lemon-yellow color appears on gently heating. Add excess of ammonia, the color deepens to orange, or with potassium hydrate to reddish brown. Egg albumin is also precipitated by the acid, but peptone gives only the color change. This reaction depends upon the presence of the tyrosin nucleus, or that of indol, in the proteid molecule.

b. Millon's reaction. Millon's reagent (mercuric and mercurous nitrate in weak nitric-acid solution) added to albumin solution gives a white coagulum in the cold which turns purple-red on heating to 70° C. or more. The reaction is due to the tyrosin grouping.

c. The biuret reaction. Excess of sodium or potassium hydrate with a few drops of 2 per cent copper sulphate in albumin solution when heated gives a violet color. Albumoses give a pinkish violet, and peptones a pink color in this reaction, but care must be taken not to use an excess of copper sulphate. The reaction seems to depend on the presence of the polypeptid groups.

d. Adamkiewicz reaction. If dilute glyoxylic acid be added to proteid solution, and concentrated sulphuric acid run under the mixture, a ring of colors is produced at the junction of the layers when gentle heat is applied; red at the bottom, then green and violet. When shaken the whole becomes violet. The reaction depends upon the tryptophane group.

2. **Precipitations.** *a. Acid precipitation.* Proteids form insoluble salts with *tannic* acid, *phospho-tungstic* acid, *hydroferrocyanic* acid, *picric* acid, etc. The proteid is changed in the reaction and cannot be recovered by breaking up the salt. Strong mineral acids, *hydrochloric* acid, *nitric* acid, etc., precipitate proteids, but the peptones are soluble in excess.

b. Heavy metal precipitation. Proteids form insoluble compounds with *mercuric chloride, lead acetate, copper sulphate, silver nitrate,* etc.

c. Alcohol. Proteids are precipitated and coagulated by an excess of alcohol. Peptone alone is recoverable from alcoholic precipitation.

d. Heat coagulations. Make the egg-albumin very faintly acid with 2 per cent acetic and heat to boiling, a white cloudy coagulum appears. Albumoses and peptones are not heat-coagulated.

e. Precipitation by neutral salts. Add crystals of ammonium sulphate to egg albumin solution to saturation, a white flocculent precipitate forms. The precipitate can be recovered as unchanged albumin by removing the excess of salt by dialysis.

Reactions Characteristic of Individual Proteids. The proteid groups most often met by the student are the *albumins, globulins, albuminates, albumoses, peptones, enzyme-coagulated proteid,* and *heat-coagulated proteid.* Each has certain characteristics.

3. **Albumins.** *a. Solubility in water and in neutral salts.* Test each statement. Albumin is soluble in distilled water, dialyze out the traces of salts. It is soluble in saturated sodium chloride and saturated magnesium sulphate. It is insoluble in saturated ammonium sulphate.

b. Heat coagulation. Mount a test tube containing 5 c.c. faintly acid egg-albumin in a 500 c.c. beaker of water which is supported by a gauze and ring stand. Suspend a thermometer bulb in the middle of the albumin solution. Gradually heat the beaker of water, stirring constantly, thus uniformly heating the albumin. Coagulation takes place at from 73° to 75° C., but turbidity a little earlier.

4. **Globulins.** *a. Solubility in water and in neutral salts.* Test the following statements, using serum globulin. Globulin is insoluble in distilled water. It is soluble in dilute neutral salt solutions—sodium chloride, magnesium sulphate, ammonium sulphate. Globulin is precipitated by adding sodium chloride or magnesium sulphate to complete saturation. Fibrinogen is precipitated by half-saturated magnesium sulphate. Globulins are precipitated by adding to their solution an equal volume of saturated ammonium sulphate, *i.e.*, by half-saturated solution.

b. Heat coagulation. Test the temperature at which globulins are heat coagulated by the method described above, on a sample of salted plasma for fibrinogen which coagulates at 56° C., and on serum globulin which coagulates at 73° C.

5. **Albuminates.** Digest egg albumin in 0.2 per cent hydrochloric acid for an hour and test:

a. Solubility. It is insoluble in neutral solutions and in saturated neutral salts, but soluble in dilute acids and alkalies.

b. Heat coagulation. It is not coagulated by heat.

6. **Albumoses and Peptones.** These proteids are formed in the alimentary canal in the process of digestion under the influence of the enzymes, pepsin and trypsin. Make a 5 per cent solution of Armour's peptone (which contains chiefly albumoses) and test:

a. Heat coagulation. These proteids are not coagulated.

b. Alcohol. When added to excess, a precipitate occurs, but when collected on a filter the precipitate may be redissolved in water.

c. General proteid reactions. These proteids fail to give many of the precipitations, but give the color changes. The biuret test yields a rose pink color.

d. Neutral salts. Albumoses are insoluble in saturated ammonium sulphate. Filter and test the filtrate for proteid. It gives the biuret test. This is due to peptones which are soluble in all salt solutions.

7. **Ferment and Heat-Coagulated Proteids.** Boiled egg white should be used for the example of the former, and fibrin for the latter. Test for the color reactions, experiment 1, which they both give. These pro-

teids are insoluble in the usual solvents, though fibrin is slightly soluble in 10 per cent sodium chloride.

Carbohydrate Reactions. The carbohydrate representatives that should be examined are:

8. **Starch.** Make a solution of starch by boiling 1 gram of starch in 100 c.c. of distilled water and test.

a. Iodine test. Shake up three or four drops of dilute iodine solution with 2 c.c. starch. A deep blue color appears. The color is discharged in dilute alkali and reappears on acidifying again. Heat also discharges the color.

b. Fehling's test. Commercial starch often contains reducing sugar. Boil 2 c.c. of starch solution with 1 c.c. of fresh Fehling. If a reddish-yellow precipitate settles on standing, the starch contains reducing sugar as an impurity. Starch does not reduce copper in the presence of an alkali.

c. Hydrolysis of starch. Boil starch solution with 5 per cent sulphuric acid for fifteen minutes. Test with Fehling's solution, first neutralizing the excess of acid. A copious precipitate of cuprous oxide shows that the starch has been converted to reducing sugar.

9. **Dextrin.** Make a 5 per cent solution of dextrin in distilled water and test:

a. Iodine. This gives a rich reddish-brown color which is characteristic.

b. Fehling. Not reduced by dextrin.

10. **Dextrose.** Test a 5 per cent solution of dextrose:

a. Iodine test. No reaction.

b. Trommer's test. Add caustic soda in excess and a few drops of 2 per cent copper sulphate and boil, or use Fehling's solution. A reduction of the copper takes place. Barfoid's solution also is reduced by dextrose, but not by maltose.

11. **Glycogen.** Make up 10 c.c. of a 1 per cent solution of glycogen and repeat the tests:

a. Iodine. This gives a wine-red color very much like that given by dextrin. The color is discharged by heating, but reappears on cooling.

b. Lead acetate. It gives a precipitate, but one must guard against the presence of proteid as an impurity.

c. Trommer's test. Glycogen does not reduce copper.

The Fats. The common fats are the oleins, palmitins, and stearins. These are glycerin salts of the fatty acids. The animal fats are mixtures of these fats in different proportions.

12. **Neutral Fat.** *a. Melting-point.* Compare neutral olive oil, some fresh rendered lard, and some tallow. The former is fluid at ordinary room temperature. Determine the melting-points of the lard and of the tallow by the method of Wiley. Fill a test tube, one-half full of water and add a two-inch top layer of alcohol. Prepare a thin flake of fat and suspend it in the test tube at the dividing line of the water and alcohol. Insert the

bulb of a thermometer at the same level. Mount the test tube with the thermometer in a beaker on a ring stand, fill the beaker with water above the level of the content of the test tube, and gradually heat with stirring of the water in the beaker. At the melting temperature the flake of fat will run into a round drop.

b. Solubility. Fat is insoluble in water, but soluble in ether, chloroform, benzol, and in alcohol.

c. Saponification. Heat some fat in an evaporating-dish, add sodium hydrate, and boil. Saponification takes place. The soap is soluble in water. Add 25 per cent sulphuric acid to some of the soap, the fatty acid is liberated and collects on the surface of the solution.

13. **Fat Acids.** Collect some of the fatty acids, wash to remove excess of alkali, and dissolve in ether.

a. Acid reaction. Add ether solution of the fatty acid to neutral litmus, or to faintly alkaline phenolphthalein. The former turns red, and the red of the latter is discharged, the acid reaction.

b. Acrolein test. Evaporate the ether from 2 c.c. of the solution, add potassium bisulphate crystals to the acid in a test tube, and raise to a high heat over a bunsen. No acrolein is given off. Repeat on neutral fat and on glycerin. Both liberate the irritating fumes of acrolein.

14. **Emulsification.** *a.* Shake up neutral olive oil and water, no emulsion is formed and the oil quickly separates.

b. Add a couple of drops of fatty acid, a very good but temporary emulsion is now formed.

c. Use rancid fat, a temporary emulsion is formed.

d. Add a little soap to either of the above, *i.e.*, *c.* A good permanent emulsion is now formed.

15. **The Salts.** A goodly series of salts is present in the body, the most important elements of which are sodium, potassium, calcium, magnesium, and iron, as chlorides, sulphates, and phosphates. Burn 50 c.c. of blood at a dull red heat, take up in water and test:

a. Chlorides. Add 1 per cent nitrate of silver, a white precipitate, insoluble in nitric acid, soluble in ammonia, and reprecipitated by nitric acid.

b. Sulphates. Add barium chloride, a white precipitate, which quickly settles and is insoluble in nitric acid.

c. Phosphates. Add nitric acid and a few drops of 1 per cent ammonium molybdate, a yellow granular precipitate of phosphorus. It is soluble in ammonia, reprecipitated in nitric acid.

d. Calcium. Make a hydrochloric acid extract of the ash of blood above, add ammonia to excess, then a solution of ammonium oxalate, a delicate white precipitate where traces are present.

e. Iron. Add hydrochloric acid and a few drops of ferrocyanide of potassium. A blue color indicates the presence of iron.

PLATE II

VARIETIES OF LEUCOCYTES

a. *Polymorphonuclear Neutrophiles.* Note the varieties in size and shape of granules, the regular staining of the nuclei, the light space around them, their relatively central position in the cell.

b. *Myelocytes.* Note the identity of granules with those just described; the even, pale stain of nuclei, their position near the surface (edge) of the cell. The two cells figured indicate the usual variations in size of the whole cell.

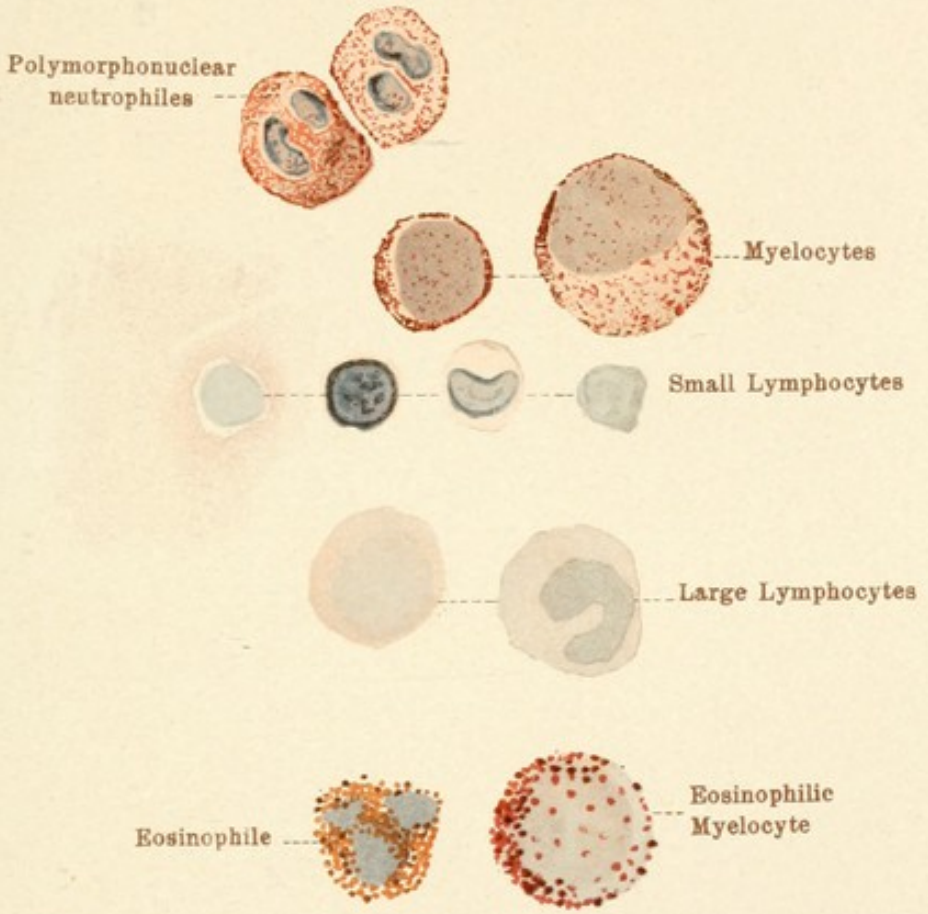
c. *Small Lymphocytes.* In the cell at the left note the transparent protoplasm; in the cell next to it note the very pale pink of protoplasm around the nucleus which is deeply stained, especially at the periphery. The next cell has an indented nucleus; its protoplasm relatively distinct. The cell on the extreme right shows no protoplasm and is probably necrotic. In all note *absence of granules* with this stain. With basic stains a blue network appears in the protoplasm.

d. *Large Lymphocytes.* Note the pale stain of nuclei and protoplasm, regularity of outline; indented nucleus in one. Every intermediate stage between these and the "*small*" lymphocytes occurs, and the distinction between them is arbitrary.

e. *Eosinophile.* Note regular shape, loose connection of granules, their copper color, their uniform and relatively large size, and spherical shape.

f. *Eosinophilic Myelocyte.* Note similarity to the ordinary myelocytes *b*, except as regards granules. Color of granules may be, as in *e*, ordinary eosinophile.

All the above were stained with the Ehrlich triacid stain, and drawn with camera lucida. Oil immersion objective $\frac{1}{12}$ and ocular No. iii. of Leitz. (Cabot.)



Varieties of Leucocytes.

R. C. Cabot fec. Lith. Anst. v. E. A. Funke. Leipzig.

CHAPTER IV

THE BLOOD

THE blood is the fluid medium of which all the tissues of the body are nourished. By means of the blood materials absorbed from the alimentary canal as well as oxygen taken from the air in the lungs are carried to the tissues, while substances which result from the metabolism of the tissues are carried to the excretory organs to be removed from the body. The blood also acts as a medium of exchange for products of glandular activity between the various tissues themselves, internal secretions, and it is a factor in the regulation of body temperature. The blood is a somewhat viscid fluid, and in man and in all other vertebrate animals, with the exception of two of the lowest, is red in color. The exact color of the blood is variable; that taken from the systemic arteries, from the left side of the heart and from the pulmonary veins is of a bright scarlet hue; that obtained from the systemic veins, from the right side of the heart, and from the pulmonary artery is of a much darker color, which varies from bluish-red to reddish-black. At first sight the red color appears to belong to the whole mass of blood, but on further examination this is found not to be the case. In reality blood consists of an almost colorless fluid, called *plasma* or *liquor sanguinis*, in which are suspended numerous minute masses of protoplasm, called *blood-corpuscles*. The corpuscles are of the two varieties, the white ameboid corpuscles, or leucocytes, and the red corpuscles, erythrocytes. The latter compose by far the larger mass of blood-cells and contain the red pigment, hemoglobin, to which the color of the blood is due.

The plasma or fluid part of the blood is a remarkably complex chemical mixture. It is kept in constant rapid circulation through the blood-vessels of the body and is, therefore, thoroughly mixed and homogeneous in character.

Quantity of the Blood. The quantity of blood in any animal under normal conditions bears a fairly constant relation to the body weight. The amount of blood in man averages $\frac{1}{12}$ to $\frac{1}{14}$ of the body weight. In other mammals the proportion of blood is also fairly constant, varying from $\frac{1}{12}$ to $\frac{1}{20}$ of the body weight. In many of the lower vertebrates the relative quantity of blood is very much less.

An estimate of the quantity in man which corresponded very nearly with this proportion has been more than once made by methods illustrated by the following data: A criminal was weighed before and after decapita-

tion; the difference in the weight representing the quantity of blood which escaped. The blood-vessels of the head and trunk were then washed out by the injection of water until the fluid which escaped had only a pale red or straw color. This fluid was then also weighed, and the amount of blood which it represented calculated by comparing the proportion of solid matter contained in it with that of the first blood which escaped on decapitation. Two experiments of this kind gave precisely similar results (Weber and Lehmann).

This quantity of blood is distributed in the different parts of the body, chiefly in the muscles, the liver, the heart, and larger blood-vessels, as shown by the following figures determined on the rabbit by Ranke (from Vierordt):

	Per cent.
Spleen	0.23
Brain and cord	1.24
Kidney	1.63
Skin	2.10
Abdominal viscera	6.30
Cartilage	8.24
Heart, lungs, and large blood-vessels	22.76
Resting muscle	29.20
Liver	29.30

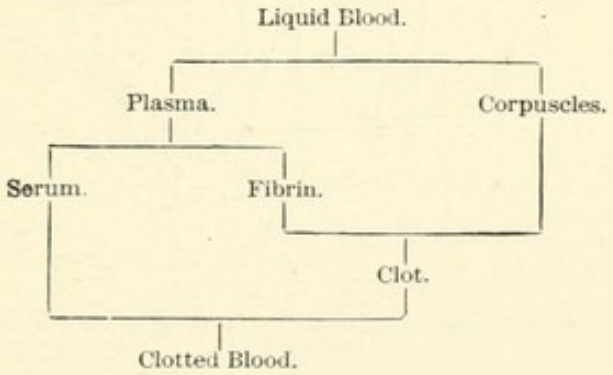
It should be remembered, in connection with these estimations, that the quantity of the blood must vary very considerably, even in the same animal, with the amount of both the ingesta and egesta of the period immediately preceding the experiment. It has been found, for example, that the quantity of blood obtainable from the body of a fasting animal rarely exceeds a half of that which is present soon after a full meal.

COAGULATION OF THE BLOOD.

The most characteristic property which the blood possesses is that of *clotting* or *coagulating*. This phenomenon may be observed under the most favorable conditions in blood which has been drawn into an open vessel. In about two or three minutes, at the ordinary temperature of the air, the surface of the fluid is seen to become semi-solid or *jelly-like*, and this change takes place, in a minute or two afterward, at the sides of the vessel in which it is contained and then quickly extends throughout the entire mass. The time which is occupied in these changes is about eight or nine minutes. The solid mass is of exactly the same volume as the previously liquid blood, and adheres so closely to the sides of the containing vessel that if the latter be inverted none of its contents escape. The solid mass is the *crassamentum* or *clot*. If the clot be watched for a few minutes, drops of a light, straw-colored fluid, the *serum*, may be seen to make its appearance on the surface, and, as it becomes greater and greater in amount, to form a complete super-

ficial stratum above the solid clot. At the same time the fluid begins to transude at the sides and at the under surface of the clot, which in the course of an hour or two floats in the liquid. The appearance of the serum is due to the fact that the clot contracts, thus squeezing the fluid out of its mass. The first drops of serum appear on the surface about eleven or twelve minutes after the blood has been drawn; and the fluid continues to transude for from thirty-six to forty-eight hours.

The clotting of blood is due to the development in the plasma of an insoluble substance called *fibrin*. This fibrin forms threads or strands through the mass in every direction. The strands adhere to each other wherever they come in contact, thus forming a very dense tangle and meshwork which incloses within itself the blood-corpuscles. The clot when first formed, therefore, includes the whole of the blood in an apparently solid mass, but soon the fibrinous meshwork begins to contract and the serum is squeezed out. When a large part of the serum has been squeezed out the clot is found to be smaller, but firmer and harder, as it is now made up largely of fibrin and blood-corpuscles. Thus in coagulation there is a rearrangement of the constituents of the blood; liquid blood being made up of plasma and blood-corpuscles, and clotted blood of serum and clot.



The rapidity with which coagulation takes place varies greatly in different animals and at different times in the same animal. Where coagulation is very slow the red corpuscles, which are somewhat heavier than plasma, often have time to settle considerably before the fibrin is formed. If the blood is rapidly cooled to something approaching 0° C. then the clot is very greatly delayed. Horse's blood is particularly favorable for demonstrating this point. In it clotting occurs so slowly that very often the red corpuscles will completely settle out, and when the blood is again warmed and the clotting takes place there is a superficial stratum differing in appearance from the rest of the clot, and is of a grayish-yellow color. This is known as the *buffy coat* or *crusta phlogistica*. The buffy coat, produced in the manner just described, commonly contracts more than the rest of the clot, on account of the absence of colored corpuscles from its meshes. When the clot is allowed to stand the white corpuscles migrate to the surface by ameboid movement,

often in such numbers that they form a distinct superficial layer, grayish-white in appearance.

That the clotting of blood is due to the gradual appearance in it of fibrin may be easily demonstrated. For example, if recently drawn blood be whipped with a bundle of twigs or wires, the fibrin may be withdrawn from the blood before it can entangle the blood-corpuscles within its meshes, as it adheres to the twigs in stringy threads relatively free from corpuscles. The blood from which the fibrin has been withdrawn no longer exhibits the power of spontaneous coagulability and it is now called *defibrinated blood.* Although these facts have long been known, the closely associated problem as to the exact manner in which fibrin is formed is by no means so simple.

Fibrin is derived from the plasma. Pure plasma may be procured by delaying coagulation in blood by keeping it at a temperature slightly above

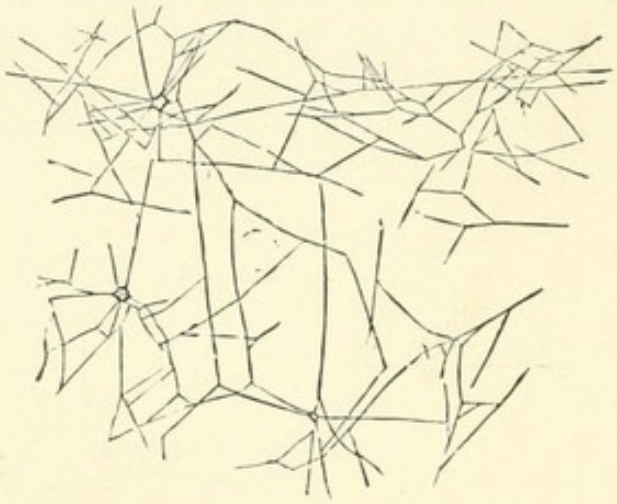


FIG. 107.—Reticulum of Fibrin, from a Drop of Human Blood, after Treatment with Rosanilin. (Ranvier.)

freezing point, until the colored corpuscles have subsided to the bottom of the containing vessel. The blood of the horse is specially suited for the purposes of this experiment. A portion of the colorless supernatant plasma, if decanted into another vessel and exposed to the ordinary temperature of the air, will coagulate, producing a clot similar in all respects to blood clot, except that it is colorless from the absence of red corpuscles. If some of the plasma be diluted with twice or three times its bulk of normal saline solution (0.9 per cent), coagulation is delayed, and the stages of the gradual formation of fibrin in it may be conveniently watched. The viscidity which precedes the complete coagulation may be actually seen to be due to the formation of fibrils of fibrin—first of all at the edge of the fluid-containing vessel, and then gradually extending throughout the mass. If a portion of plasma, diluted or not, be whipped with a bundle of twigs the fibrin may be obtained as a solid, stringy mass, just in the same way as from the entire

blood, and the resulting fluid no longer retains its power of spontaneous coagulability.

Theories of Coagulation. It is evident that the blood plasma contains some substance or substances which take part in the formation of fibrin. By numerous investigations it has been found that the direct antecedent of the fibrin is the proteid substance, *fibrinogen*. This fibrinogen exists in the blood plasma at all times, but is somewhat increased under certain conditions. The fibrinogen is reacted on by another substance known as *thrombin*, or by the historical term *fibrin ferment*. We shall not present the numerous theories which have been held concerning blood coagulation, many of which have been more or less disproven, but shall try to present

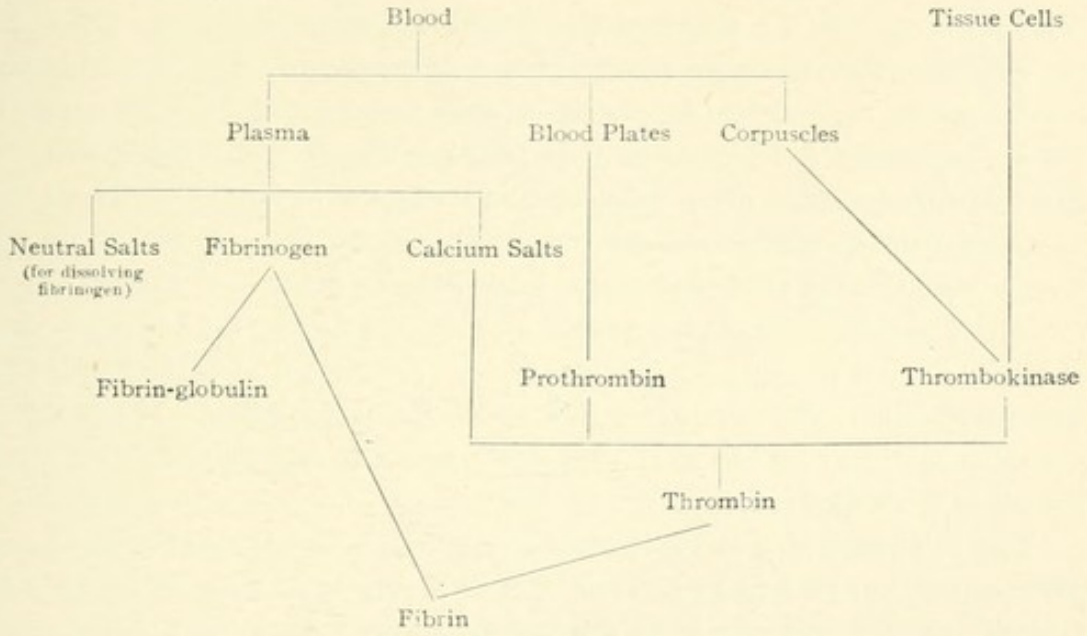


FIG. 108.—Schema of Coagulation.

the condensed statement of the present explanations of this intricate phenomenon. One may start from the statement that the fibrinogen of the plasma when acted upon by the thrombin, also of the plasma, produces an insoluble substance, fibrin. The chief interest centers around the origin and character of the fibrinogen, the origin and nature of the thrombin, and the conditions which influence its activity.

The *fibrinogen* is present in blood plasma of the circulating blood of the body at all times. It can be separated from plasma by various chemical means, and when purified can be made to form fibrin under proper conditions. All observers are agreed that this proteid is the immediate precursor of the insoluble fibrin. Its origin in the blood has been traced with some degree of certainty to the disintegration of the white blood-corpuscles.

The *thrombin* is the substance which reacts on the fibrinogen in the processes of fibrin formation. It does not exist in the living blood-vessels, or at

least is present only in minute traces, but makes its appearance immediately the blood is drawn. Its origin is therefore of peculiar interest.

It has been claimed by some, notably Peckelharing, that thrombin is a calcium compound. At any rate, it is definitely proven that calcium is a necessary element in the formation of the clot.

The substance thrombin, fibrin ferment, quickly appears in considerable quantity when blood is drawn under ordinary conditions. Its appearance is due to at least three antecedent substances, *prothrombin* (thrombogen), *calcium*, and *thrombokinase*. The sources of these substances and the part taken by each in the process of coagulation are as follows: If blood be drawn, centrifugalized, and the blood plates separated, freed from plasma, and suspended in water, their solution will cause the formation of fibrin from fibrinogen in the presence of calcium and thrombokinase. The blood platelets are, therefore, the source of the thrombogen. The thrombokinase can be traced to its origin in the tissue cells and the formed elements of the blood, especially the leucocytes. If blood is drawn from the vessels with due precautions not to allow it to come in contact with the cut vessel, or other tissue, clotting is very much delayed. The plasma if separated by the centrifuge will remain unclotted for a long time as shown by Howell for the terrapin's plasma. This plasma will quickly clot at any time if a few drops of tissue extract in salt solution be added. A solution of extract of washed white corpuscles acts to increase the rapidity of coagulation. If precautions are taken to draw the blood in such a manner as to remove the calcium from the plasma, no clot is formed.

The calcium which exists in solution in the plasma to the extent of 0.026 per cent can be removed by precipitation with oxalate solution, or by fluorides. Oxalate plasma contains both prothrombin and thrombokinase, and whenever calcium chloride is added to slight excess coagulation takes place. In fluoride plasma one must add both calcium and thrombokinase as that substance seems to prevent the setting free of thrombokinase from the corpuscles. The prothrombin is not interfered with by fluoride.

In a word, one may say that the coagulation of the blood takes place because of the formation of fibrin from fibrinogen by the action of thrombin. The fibrinogen is constantly present in the plasma. The thrombin is formed by the interaction of three substances, prothrombin, thrombokinase, and calcium. The prothrombin arises chiefly from the disintegration of the blood platelets when the blood leaves the blood-vessels. The thrombokinase originates in tissue cells of the blood and of the organs of the body in general. The calcium is present in the blood plasma at all times.

Conditions Affecting Coagulation. From the preceding discussion it is evident that the rapidity of the coagulation of the blood will be influenced by anything that will influence the formation of the fibrin factors or their interaction. The most important influences are the following:—

Temperature. Cold retards coagulation. Gentle warmth, 40° C., hastens but a temperature above 56° C. destroys clotting, since that temperature heat-coagulates the fibrinogen.

Contact with Foreign Bodies. Such contact hastens clotting. This is due to the influence of such bodies on the formation of fibrin factors, especially the substances that arise from the disintegration of the leucocytes.

Condition of the Blood-Vessel Walls. Intravascular clotting often takes place upon injury of the endothelial lining of the blood-vessel, probably from the liberation of thrombokinase in quantity too great for elimination by the healthy portion of the wall. The healthy endothelium no doubt is an important factor in eliminating the small amounts of the fibrin factors that must be constantly forming. The open wounds and lacerations of tissue that accompany the loss of blood by accident are the very conditions most favorable to clotting, since large amounts of tissue extract, thrombokinase, are formed under these conditions.

Neutral Salts. The addition of neutral salts in the proportion of 2 or 3 per cent and upward. When added in large proportions, most of these saline substances prevent coagulation altogether. Coagulation, however, ensues on dilution with water. The time during which salted blood can be thus preserved in a liquid state, and coagulated by the addition of water, is quite indefinite.

Oxalates and Fluorides. These and other precipitants of calcium prevent clotting by removing this substance.

Peptone. The injection of commercial peptone in the blood-vessels of an animal to the extent of 0.5 gram of peptone per kilo weight of the body of the animal will deprive the blood of the power of coagulation. If a smaller quantity be injected the coagulation of the blood will be delayed. If peptone blood is drawn and centrifuged, the plasma obtained, which is called *peptone plasma*, can be made to coagulate by diluting sufficiently with water and letting it stand a long time. Peptone plasma in the blood-vessels of the animal gradually regains the power to coagulate.

MORPHOLOGY OF THE BLOOD.

The corpuscles floating in the fluid plasma of the blood, when separated by a centrifugal machine are found to make up 45 to 50 per cent of the total mass of the blood. These corpuscles, or formed elements, are of three varieties, the red corpuscles or *erythrocytes*, the white corpuscles *leucocytes*, and the blood platelets which have been called *thrombocytes*.

Red Corpuscles or Erythrocytes. Human red blood-corpuscles are circular, biconcave discs with rounded edges, from 7 μ to 8 μ in diameter, and about 2 μ in thickness. When viewed singly they appear of a pale yellowish tinge; the deep red color which they give to the blood being ob-

servable in them only when they are seen *en masse*. They are composed of a colorless, structureless, and transparent filmy framework or *stroma*, infiltrated in all parts by the red coloring matter, the *hemoglobin*. The *stroma* is tough and elastic, so that as the corpuscles circulate they admit of elongation and other changes of form in adaptation to the vessels, yet recover their natural shape as soon as they escape from compression.

Number and Character of the Red Corpuscles. The normal number of red blood-cells in a cubic millimeter of human blood was estimated by Welcker, in 1854, to be 5,000,000 in men and 4,500,000 in women. Numerous recent observations, however, have shown that these estimates are a little low, especially in men, and the average number has been placed by different authorities at various points between 5,000,000 and 5,500,000. Still the original numbers as given by Welcker are accepted at the present day as being sufficiently accurate for ordinary purposes. It has been also shown that there are many distinct physiological variations in the number, depending

FIG. 109.

FIG. 110.

FIG. 109.—Red Corpuscles in Rouleaux. The rounded corpuscles are white or uncolored.

FIG. 110.—Corpuscles of the Frog. The central mass consists of nucleated colored corpuscles. The other corpuscles are two varieties of the colorless form.

on the time of day, digestion, sex, etc. The number of red cells usually diminishes in the course of each day, while the leucocytes increase in number. It has been suggested that this is due to the influence of digestion and exercise.

It has generally been found that within half an hour or an hour after a full meal the number of red cells begins to diminish, and that this keeps up for from two to four hours, when it is followed by a gradual rise to the normal. The usual fall is 250,000 to 750,000 per cubic millimeter. These results are most marked after a largely fluid meal, and are probably due to dilution of the blood as a result of the absorption of fluids. In animals the number of red cells is increased by fasting, but in man the results are variable, some authorities claiming an increase and others a decrease. In childhood there

is no difference between the sexes in the number of red cells per cubic millimeter, but after menstruation is established a relative anemia develops in women. Welcker's original estimate placed the difference at 500,000 per cubic millimeter, and these figures have been generally accepted, though Leichtenstein asserts that the difference is 1,000,000.

Menstruation in healthy subjects has practically no effect, as not more than 100–200 cubic centimeters of blood are lost normally in the course of

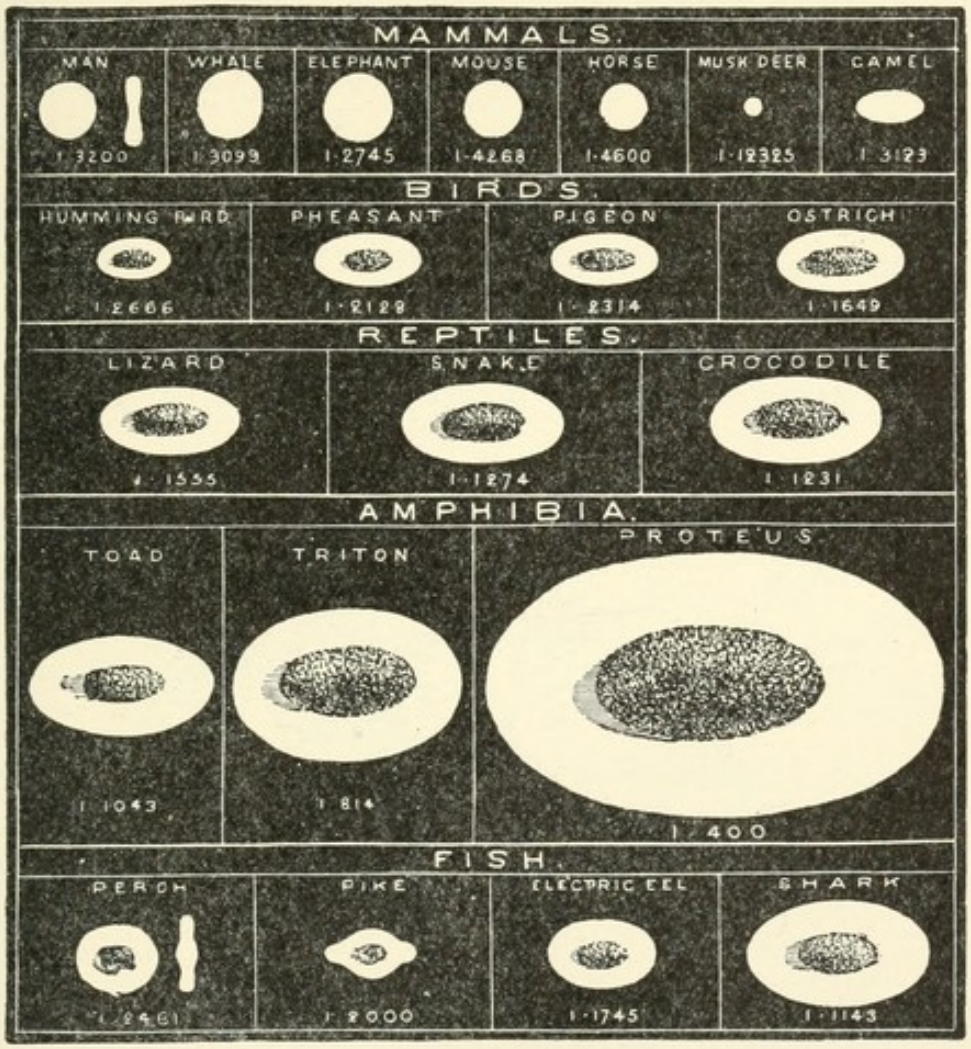


FIG. 111.—The Illustration is Somewhat Altered from a Drawing by Gulliver, in the Proceed. Zool. Society, and exhibits the typical characters of the red blood-cells in the main Divisions of the Vertebrata. The fractions are those of an inch, and represent the average diameter. In the case of the oval cells, only the long diameter is here given. It is remarkable, that although the size of the red blood-cells varies so much in the different classes of the vertebrate kingdom, that of the white corpuscles remains comparatively uniform, and thus they are, in some animals, much greater, in others much less, than the red corpuscle existing side by side with them.

several days. Under such circumstances the normal diminution of red cells per cubic millimeter is probably less than 150,000, though Sfameni has placed the loss at about 225,000. In fact an increase has been claimed. The leucocytes are slightly increased during menstruation. It is now the general opinion that pregnancy has little or no effect on the number of red cells, and

that any anemia must be due to abnormal conditions. Post-partum anemia should not last longer than two weeks.

The red corpuscles are not all alike. In almost every specimen of blood a certain number of corpuscles smaller than the rest may be observed. They are termed *microcytes*, or *hematoblasts*, and are probably immature corpuscles.

A peculiar property of the red corpuscles, which is exaggerated in inflammatory blood, may be here again noticed, *i.e.*, their great tendency to adhere together in rolls or columns (rouleaux), like piles of coins. These rolls quickly fasten together by their ends, and cluster; so that, when the blood is spread out thinly on a glass, they form a kind of irregular network, with crowds of corpuscles at the several points corresponding with the knots of the net, figure 109. Hence the clot formed in such a thin layer of blood looks mottled with blotches of pink upon a white ground.

The red corpuscles are constantly undergoing disintegration in different parts of the circulatory system, particularly in the spleen. The liberated hemoglobin contributes to the formation of the bile pigments in the liver.

Development of the Red Blood-Corpuscles.—The first formed blood-corpuscles of the human embryo differ much in their general characters

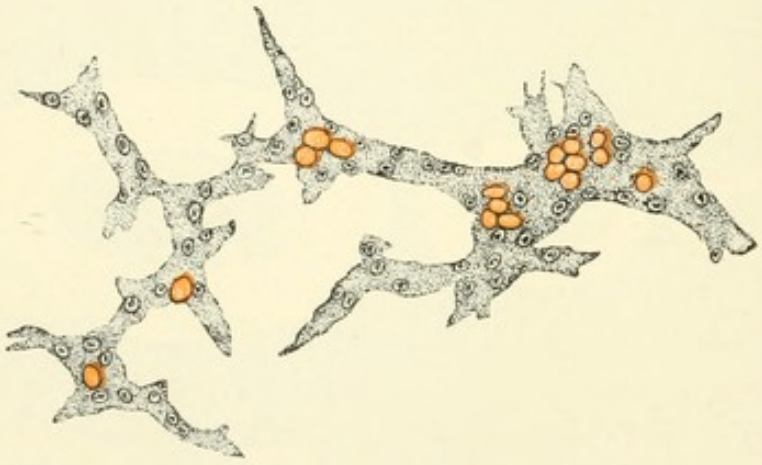


FIG. 112.—Part of the Network of Developing Blood-Vessels in the Vascular Area of a Guinea-Pig. *bl*, Blood-corpuscles becoming free in an enlarged and hollowed-out part of the network; *a*, process of protoplasm. (E. A. Schäfer.)

from those which belong to the later periods of intra-uterine, and to all periods of extra-uterine life. Their manner of origin is at first very simple.

Surrounding the early embryo is a circular area, called the vascular area, in which the first rudiments of the blood-vessels and blood-corpuscles are developed. Here the nucleated embryonal cells of the mesoblast, from which the blood-vessels and corpuscles are to be formed, send out processes in various directions, and these, joining together, form an irregular meshwork. The nuclei increase in number, and collect chiefly in the larger masses of protoplasm, but partly also in the processes. It appears that hemo-

globin then makes its appearance in certain of these nucleated embryonal cells, which thus become the earliest red blood-corpuscles. The protoplasm of the cells and their branched network in which these corpuscles lie then become hollowed out into a system of canals enclosing fluid, in which the red nucleated corpuscles float. The corpuscles at first are from about 10 μ to 16 μ in diameter, mostly spherical, and with granular contents, and a well-marked nucleus. Their nuclei, which are about 5 μ in diameter,

FIG. 1

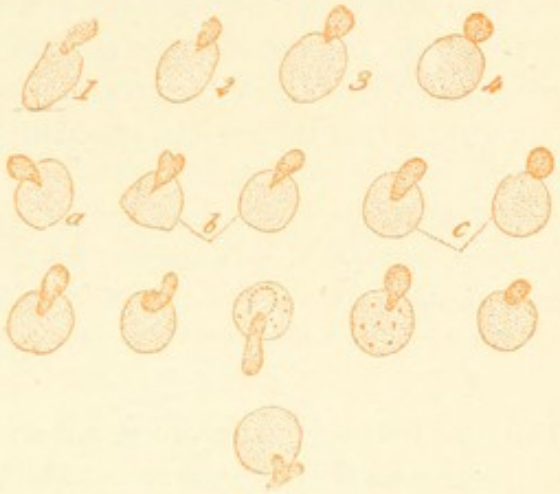


FIG. 114.

FIG. 113.—Multiplication of the Nucleated Red Corpuscles. Marrow of young kitten after bleeding, showing above karyokinetic division of erythroblast, and below the formation of mature from immature erythrocytes. (Howell.)

FIG. 114.—Shows the Way in which the Nucleus Escapes from the Nucleated Red Corpuscles. 1, 2, 3, 4, represent different stages of the extrusion noticed upon the living corpuscles. *a*, Specimen from the circulating blood of an adult cat, bled four times; *b*, specimen from the circulating blood of a kitten forty days old, bled twice; *c*, specimens from the blood of a fetal cat, 9 cm. long. Others from the marrow of an adult cat, two of the figures showing the granules present in the corpuscles, which have been interpreted erroneously as a sign of the disintegration of the nucleus. (Howell.)

are central, circular, very little prominent on the surfaces of the corpuscles, and apparently slightly granular.

The corpuscles then strongly resemble the colorless corpuscles of the fully developed blood but for their color. They are capable of ameboid movement and multiply by division.

When, in the progress of embryonic development, the liver is formed, the multiplication of blood-cells in the whole mass of blood ceases, and new blood-cells are produced by this organ, and also by the spleen. These are at first colorless and nucleated, but afterward acquire the ordinary blood tinge, and resemble very much those of the first set. They also multiply by division. The bone marrow also begins to form red corpuscles, though at first in small amounts only. This function develops rapidly, however, so that at birth the marrow represents the chief seat of production of the red cells. Nevertheless, nucleated red cells are usually found at birth, sometimes in considerable quantities in the liver and in the spleen. Non-nucleated red cells begin to appear soon after the first month of fetal life, and gradually increase so that at the fourth month they form one-fourth of the whole amount of

colored corpuscles. At the end of fetal life they almost completely replace the nucleated cells. In late fetal life the red cells are formed in almost the same way as in extra-uterine life.

Various theories have prevailed as to the mode of origin of the non-nucleated colored corpuscles. For a time it was thought that they were of endoglobular origin, and merely fragments of some original cell, being produced by subdivision of the cell body itself. This theory easily accounted for the absence of the nuclei, but it has not been supported by recent investigations. At present it is the general belief that the non-nucleated cells, or erythrocytes, are derived from nucleated cells by a process of mitotic division, and further that their nuclei gradually shrink or fade and are then extruded.

FIG. 115.—Colored Nucleated Corpuscles, from the Red Marrow of the Guinea-Pig. (E. A. Schäfer.)

The use of some of the more recent stains seems to prove that there are traces of nuclear material in the non-nucleated corpuscles.

After infancy and early childhood the origin of erythrocytes is practically limited to the red marrow of the bones. The mother cells, or *erythroblasts*, are constantly forming and setting free erythrocytes, the rate varying greatly at different periods.

The Colorless Corpuscles or Leucocytes. In human blood the white corpuscles, *leucocytes*, are nearly spherical masses of granular protoplasm without cell wall. In all cases one or more nuclei exist in each corpuscle. The corpuscles vary considerably in size but average 10 μ in diameter.

The number of leucocytes in a cubic millimeter of blood is estimated at 7,500 to 8,000. The proportion of white corpuscles to red, therefore, is about one of the former to 700 of the latter. This proportion is not very constant in health and great variations occur under the influence of disease, especially in certain infectious diseases in which the number of white corpuscles is markedly increased.

After a full meal the white cells in a healthy adult are increased in number about one-third, the increase beginning within an hour, attaining a maximum in three or four hours, and then gradually falling to normal. This process is frequently modified by the character of the food, the greatest increase occurring with an exclusively meat diet, while a purely vegetarian diet has usually no effect. The increase is also more marked in children, and especially in infants. The essential factor is probably the absorption of albuminous matter in considerable quantities. This causes proliferation of leucocytes in the adenoid tissue of the gastro-intestinal tract.

In pregnancy there is often a moderate increase in the number of white

cells during the later months. This does not begin until after the third month, and is most marked and constant in primiparæ. After parturition the leucocytes gradually diminish under normal conditions, and usually reach the normal within a fortnight. The essential factor is probably the general stimulation in the maternal organism. It is well established that the white cells are very numerous in the new-born, though different observers have made very conflicting estimates. Still all agree that there is a very rapid decrease in their numbers during the first few days, and that this is followed by a less marked increase, which continues for many months. According to Rieder, who is perhaps the most reliable, there are at birth from 14,200 to 27,400 per cubic millimeter, and after the fourth day from 12,400 to 14,800.

Varieties of Leucocytes. The colorless corpuscles present greater diversities of form than the red ones, plate II. They are usually classified according to their reaction to staining agents, or to the presence or absence of granules in their cytoplasm. Kanthack and Hardy offer the following classification, based upon both phenomena:

Leucocytes.

A. Oxyphile (staining with acid dyes)	1. Finely granular. 2. Coarsely granular eosinophile.
B. Basophile (staining with basic dyes)	1. Finely granular.
C. Hyaline	1. Small lymphocyte. 2. Large myelocyte.

The *finely granular oxyphile* constitutes 75 per cent of all leucocytes. It has an average diameter of 10 μ, and possesses *phagocytic* action to a marked degree—that is, it possesses the power of ingesting foreign particles. Its nucleus consists of several lobes united by threads of chromatin. This cell was formerly known under the term *neutrophile*, because of its supposed reaction to neutral dyes.

The *coarsely granular* form of *eosinophile* constitutes only 2 per cent of the leucocytes. It has a diameter of 12 μ and a reniform nucleus.

The *basophile* cell is rarely found in normal blood. It may occur occasionally during periods of digestion. It is a small, spherical cell, with an irregular nucleus and a diameter of 7 μ.

The *small hyaline* leucocyte is also called a *lymphocyte*, because of the large numbers found in adenoid tissue, and is supposed to be an immature form. The nucleus is proportionally large, and is surrounded by but little protoplasm in which no granules can be detected. The cell is about the size of a red blood-cell, and constitutes from 10 to 20 per cent of all leucocytes.

The *large hyaline* or *myelocyte* varies in diameter from 8.5 to 10 μ. Its nucleus is spherical or reniform, and is surrounded by more protoplasm than in the case of the lymphocyte. It forms about 10 per cent of the leucocytes.

Ameboid Movement of Leucocytes. The remarkable property of the color-

less corpuscles of spontaneously changing their shape was first demonstrated by Wharton Jones in the blood of the skate. If a drop of blood be examined with a high power of the microscope, under conditions by which loss of moisture is prevented, and at the same time the temperature is maintained at about that of the body, 37° C., the colorless corpuscles will be observed slowly to alter their shapes, and to send out processes at various parts of their

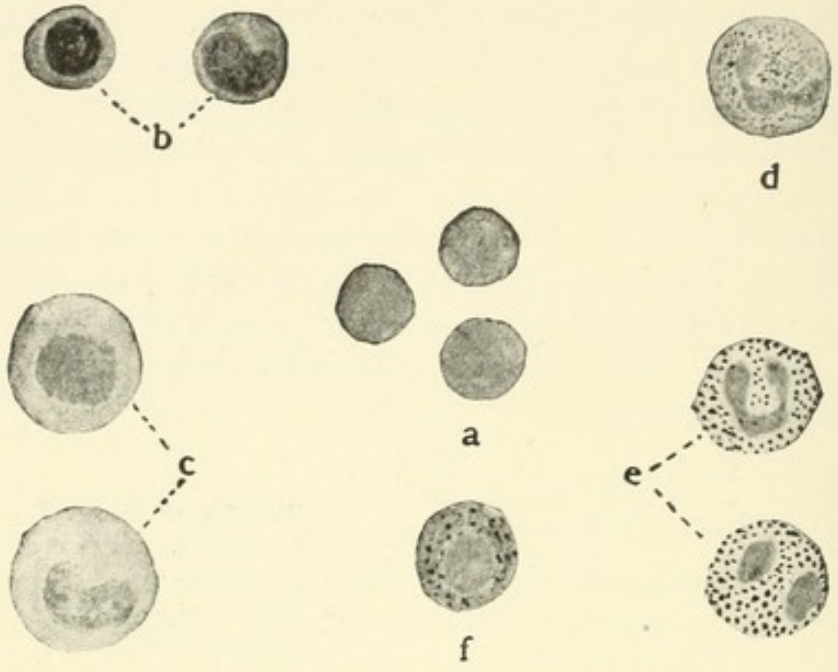


FIG. 116.—(*a*) Red blood-corpuscle for comparison; (*b*) small hyaline cell or lymphocyte; (*c*) large hyaline cell or myelocyte; (*d*) fine granular oxyphile; (*e*) coarse granular oxyphile or eosinophile; (*f*) basophile. (F. C. Busch.)

circumference. The ameboid movement which can be demonstrated in human colorless blood-corpuscles, can be most conveniently studied in the newt's blood. Processes are sent out from the corpuscle. These may be withdrawn, but more often the protoplasm of the whole corpuscle flows gradually forward to the position occupied by the process, thus the corpuscle changes its position. The change of position of the corpuscle can also take place by a flowing movement of the whole mass, and in this case the loco-

FIG. 117.—Human Colorless Blood-Corpuscle, Showing its Successive Changes of Outline Within Ten Minutes when kept Moist on a Warm Stage. (Schofield.)

motion is comparatively rapid. The activity both in the processes of change of shape and also of change in position is much more marked in some corpuscles than in others. Klein states that in the newt's blood the changes are especially noticeable in a variety of the colorless corpuscle, which consists of a mass of finely granular protoplasm with jagged outline and contains

three or four nuclei, or in large irregular masses of protoplasm containing from five to twenty nuclei.

The property which the colorless corpuscles possess of passing through the walls of the blood-vessels will be described later on.

The Blood Plates or Thrombocytes. A third variety of corpuscle found in the blood is known as the *blood plate*. They are circular or elliptical in shape, of nearly homogeneous structure, and vary in size from 0.5 to 5μ.

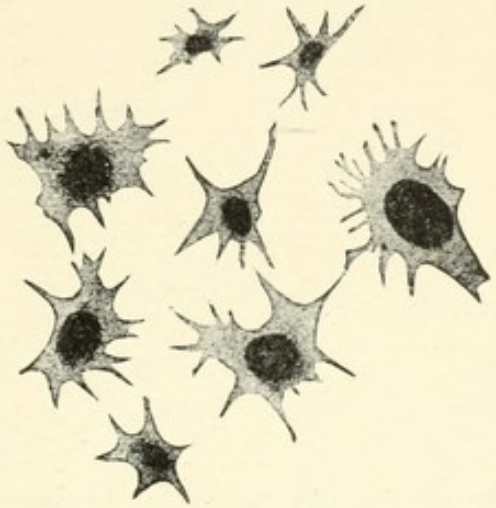


FIG. 118.—Blood Plates, Showing Chromatic Centers Regarded by some as Nuclei, and Exhibiting Ameboid Movement. (Schäfer, from Kopsch.)

Hence they are smaller than the red corpuscles. They vary in number from 5,000 to 45,000 per cubic millimeter and are preserved by drawing fresh blood directly into Hayem's or other preserving fluid. Chemically they contain a nucleo-proteid, and it is supposed that they take part in the phenomenon of coagulation. According to Deetjen and others, ameboid movement has been demonstrated in these bodies.

CHEMICAL COMPOSITION OF THE BLOOD.

In considering the chemical composition of the blood, it will be convenient to take in order the composition of the various chief factors into which the blood may be separated, viz., *The Plasma ; The Serum ; The White Corpuscles ; The Red Corpuscles.*

The Composition of the Plasma. The plasma is the liquid part of the blood in which the corpuscles float.

It contains the fibrin factors, inasmuch as when drawn from the blood-vessels it undergoes coagulation and splits up into fibrin and serum. It differs from the serum in containing fibrinogen, but in appearance and in reaction it closely resembles that fluid. Its alkalinity, however, is greater than that of the serum obtained from it. It may be freed from corpuscles by the centrifugal machine, or by the other means enumerated below.

The chief methods of obtaining plasma free from corpuscles are: 1. By cold. The temperature should be about 0° C. and may be two or three degrees higher, but not lower. 2. The addition of neutral salts, in certain proportion, either as solids or in solution, *e.g.*, of sodium sulphate, if solid 1 part to 12 parts of blood; if a saturated solution 1 part to 6 parts of blood. Or magnesium sulphate, saturated solution 1 part to 4 of blood. 3. By mixing frog's blood with an equal part of a 5 per cent solution of cane sugar, and getting rid of the corpuscles by filtration. 4. By the injection of commercial peptone into the veins of certain mammals previous to bleeding them to death, allowing the corpuscles to subside or by subjecting the blood to the action of a centrifugal machine by the rapid rotation of which the whole of the solids are driven to the outer end of the tubes in which the blood is placed.

PERCENTAGE COMPOSITION OF PLASMA.

Water		90.29
Solids—		
1. Proteids—		
Fibrinogen, Paraglobulin, Serum albumin	8.289	
2. Extractives	.566	
3. Inorganic salts	.850	
		9.71
		100.00

Water. The water of the plasma varies in amount according to the amount of food, drink, and exercise, or other circumstances. It amounts to about 90 per cent.

Proteids. Fibrinogen is the substance in plasma which is converted into fibrin on coagulation. It belongs to the class of proteids called globulins. It is precipitated from plasma with serum globulin by saturation with $MgSO_4$ and NaCl. It is soluble in dilute salt solutions but is not soluble in water. It can be distinguished from serum globulin by a number of special reactions; 1. Its coagulation temperature is lower, 55° to 56° C. 2. It is completely precipitated by saturation with NaCl as well as with $MgSO_4$. 3. It gives rise to an insoluble proteid, *fibrin*. It may be, however, that fibrinogen is not a simple proteid, but a mixture or loose chemical combination of two or more proteids. Fibrinogen is present in plasma to the extent of 0.2 to 0.5 per cent.

Serum globulin or *paraglobulin* is similar to fibrinogen in its reactions. It is completely precipitated by $MgSO_4$; incompletely by NaCl, and coagulates at a temperature of 75° C. It is likewise soluble in dilute salt solutions but insoluble in water. It is present in plasma in from 3.5 to 4 per cent.

Serum albumin is the proteid which predominates in human plasma. It is readily obtained in crystalline form; is soluble in $MgSO_4$ and NaCl solutions, but insoluble in saturated ammonium sulphate solutions; and coagulates in neutral or acid solutions at from 73° to 75° C.

Extractives. The extractives are the nitrogen-containing substances such as urea, uric acid, creatin, creatinin, etc.; glycogen, dextrose, choles-

terin, etc., a total of 0.5 to 0.6 per cent. The dextrose content amounts to from 0.1 to 0.15 per cent.

Ferments are also found in blood; first, a diastatic ferment converting amyloids into sugars; second, a glycolytic ferment causing a disappearance of sugar; third, a fat-splitting ferment, lipase; and fourth, fibrin ferment (thrombin), or its precursor, prothrombin.

Inorganic Substances. The blood plasma contains about 0.8 per cent of inorganic salts distributed as follows, the sodium chloride predominating:

Parts in 1,000 of plasma.

Chlorine	3.536
Sulphuric acid	.129
Phosphoric acid	.145
Potassium	.314
Sodium	3.410
Phosphate of lime	.298
Phosphate of magnesia	.218
Oxygen	.455
	8.505

The Serum. The serum is the liquid part of the blood or of the plasma which remains after the fibrin has been formed and removed. It is a transparent, yellowish, faintly alkaline fluid, with a specific gravity of from 1025 to 1032. Serum may be obtained from blood-corpuscles by allowing blood to clot in large test tubes, or by subjecting test tubes of whipped blood to the action of a centrifugal machine for some time. Serum is chemically very much the same as plasma except that it has lost the fibrinogen in the process of clotting and has gained the by-products of that process—thrombin, thrombokinase, and fibrin-globulin. The salts of serum are practically those of plasma.

The Composition of the White Corpuscles. The white corpuscles are comparatively undifferentiated cellular elements, hence possess the chemical composition of protoplasm. Lillienfeld has made an analysis of the leucocytes of thymus gland from the calf, which contain 11.49 per cent of solids, as follows:

In 100 Parts of Dry Substance of Corpuscles of Calf.

	Per cent.
Proteid	1.76
Leuconuclein	68.78
Histon	8.76
Lecithin	7.51
Fat	4.02
Cholesterin	4.40
Glycogen	0.80
	96.03

The most noteworthy substance in this table is the nucleohiston content, first isolated by Kossel and Lillienfeld. Beside the substances in the above table, the white corpuscles contain salts of potassium, sodium, calcium, and magnesium. The potassium phosphate is present in greatest amount.

The Composition of the Red Corpuscles. Analysis of a thousand parts of moist blood-corpuscles shows the following result:

Water		688
Solids—		
Organic	303.88	312=1,000
Mineral	8.12	

Of the solids the most important is *Hemoglobin*, the substance to which the blood owes its color. It constitutes, as will be seen from the appended table, more than 90 per cent of the organic matter of the corpuscles. Besides hemoglobin the corpuscles contain proteid and fatty matters, the former chiefly consisting of *globulins*, and the latter of *cholesterin* and *lecithin*.

In 1,000 parts of *organic* matter are found:

Hemoglobin	905.4
Proteids	86.7
Fats	7.9=1,000

Of the *inorganic salts* of the corpuscles, the iron omitted, there are present, in 1,000 parts of corpuscles (Schmidt):

Potassium chloride	3.679
Potassium phosphate	2.343
Potassium sulphate	.132
Sodium phosphate	.633
Calcium phosphate	.094
Magnesium phosphate	.060
Soda	.341=7.282

Hemoglobin. Of the substances in the erythrocytes, by far the most important from every point of view is the pigment, *hemoglobin*. It composes about 90 per cent of the total solids of the corpuscles; therefore, between 14 and 15 per cent of the blood itself. Hemoglobin is the most complex compound in the body, having a molecule of the enormous molecular weight of 16,669. Hemoglobin is intimately distributed throughout the stroma of the corpuscle, and when dissolved out it undergoes crystallization.

Its percentage composition is C 53.85; H 7.32; N 16.17; O 21.84; S 0.63; Fe 0.42. Jacquet gives the empirical formula for the hemoglobin of the dog, $C_{758}H_{1203}N_{195}S_3FeO_{218}$. The most interesting of the properties of hemoglobin are its powers of crystallizing and its attraction for oxygen and other gases.

Hemoglobin Crystals. The hemoglobin (oxyhemoglobin) of the blood of various animals possesses the power of crystallizing to very different ex-

tents. In some the formation of crystals is almost spontaneous, whereas in others it takes place either with great difficulty or not at all. Among the animals whose blood coloring-matter crystallizes most readily are the guinea-pig, rat, squirrel, and dog; and in these cases to obtain crystals it is generally sufficient to dilute a drop of recently drawn blood with water

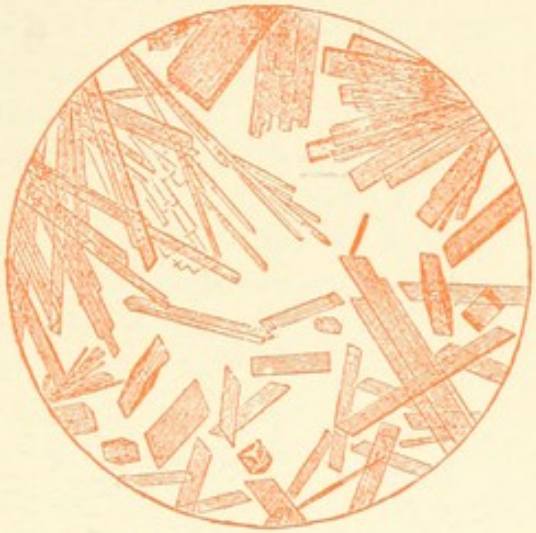


FIG. 119.—Crystals of Oxyhemoglobin—Prismatic, from Human Blood.

and to expose it for a few minutes to the air. In many instances other means must be adopted, *e.g.*, the addition of alcohol, ether, or chloroform, rapid freezing, and then thawing, the application of an electric current, a tempera-

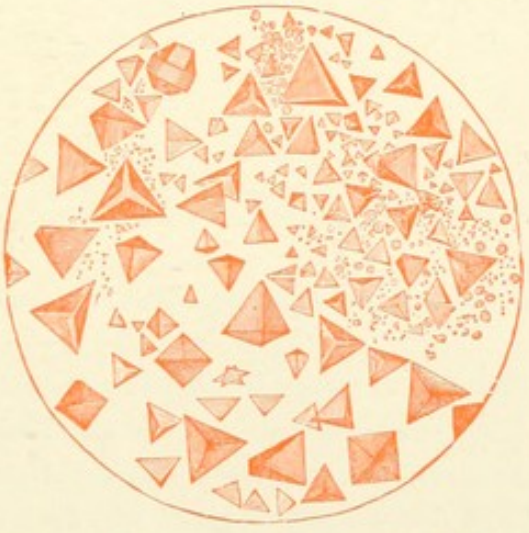


FIG. 120.—Oxyhemoglobin Crystals—Tetrahedral, from Blood of the Guinea-pig.

ture of 60° C., the addition of sodium sulphate, or the addition of decomposing serum of another animal.

The hemoglobin of human blood crystallizes with difficulty, as does also that of the ox, the pig, the sheep, and the rabbit.

The forms of hemoglobin crystals, as will be seen from figures 119 and 120, differ greatly. Hemoglobin crystals are soluble in water. Both the crystals themselves and also their solutions have the characteristic color of arterial blood.

A dilute solution of oxyhemoglobin gives a characteristic appearance with the spectroscope. Two absorption bands are seen between the solar lines *D*, which is the sodium band in the yellow, and *E*, see the frontispiece, one in the yellow, with its middle line some little way to the right of *D*. This band is very intense, but narrower than the other, which lies in the green near to the left of *E*. Each band is darkest in the middle and fades away at the sides. As the strength of the solution increases, the bands become broader and deeper. Both the red and the blue ends of the spectrum become encroached upon until the bands coalesce to form one very broad band when only a slight amount of the green and part of the red remain unab-

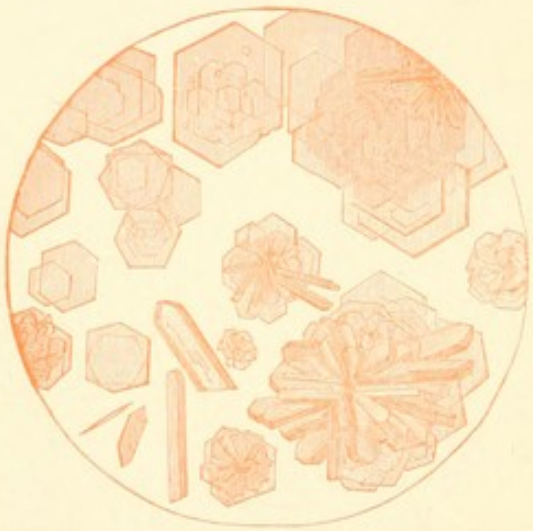


FIG. 121.—Hexagonal Oxyhemoglobin Crystals, from Blood of Squirrel. On these hexagonal plates prismatic crystals, grouped in a stellate manner, not unfrequently occur (after Funke).

sorbed. Any further increase of strength leads to complete absorption of the spectrum.

If crystals of hemoglobin are exposed to an atmosphere of oxygen they take up oxygen and form oxyhemoglobin, each gram of the pigment fixing a definite amount of oxygen, see chapter on Respiration. When subjected to a mercurial air pump the oxygen is given off, and the crystals become of a purple color. A solution of the oxyhemoglobin in the blood-corpuscles may be made to give up oxygen, and to change color in a similar manner. One gram of oxyhemoglobin liberates 1.59 c.c. oxygen, or according to Hüfner's later determinations, 1.34 c.c.

This change may be also effected by passing through the solution of blood or of oxyhemoglobin, hydrogen or nitrogen gas, or by the action of

reducing agents, of which Stokes's fluid* or ammonium sulphide are the most convenient.

With the spectroscope, a solution of deoxidized or *reduced hemoglobin* is found to give an entirely different appearance from that of oxidized hemoglobin. Instead of the two bands at D and E we find a single broader but fainter band occupying a position midway between the two, and at the same time less of the blue end of the spectrum is absorbed. Even in strong solutions this latter appearance is found, thereby differing from the strong solution of oxidized hemoglobin which lets through only the red and orange rays; accordingly, to the naked eye the one (reduced-hemoglobin solution) appears purple, the other (oxyhemoglobin solution) red. The deoxidized crystals or their solutions quickly absorb oxygen on exposure to the air, becoming scarlet. If solutions of blood be taken instead of solutions of hemoglobin, results similar to the whole of the foregoing can be obtained.

Venous blood never, except in the last stages of asphyxia, fails to show the oxyhemoglobin bands, inasmuch as the greater part of the hemoglobin even in venous blood exists in the more highly oxidized condition.

Action of Gases on Hemoglobin. *Carbonic oxide* gas passed through a solution of hemoglobin causes it to assume a cherry-red color and to present a slightly altered spectrum; two bands are still visible but are slightly nearer the blue end than those of oxyhemoglobin, see plate I. The amount of carbonic oxide taken up is equal to the amount of the oxygen displaced. Although the carbonic-oxide gas readily displaces oxygen, the reverse is not the case, and upon this property depends the dangerous effect of coal-gas poisoning. Coal-gas contains much carbonic oxide, and, when breathed, the gas combines with the hemoglobin of the blood and produces a compound which cannot easily be reduced. This compound (carboxyhemoglobin) is not an oxygen-carrier, and death may result from suffocation due to the want of oxygen, notwithstanding the free entry of pure air into the lungs. Crystals of carbonic-oxide hemoglobin closely resemble in form those of oxyhemoglobin.

Nitric oxide produces a similar compound to the carbonic-oxide hemoglobin, which is even less easily reduced.

Nitrous oxide reduces oxyhemoglobin, and therefore leaves the reduced hemoglobin in a condition actively to take up oxygen.

Sulphuretted hydrogen, if passed through a solution of oxyhemoglobin, reduces it and an additional band appears in the red. If the solution be then shaken with air, the two bands of oxyhemoglobin replace that of reduced hemoglobin, but the band in the red persists.

* *Stokes's Fluid* consists of a solution of *ferrous sulphate*, to which ammonia has been added and sufficient tartaric acid to prevent precipitation. Another reducing agent is a solution of *stannous chloride*, treated in a way similar to the ferrous sulphate, and a third reagent of like nature is an aqueous solution of yellow *ammonium sulphide*, NH_4HS.

Methemoglobin. If an aqueous solution of oxyhemoglobin is exposed to the air for some time, its spectrum undergoes a change; the two *d* and *e* bands become faint, and a new line in the red at C is developed. The solution, too, becomes brown and acid in reaction, and is precipitable by basic lead acetate. This change is due to the decomposition of oxyhemoglobin, and to the production of *methemoglobin*. On adding ammonium sulphide, reduced hemoglobin is produced, and on shaking this up with air, oxyhemoglobin is again produced. Methemoglobin is probably a stage in the deoxidation of oxyhemoglobin. It appears to contain less oxygen than oxyhemo-

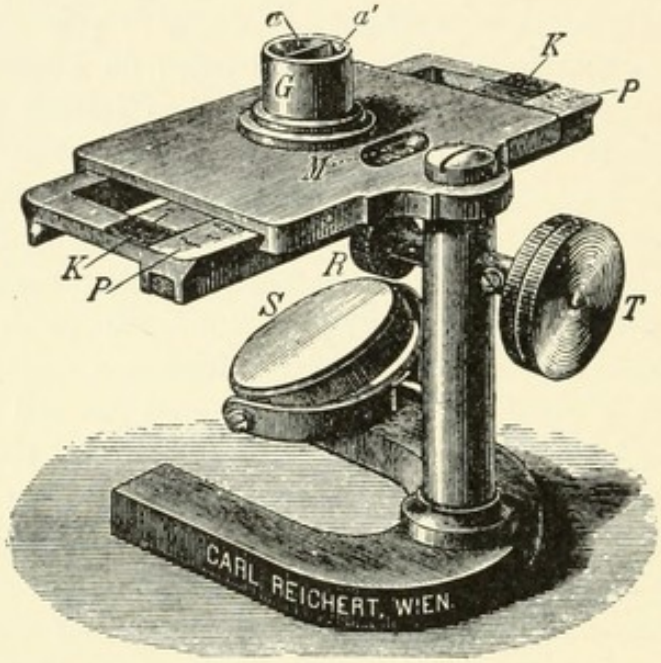


FIG. 122.—Fleischl's Hemoglobinometer.

globin, but more than reduced hemoglobin. Its oxygen is in more stable combination, however, than is the case with the former compound.

Estimation of Hemoglobin. The most exact method is by the estimation of the amount of iron (dry hemoglobin containing 0.42 per cent of iron) in a given specimen of blood, but as this is a somewhat complicated process, various methods have been proposed which, though not so exact, have the advantage of simplicity. Of the several varieties of hemoglobinometer, one of the best adapted to its purpose is that invented by Professor Fleischl, of Vienna. In this instrument the amount of hemoglobin in a solution of blood is estimated by comparing a stratum of diluted blood with a standard solid substance of uniform tint similar spectroscopically to diluted blood. The Fleischl instrument has been recently modified and made more accurate by Miescher. The Fleischl-Miescher apparatus consists of a stand with a metal plate having a circular opening and a plaster mirror below, *S*, figure 122, which casts light through the opening. Beneath the plate is a metal framework containing a colored glass wedge, and along the side of

the same is a scale graduated so as to indicate the percentage of hemoglobin corresponding to the shades of the different parts of the wedge. This framework can be moved by the wheel *T* which fits into a rack on its lower surface. The scale can be read through a small opening *M* in the plate. Into the large circular opening of the plate fits a cylindrical metal cell *G* with a glass bottom and divided by a metal partition into two equal parts. One of these halves lies over the wedge and is filled with distilled water. The other contains the solution of blood in which the hemoglobin is to be estimated. The apparatus is usually supplied with three cells. Of these, the first two are used in estimating the hemoglobin according to Miescher's modification of Fleischl's original method. This is the method now generally used. These cells are furnished with a glass cover having a groove which fits upon the partition of the cell. Over this cover is placed a diaphragm with a longitudinal slit, which only permits of the central part of each side of the cell being seen. The third cell is for use when the original Fleischl method is employed.

The patient's ear or finger is pricked, and the blood from the wound sucked up into the graduated pipet until it reaches the mark $\frac{1}{2}$, $\frac{2}{3}$, or $\frac{1}{1}$, a one per cent solution of sodium carbonate is then sucked in until the upper mark is reached. The pipet is then well shaken in order to mix the blood thoroughly. One-half of each of the two cells, which are respectively 12 and 15 millimeters high, are then filled with the mixture, the other half being filled with water. An important point is that the liquids should completely fill the cells. The cover-glasses and diaphragms are then applied and the cells are ready for examination. This must be done by artificial light. Moreover, in order to have accurate results, light of the same intensity should be always used. One of the cells is placed on the plate and the wheel *T* turned until the colors of the two halves exactly correspond. When this point is reached, the result is read off on the scale through the opening *M*. This should be repeated several times with each of the cells, and the average of the readings taken. The result obtained with the 12-millimeter cell should be multiplied by $\frac{5}{4}$ to bring it up to that of the larger. For example, suppose the result of several readings to be:

With the large cell (15 mm.)	54.00
With the small cell (12 mm.)	42.00

If the readings obtained with the large cell are exactly correct, then the readings with the smaller one should be 43.2, since $54 \times \frac{4}{5} = 43.2$. Or, if the readings with the smaller cells are exact, the readings with the larger should be 52.5, since $42 \times \frac{5}{4} = 52.5$. Hence the mean of 54 and 52.5, namely 53.25, should be taken as the correct figure. On looking at the corrected table of hemoglobin values supplied with each instrument, we would find that this number on the scale corresponds to a solution containing 400 milligrams

of hemoglobin per 1,000 cubic centimeters of solution. But our original dilution was either 1 : 200, 1 : 300, or 1 : 400, according as our pipet had been filled with blood up to the mark $\frac{1}{1}$, $\frac{2}{3}$, or $\frac{1}{2}$; so that in order to obtain the actual percentage of hemoglobin in the blood under examination we should be obliged to multiply our result by 200, 300, or 400. In the example we have taken, the amount of hemoglobin would be, if our dilution was 1 : 200, 400 × 200 = 80,000 milligrams = 80 grams in 1,000 cubic centimeters = 8 grams in 100 cubic centimeters, or 8 per cent.

Another very simple method of approximately determining the hemoglobin percentage is the hemoglobin scale devised by T. W. Talquist. This consists of a series of shades of color corresponding to undiluted blood of various hemoglobin values, ranging from ten to one hundred per cent of an arbitrary scale. This scale is included in a book, the remaining pages of which consist of filter paper, which is used for absorbing the specimen of blood whose hemoglobin percentage is to be estimated. The blood-stained filter paper is compared with the hemoglobin scale by direct daylight until a shade is found with which it corresponds. For approximate results this method has proved very satisfactory.

Derivatives of Hemoglobin. *Hematin.* By the action of heat or of acids or alkalies in the presence of oxygen, hemoglobin can be split up into a substance called *Hematin*, which contains all the iron of the hemoglobin from which it was derived, and a proteid residue. Of the latter it is impossible to say more than that it probably consists of one or more bodies of the globulin class. If there be no oxygen present, instead of hematin a body called *hemochromogen* is produced, which, however, will speedily undergo oxidation into hematin.

Hematin is a dark brownish or black non-crystallizable substance of metallic luster. Its percentage composition is C, 64.30; H, 5.50; N, 9.06; Fe, 8.82; O, 12.32; which gives the formula $C_{68}H_{70}N_8Fe_2O_{10}$ (Hoppe-Seyler). It is insoluble in water, alcohol, and ether; soluble in the caustic alkalies; soluble with difficulty in hot alcohol to which is added sulphuric acid. The iron may be removed from hematin by heating it with fuming hydrochloric acid to 160° C., and a new body, *hematoporphyrin*, the so-called iron-free hematin, is produced. Hematoporphyrin ($C_{68}H_{74}N_8O_{12}$, Hoppe-Seyler) may also be obtained by adding blood to strong sulphuric acid, and if necessary filtering the fluid through asbestos. It forms a fine crimson solution, which has a distinct spectrum, viz., a dark band just beyond D, and a second all but midway between D and E. It may be precipitated from its acid solution by adding water or by neutralization, and when redissolved in alkalies presents four bands, a pale band between C and D, a second between D and E, nearer D, another nearer E, and a fourth occupying the chief part of the space between *b* and F.

Hematin in Acid Solution. If an excess of acetic acid is added to

blood, and the solution boiled, the color alters to brown from decomposition of hemoglobin and the setting free of hematin; by shaking this solution with ether, a solution of hematin in acid solution is obtained. The spectrum of the ethereal solution shows no less than four absorption bands, viz., one in the red between C and D, one faint and narrow close to D, and then two broader bands, one between D and E, and another nearly midway between *b* and F. The first band is by far the most distinct, and the acid aqueous solution of hematin shows it plainly.

Hematin in Alkaline Solution. If a caustic alkali is added to blood and the solution is boiled, alkaline hematin is produced, and the solution becomes olive green in color. The absorption band of the new compound is in the red, near to D, and the blue end of the spectrum is absorbed to a considerable extent. If a reducing agent be added, two bands resembling those of oxy-

FIG. 123.—Hematoidin Crystals. (Frey.)

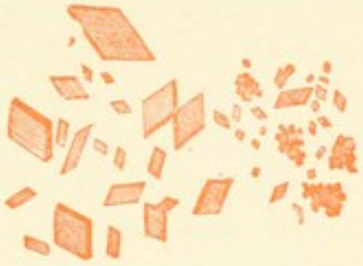


FIG. 123a.—Hemin Crystals. (Frey.)

hemoglobin, but nearer to the blue, appear; this is the spectrum of *reduced hematin*, or *hemochromogen*. On violently shaking the reduced hematin with air or oxygen the two bands are replaced by the single band of alkaline hematin.

Hematoidin. This substance is found in the form of yellowish crystals, figure 123, in old blood extravasations and is derived from the hemoglobin. Their crystalline form and the reaction they give with fuming nitric acid seem to show them to be closely allied to *Bilirubin*, the chief coloring matter of the bile, and in composition they are probably either identical or isomeric with it.

Hemin. One of the most important derivatives of hematin is hemin. It is usually called *Hydrochloride of Hematin*, but its exact chemical composition is uncertain. Its formula is said to be $C_{32}H_{30}N_4FeO_3HCl$, and it contains 5.18 per cent of chlorine, but by some it is looked upon as simply crystallized hematin. Although difficult to obtain in bulk, a specimen may be easily made for the microscope in the following way:—A small drop of dried blood is finely powdered with a few crystals of common salt on a glass slide and spread out; a cover-glass is then placed upon it, and glacial acetic acid added by means of a capillary pipet. The blood at once turns a brownish color. The slide is then heated, and the acid mixture evaporated to dryness

at a high temperature. The excess of salt is washed away with water from the dried residue, and the specimen may then be dried and mounted. A large number of small, dark, reddish black crystals of a rhombic shape, sometimes arranged in bundles, will be seen if the slide be subjected to microscopic examination, figure 123a.

The formation of these hemin crystals is of great interest and importance from a medico-legal point of view, as it constitutes the most certain and delicate test we have for the presence of blood (not of necessity the blood of man) in a stain on clothes, etc. It exceeds in delicacy even the spectroscopic test. Compounds similar in composition to hemin, but containing hydrobromic or hydriodic acid, instead of hydrochloric, may be also readily obtained.

Variations in the Composition of Healthy Blood. The conditions which appear most to influence the composition of the blood in health are these: Diet, Exercise, Sex, Pregnancy, and Age.

Sex. The blood of men differs from that of women, chiefly in being of somewhat higher specific gravity, from its containing a relatively larger quantity of red corpuscles.

Pregnancy. The blood of pregnant women has rather lower than the average specific gravity. The quantity of the colorless corpuscles is increased in the later months, especially in primiparæ; it is also claimed that the fibrin is increased in amount.

Age. The blood of the fetus is very rich in solid matter, and especially in colored corpuscles; and this condition, gradually diminishing, continues for some weeks after birth. The quantity of solid matter then falls during childhood below the average, rises during adult life, and in old age falls again.

Diet. Such differences in the composition of the blood as are due to the temporary presence of various matters absorbed with the food and drink, as well as the more lasting changes which must result from generous or poor diet respectively, need be here only referred to.

Effects of Bleeding. The result of bleeding is to diminish the specific gravity of the blood, and so quickly that in a single venesection the portion of blood last drawn has often a less specific gravity than that of the blood that flowed first. This is, of course, due to absorption of fluid from the tissues of the body. The physiological import of this fact, namely, the instant absorption of liquid from the tissues, is the same as that of the intense thirst which is so common after either loss of blood, or the abstraction from it of watery fluid, as in cholera, diabetes, and the like.

For some little time after bleeding, the want of colored corpuscles is well marked, but with this exception: no considerable alteration seems to be produced in the composition of the blood for more than a very short time; the loss of the other constituents, including the colorless corpuscles, being very quickly repaired.

Variations in Different Parts of the Body. The composition of the blood, as might be expected, is found to vary in different parts of the body. Thus arterial blood differs from venous; and although its composition and general characters are uniform throughout the whole course of the systemic arteries, they are not so throughout the venous system, the blood contained in some veins differing markedly from that in others.

Differences between Arterial and Venous Blood. The differences between arterial and venous blood are these:

Arterial blood is bright red, from the fact that almost all its hemoglobin is combined with oxygen, oxyhemoglobin, while the purple tint of venous blood is due to the deoxidation of a certain quantity of its oxyhemoglobin, and its consequent reduction to the purple variety (deoxidized, or purple hemoglobin).

Arterial blood coagulates somewhat more quickly.

Arterial blood contains more oxygen than venous, and less carbonic acid.

Some of the veins contain blood which differs from the ordinary standard considerably. These are the Portal, the Hepatic, and the Splenic veins.

Portal Blood. The blood which the portal vein conveys to the liver is supplied from two chief sources; namely, from the gastric and mesenteric veins, which contain the soluble elements of food absorbed from the stomach and intestines during digestion, and from the splenic vein. It must, therefore, combine the qualities of the blood from each of these sources.

The blood in the gastric and mesenteric veins will vary much according to the stage of digestion and the nature of the food taken, and can therefore be seldom exactly the same. Speaking generally, and without considering the sugar and other soluble matters which may have been absorbed from the alimentary canal, this blood appears to be deficient in solid matters, especially in colored corpuscles, owing to dilution by the quantity of water absorbed, to contain an excess of proteid matter, and to yield a less tenacious kind of fibrin than that of blood generally.

The blood of the *portal vein*, combining the peculiarities of its two factors, the splenic and mesenteric venous blood, is usually of lower specific gravity than blood generally, is more watery, contains fewer colored corpuscles, more proteids, and yields a less firm clot than that yielded by other blood, owing to the deficient tenacity of its fibrin.

Guarding (by ligature of the portal vein) against the possibility of an error in the analysis from regurgitation of hepatic blood into the portal vein, recent observers have determined that *hepatic venous blood* contains less water, proteids, and salts than the *blood of the portal veins;* but that it yields a much larger amount of extractive matter, in which is one constant element, namely, *grape-sugar*, which is found, whether saccharine or farinaceous matter has been present in the food or not.

GLOBULOCIDAL AND OTHER PROPERTIES OF SERUM.

Cytolysis. It has been known for some time that the sera of certain animals when injected into the circulation of animals of another species will cause destructive changes in the blood-corpuscles, accompanied by symptoms of poisoning, which may even end fatally. These results served to bring into disrepute the use of foreign blood in transfusion, which has consequently been practically abandoned. This discharge of the hemoglobin of the red blood-corpuscles and solution in the plasma (laking) is now included in the general term *Cytolysis*, and more specifically known as *Hemolysis*. Agents which produce such an effect are known as hemolytic or hemotoxic agents. Sera of one species are not hemolytic for blood of all other species, but the serum of one animal may be made to acquire such properties for the blood of another.

This adaptation is brought about in the following way: For instance, the blood of the guinea-pig, which is not normally lytic for the red cells of the rabbit, may be adapted to the latter by previously, at several successive intervals (three to seven days) injecting into the abdominal cavity or subcutaneous tissues of the guinea-pig small quantities of rabbit's blood. If now a small quantity of serum be obtained from the guinea-pig by the usual methods and mixed in a test tube with some of the rabbit's blood diluted with physiological salt solution, hemolysis occurs. That is, the coloring matter of the rabbit's red blood-cells goes into solution and the cells appear under the microscope as shadow corpuscles or ghosts, devoid of hemoglobin. Such an artificially produced hemolytic serum is only lytic for the blood of the animal species for which it has been adapted. It is true that it may also show slightly lytic properties for closely allied species. It has therefore been suggested as a possible valuable aid in determining relationships of various animal species.

Concerning the nature of the lytic substance, it has been found that it probably consists of two bodies acting conjointly, for if the serum be heated to 56° C. for a short time, its lytic powers are lost, but may be restored by adding a little serum of another animal of the same species which has not been adapted, and whose serum is consequently not in itself lytic. Of these two bodies, therefore, one is stable and is formed only in the adapted serum, while the other is more unstable or labile (destroyed at 56° C.) and exists normally in the blood plasma. The former is known as the immune body and the latter as alexin. Lysis occurs only when both are present at the same time, and not through the agency of one or the other singly.

This cytolytic adaptation has been extended to include other cells besides the red blood-corpuscles. Thus in a similar manner *leucolytic*, *hepatolytic*, *nephrolytic*, and a number of other lytic sera have been developed.

It is further possible, under certain circumstances, that substances may

be developed in the tissues which are lytic for other tissue cells of the same animal, *autolytic substances*. This may be an important physiological process in the elimination of worn-out tissue cells, cellular elements in injury, inflammation, etc.

Agglutinative Substances. A further property of adapted sera is that of agglutination. The adaptation is secured in the same way as in the production of cytolysins. In fact, both cytolysis and agglutination may occur at the same time. The normal blood serum of some animals may be agglutinative for the blood-cells of some other species. In normal serum, agglutinative and cytolytic properties may be present together or one only may be normally present.

The activity of agglutinative substances is not destroyed at a temperature of 56° C. They do become inert, however, at 70° C., and, furthermore, they cannot be restored by adding normal serum, as is the case with cytolysins.

Precipitins. Other forms of adaptive substances which may be found in animal serum are those which, when mixed with the substances by means of which adaptation has been secured, form a precipitate. By this means blood of different species of animals may be detected even when in a dried state. It has been suggested as a possible valuable aid in medico-legal cases, since human blood in a dilution of 1 to 50,000 has been recognized by this means.

Physical Factors. Diffusion, Osmosis, Dialysis. The term *diffusion* has long been applied to the regular mixing of the molecules of two gases when brought into contact in a confined space, this interpenetration being due to the to-and-fro movements of their molecules. More recently it has been applied to the mixing of the molecules of two solutions when brought into contact, as it has been found that they act in the same way and obey the same laws as gases. If, however, the two solutions are separated by a membrane, permeable to the solutions, diffusion will still occur. To this form of diffusion the term *Osmosis* has been applied in the case of water, and *Dialysis* in the case of diffusible substances. All bodies can be divided into two groups, *crystalloids* and *colloids*. To the former group belong bodies having a crystalline form, which readily go into solution in water. All such bodies are diffusible (dialyz-

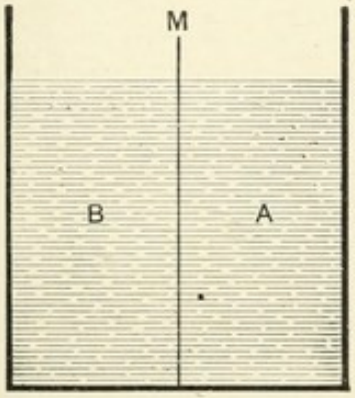


Fig. 124.

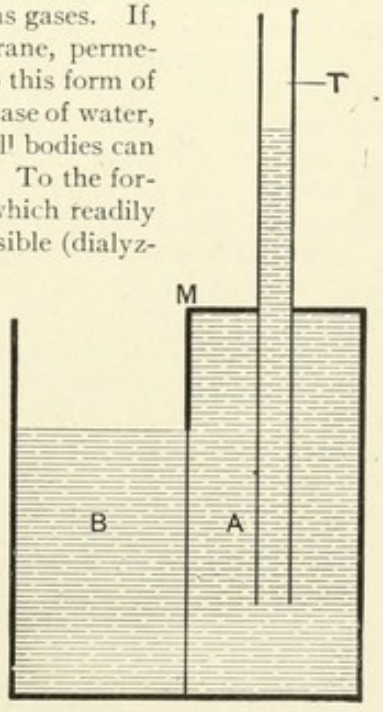


Fig. 125.

able), their power of dialysis, however, varying considerably. To the second group belong such bodies as have no crystalline form (amorphous). These are generally bodies with a large molecule, which form colloidal suspensions in water, and are only slightly or not at all diffusible. An exception to this second group is hemoglobin, which has a very large molecule but is crystalline and is diffusible. The following may serve as simple illustrations:

Take a jar and divide it in two equal parts by an animal membrane, *M*, figure 143, and place an equal amount of distilled water in the two sides, *A* and *B*. Now, since the molecules of water act like those of a gas, and are continually moving to and fro, bombarding all the surfaces of their retainer, the molecules of water in *A* and *B* will be continually striking all the surfaces of *A* and *B*; but since the membrane is permeable to the water molecules, there will be a continual interchange of molecules between *A* and *B*. If now, in one side *A* we place a solution of sodium chloride, still keeping water in *B*, the membrane being permeable to the sodium chloride, the first thing we should notice would be an increase in the amount of water in *A*. Formerly it would have been said that "the salt had attracted the water." Now we should say that the salt had a certain osmotic pressure. The salt, however, being able to pass (dialyze) through the membrane, will do so, and this will continue until the strength of the two salt solutions, and therefore the osmotic pressure on both sides, is equal.

Osmotic Pressure. If now in *A* we place a solution of some soluble colloidal substance to which the membrane is impermeable, or else replace the membrane, *M*, we used in our former experiment by one which is not permeable to the sodium chloride, and arrange our jar as in figure 125, so as to be able to read off any increase of water which may pass into *A*, we will notice that the amount of liquid in *A* will continue to increase up to a certain point. Once that point is reached, there will be no further change, since the substance in solution, in *A*, cannot pass through the membrane as in the previous example. This pressure can be measured and expressed in millimeters of mercury. It is constant for all solutions of this substance that are of the same concentration when measured under like conditions of temperature and pressure, and is called the *Osmotic pressure* of this solution.

Of the numerous explanations regarding the nature of osmotic pressure which have been more or less satisfactory, a simple one, and one that can be easily understood, is as follows: In figure 125 one surface of the membrane is being bombarded by the molecules of a non-diffusible substance mixed with those of a diffusible one (water); while the other surface is being bombarded entirely by water molecules. The former condition permits less water to diffuse out, since fewer molecules get to the surface of the membrane; while the latter permits all of the molecules which reach it to pass through.

Osmotic pressure can be estimated in several different ways in addition to the above, viz., the determination of the freezing point of the solution, determination of the boiling point, determination of the electrical conductivity. The results obtained with the various methods agree very closely. The following solutions have the same osmotic pressure: Sodium chloride, 0.64 per cent; potassium nitrate, 1.09 per cent; sugar 5.5 per cent.

Isotonic Solutions. Solutions that have the same osmotic pressure are called *isotonic*. The term isotonic is a relative one, implying a comparison with some other solution taken as a standard. In physiology it has been customary to take blood-plasma as a standard. A solution of 0.64 per cent sodium chloride is isotonic for the blood-plasma of the frog, and a 0.9 per cent solution for that of man. Further, any solution which is of a lower osmotic pressure than the standard solution is said to be *hypoisotonic* (*hypotonic*) in relation to that solution. A solution of a higher osmotic pressure is said to be *hyperisotonic* (*hypertonic*).

Water passes in the Direction of the Arrows.

Hypertonic saline solution.....(2 per cent)

↑

Blood-plasma

↑↓

Isotonic saline solution.....(0.64 per cent)

↑

Hypotonic saline solution.....(0.3 per cent)

If a hypotonic solution be mixed with blood, water from the hypotonic solution passes through the cell membrane of the red corpuscles into the stroma, and causes it to swell. The hemoglobin at the same time passes out and goes into solution in the diluted plasma. On the other hand, the addition of a hypertonic solution to the plasma causes the red corpuscles to lose their water and become crenated. The principles of osmosis have been derived from the action of substances separated by dead animal or plant membranes. It must be, however, remembered that in the application of these principles to processes occurring in the living organism, the cells, forming the various membranes, are an important modifying factor. It is probable that physico-chemical processes, occurring in the protoplasm the cell, may change its permeability to the same substance at different times.

THE CHARACTER AND COMPOSITION OF LYMPH.

The lymph is the fluid which immediately surrounds the tissue cells of the living body. It fills up the spaces between the cells themselves and between the cells and the blood-vessels which ramify among the cell-masses. The lymph, therefore, is an intermediate fluid between blood-plasma on the one hand, and the tissue cells on the other, receiving its ingredients by the passage of fluid from the plasma through the walls of the finer blood-vessels in the one direction, and by the discharge of the substances from the cells themselves in the other.

The Chemical Composition of the Lymph. Since the chief source of the lymph is the blood-plasma, one would naturally expect that its chemical composition would be very similar to that of plasma, which is in fact the case. The variations that are noted in lymph taken from definite sources no doubt have their origin in the fact that the lymph passes through these organs slowly, and that ingredients peculiar to the necessities of the function and growth of the differentiated tissue of the organ are taken from the lymph in special organs. Lymph obtained from a human lymphatic fistula has been analyzed; the figures from Hammarsten are as follows, though considerable variations appear in the analyses from other authorities:

ANALYSIS OF LYMPH.

	Per cent
Water	94.5 to 96.5
Solids	3.7 to 5.5
Albumins	3.4 to 4.1
Ethereal extract	0.06 to 0.13
Sugar	0.1
Salts	0.8 to 0.9
Sodium chloride	0.55 to 0.58
Sodium carbonate	0.24
Disodic phosphate	0.028

The most notable fact to be derived from this composition table is the low percentage of proteids present in the lymph.

The Formation of Lymph. The manner in which the substances in the lymph pass through the walls of the capillaries from the plasma is a

question which has been surrounded with considerable difficulty. It is thought by Ludwig and many of his followers that the process involved is merely one of filtration. Certainly the blood pressure in the capillaries is in the main greater than that of the pressure of the lymph in the surrounding tissues, and this positive pressure will contribute so much to the direct ingredients of the blood-plasma through the capillary walls. It is true, as a matter of experiment, that anything which contributes to an increase in the capillary pressure is very apt to produce an edema of the corresponding tissues. Since the colloidal materials represented by the proteid are non-diffusible, one would by this theory expect to find a diminished percentage in the lymph, which is true, though not to the extent which the theory demands.

Heidenhain was the first to question the adequacy of the blood pressure and filtration hypothesis. He showed that many of the conditions under which lymph formation takes place are not sufficient to produce filtrations of the material found. He advanced the hypothesis that the living endothelial lining of the blood-vessels exerted a secretory activity in lymph production. He discovered that various substances known as lymphagogues when introduced into the circulatory system produce a remarkable increase in the flow of lymph from the thoracic duct. Further, he noticed that the concentration of the lymph was changed, *i.e.*, increased. It has been suggested that these substances act to change the normal resistance of the endothelial cells, and this has been offered as a criticism. Nevertheless many drugs act to increase the flow of lymph in a way which cannot be presumed to be other than normal, *i.e.*, they stimulate the physiological processes going on in the endothelial cells. Such observations contribute strongly to the view advanced by Heidenhain. Many investigations have been brought to the support of the hypothesis that lymph formation is largely a process of secretion, yet it seems at the present time that we cannot wholly deny that filtration and osmosis play a part in the processes. Certainly the permeability or activity of the endothelial lining of the blood-vessels varies greatly at different times in the life of an individual, and this variation in function is associated with the marked change in the character and quantity of lymph produced.

The second factor in lymph formation, the activity of the tissue in taking up or discharging materials into the lymph-mass, must not be ignored altogether.

LABORATORY EXPERIMENTS FOR THE EXAMINATION OF THE BLOOD.

1. **Microscopical Examination of the Blood.** Mount a drop of frog's blood in 0.7 per cent sodium chloride and examine with the low power of a compound microscope. The red corpuscles will appear as oval nucleated

discs with a faint yellowish color, figure 110. Here and there white granular cells of irregular outline will be noted, the white corpuscles. Examine the drop of blood with a high magnifying power and sketch the outline of the blood cells. Select the white corpuscle which is most irregular in outline and make a series of outline drawings once every minute to show its ameboid movements, figure 117.

Draw a drop of your own blood by puncturing the tip of the finger, under sterile conditions, and mount in a drop of 0.9 per cent physiological saline. Examine with a high power, note the small biconcave red corpuscles which appear faintly yellow in color and even adhere in rouleaux, figure 109. The white corpuscles will appear as somewhat larger granular discs differing in form and size. By mounting a drop of blood on a warm stage the ameboid movements of the white corpuscles can be observed with comparative ease.

2. **Action of Fluids on the Red Corpuscles.** *Water.* When water is added gradually to frog's blood, the oval disc-shaped corpuscles become spherical and gradually discharge their hemoglobin, a pale, transparent stroma being left behind. Human red blood cells change from a discoidal

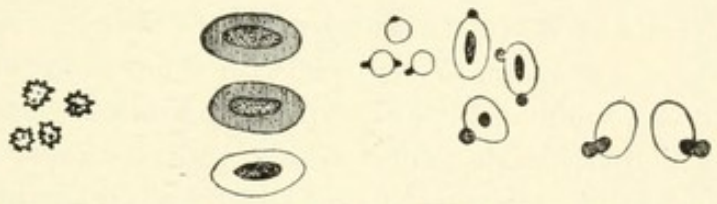


FIG. 126. FIG. 127. FIG. 128. FIG. 129.

FIG. 126.—Effect of Hypertonic Salt-Solution on the Red Blood-Corpuscles of Man.
FIG. 127.—Effect of Acetic Acid. FIG. 128.—Effect of Tannin. FIG. 129.—Effect of Boric Acid.

to a spheroidal form and discharge their cell-contents, becoming quite transparent and all but invisible (ghost corpuscles).

Hypertonic Salt-Solutions. Mount a drop of human blood in 2 per cent sodium-chloride solution. The red blood cells lose their disc shape and become spherical with spinous projections or crenations, figure 126.

The original form of the red blood cells can be restored by transferring them to isotonic salt-solution.

Dilute Acetic Acid. This reagent causes the nucleus of the red blood cells in the frog to become more clearly defined; if the action is prolonged, the nucleus becomes strongly granulated, and all the coloring matter seems to be concentrated in it, the surrounding cell-substance and outline of the cell becoming almost invisible; after a time the cells lose their color altogether. The cells in figure 127 represent the successive stages of the change. A similar loss of color occurs in the red cells of human blood, which, from the absence of nuclei, seem to disappear entirely.

Alkalies. Alkalies cause the red blood-corpuscles to absorb water and finally to disintegrate.

Chloroform and Ether. These reagents when added to the red blood cells of the frog cause them to part with their hemoglobin; the stroma of the cells becomes gradually broken up. A similar effect is produced on the human red blood cell.

Tannin and Boric Acid. When a 2 per cent fresh solution of tannic acid is applied to frog's blood it causes the appearance of a sharply defined little knob, projecting from the free surface (*Roberts' macula*). The coloring matter becomes at the same time concentrated in the nucleus, which grows more distinct, figure 128. A somewhat similar effect is produced on the human red blood-corpuscle.

A 2 per cent solution of boric acid applied to nucleated red blood cells of the frog will cause the concentration of all the coloring matter in the nucleus; the colored body thus formed gradually quits its central position, and comes to be partly, sometimes entirely, protruded from the surface of the now colorless cell, figure 129. The result of this experiment led Brücke to distinguish the colored contents of the cell (*zoöid*) from its colorless stroma (*ecoid*). When applied to the non-nucleated mammalian corpuscle its effect merely resembles that of other dilute acids.

3. **Phagocytosis in White Corpuscles.** Mix some very fine pigment granules, powdered vermilion, or charcoal with a few drops of frog's blood, let stand for 10 or 20 minutes, then mount a drop on the glass slide and examine under a high-magnifying microscope. In a favorable field here and there will be found some white corpuscles which have taken up the pigment. Colored corpuscles have been observed with fragments of pigment embedded in their substance. White corpuscles have also been seen in diseased states of the body to contain micro-organisms, for example, bacilli, and are said to have the power of destroying these organisms, which gives them the name *phagocytes*.

4. **Enumeration of the Blood-Corpuscles.** Several methods are employed for counting the blood-corpuscles, most of them depending upon

FIG. 130.—Thoma-Zeiss Hemacytometer, glass slide.

the same principle, *i.e.*, the dilution of a minute volume of blood with a given volume of a colorless solution similar in specific gravity to blood-plasma, so that the size and shape of the corpuscles are altered as little as possible. A minute quantity of the well-mixed solution is then taken, examined under the microscope, either in a flattened capillary tube (Malassez) or in a cell (Hayem and Nachet, Gowers) of known capacity, and the number of corpuscles in a measured length of the tube, or in a given area of the cell, is counted. The length of the tube and the area of the cell are ascertained by means of a micrometer scale in the microscope ocular; or in the case of Gowers' modi-

fication, by the division of the cell area into squares of known size. Having ascertained the number of corpuscles in the diluted blood, it is easy to find out the number in a given volume of normal blood.

The hemacytometer, which is most used at the present time, is known as the Thoma-Zeiss hemacytometer. It consists of a carefully graduated pipet, in which the dilution of the blood is done; this is so formed that the capillary stem has a capacity equalling one-hundredth of the bulb above it. If the blood is drawn up in the capillary tube to the line marked 1, figure 131, the saline solution may afterward be drawn up the stem to the line 101; in this way we have 101 parts of which the blood forms 1. As the content of the stem can be displaced unmixed we shall have in the mixture the proper dilution. The blood and the saline solution are well mixed by shaking the pipet, in the bulb of which is contained a small glass bead for the purpose of aiding the mixing. The other part of the instrument consists of a glass slide, figure 130, upon which is mounted a covered disc, *m*, accurately ruled so as to present one square millimeter divided into 400 squares of one-twentieth of a millimeter each. The micrometer thus made is surrounded by another annular cell, *c*, which has such a height as to make the cell project exactly one-tenth millimeter beyond *m*. If a drop of the diluted blood be placed upon *m*, and *c* be covered with a perfectly flat cover-glass, the volume of the diluted blood above each of the squares of the micrometer, *i.e.*, above each $\frac{1}{400}$, will be $\frac{1}{4000}$ of a cubic millimeter. An average of ten or more squares is then taken, and this number multiplied by 4000×100 gives the number of corpuscles in a cubic millimeter of undiluted blood. A separate pipet is used for making dilutions for counts of leucocytes. In this, the dilution is made of one part of blood and ten parts of diluting fluid. Acetic acid, 0.2 of one per cent, is usually employed for this purpose.

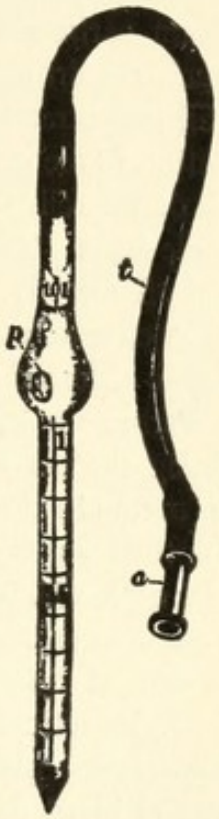


FIG. 131. — Thoma-Zeiss Hemacytometer, pipet.

5. **The Percentage of Corpuscles and Plasma in Human Blood.** Fill the two graduated capillary tubes of a hematocrite with blood drawn from the tip of your own finger, insert into the instrument, and centrifuge as rapidly as possible. The experiment must be performed within the time limit of clotting in order to be successful. The corpuscles will be thrown down and the percentage of plasma and corpuscles can be read off directly. Should one fail to fill the tube exactly full, then the percentage of plasma and corpuscles can be calculated from the proportion which each bears to the quantity in the tube.

6. **Estimation of the Percentage of Hemoglobin.** The per cent of hemoglobin in a sample of blood can be obtained by the instrument known as Fleischl's hemometer, see figure 122. The principle of this instrument rests on a comparison of the color of the sample of dilute blood with a standard glass wedge of uniform tint similar to that of blood. Fill one of the chambers in the cells of the instrument half full with a 2 per cent solution of sodium carbonate. Now draw a drop of blood from the tip of a finger. Touch the drop with the end of the standardized capillary tube, using care to fill it accurately. Quickly wash this sample of blood out in the carbonate solution in the cell and finish filling the cell. Put distilled water in the other half of the cell, mount in the instrument, and examine in a dark room, using candle-light. The glass wedge is graduated in percentage which can be read off directly. This instrument is usually provided with several cells, in which case as many samples may be taken and the average of the readings used to determine the percentage.

Perhaps a more convenient and certainly a quicker method for determining the percentage of hemoglobin is Talquist's hemoglobinometer. By this method a drop of blood is drawn directly on to absorbent paper furnished with the instrument, and the resulting stain is compared directly with a paper color scale which is graduated in percentage. In this method the comparison is made in ordinary daylight, and because of its rapidity it is very convenient for clinical examinations.

7. **Reaction of Blood-Plasma.** Wet a piece of neutral litmus paper (some prefer glazed paper), then touch one end of the strip with a drop of blood drawn from your finger under sterile conditions. After a few moments wash off the excess of corpuscles in neutral distilled water. The deeper blue at the point of contact with the blood indicates alkalinity.

8. **The Specific Gravity of Blood.** From standard mixtures of chloroform and benzol with specific gravity of 1.050, 1.060, and 1.070 make up a set of specific-gravity solutions of 1.050, 1.052, 1.054, etc., to 1.070. These standards may be kept in stoppered 4-dram vials, or in test tubes. The specific gravity of blood is determined by inserting with a pipet a drop of freshly drawn blood into the middle of one of the solutions, say 1.056. Since the blood does not mix with the chloroform and benzol the drop will rise or sink according to its relative specific gravity. By a few trials one may quickly find a specific gravity in which the drop of blood floats without rising or sinking. This represents the specific gravity of the drop of blood.

This method permits rapid clinical application and has proven of considerable interest in the hands of clinists.

9. **The Isotonicity of Blood.** The absorption or loss of water by the corpuscles of blood in solutions of other concentrations than that of blood-plasma can be used as a means of determining the isotonicity of blood.

Make up a series of solutions of sodium chloride, varying by tenths, from 0.5 to 1.2 per cent. Prepare a series of slides with vaseline rings and mount drops of human blood in drops of saline of 0.6, 0.7, 0.8, 0.9, 1, and 1.1 per cent, examine every ten minutes under a high-power microscope. The corpuscles of some of the slides will swell up and may disintegrate, others will show crenation as in figure 126. In the isotonic solutions the corpuscles will appear of their normal size and condition.

10. **Coagulation of Blood.** *a. Normal Clot.* Anesthetize a dog, insert a cannula into the carotid or femoral artery, and draw samples of blood into two or three clean, dry test tubes. Draw one sample into a test tube that has had its sides oiled. Note the exact time at which the blood was drawn into the test tubes and set the test tubes in a test-tube rack. Examine at intervals of 30 seconds by gently inclining the test tubes. Presently

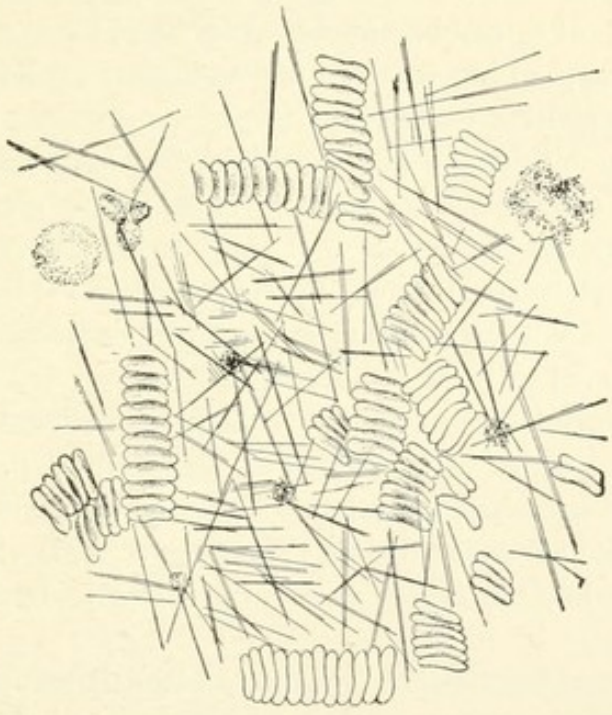


FIG. 132.—Miscroscopic View of Clot Showing Fibrin Network.

it will be noted that the blood becomes more viscous and does not flow freely up the sides of the test tubes. Later the whole mass will become jelly-like and will retain the form of the test tube. Note the time of the first slight change, and also when the clot becomes more perfect. The sample in the oiled test tube will be found to clot more slowly.

If the test tubes of clotted blood are left standing for a day, the coagulum will become similar in size and a transparent yellowish blood will make its appearance on the surface or between the sides of the clot and the test-tube wall. This fluid is the serum and it is squeezed out by the shrinking of the fibrin which holds the corpuscles in its meshes.

b. Microscopic Examination of the Process of Clotting. Take a drop of

fresh blood from the tip of your finger under sterile conditions and mount on a microscopic slide in a few drops of salt-solution, and examine immediately under the high power. Small threads of fibrin will presently be seen to form across the field, usually being most clearly obvious where fragments of white corpuscles are noted, see figures 107 and 132. The threads of fibrin become more apparent when stained with rosanilin.

c. Whipped Blood. Draw a sample of blood into a glass tumbler, enough to fill it one-half or two-thirds full. Immediately begin vigorously stirring the blood with a bunch of stiff wires or a pencil, and keep it up until the time of clotting has passed, 5 or 10 minutes. In this instance the wires will break up and collect the fibrin as fast as it forms, and no firm mass will be produced. The remaining fluid is called *whipped blood.* The *fibrin* can be removed from the wires and washed in tap water until all the adherent red corpuscles are removed. This mass of fibrin is white, elastic, and composed of a network of thread-like fibers. It is these fibers extending through and through the mass of blood which makes it retain the form of the vessel when undisturbed clotting occurs.

d. The Influence of Salt-Solution on Blood-Clotting. Add 20 c.c. of saturated magnesium sulphate, 1 per cent sodium oxalate, and 2.5 per cent of sodium chloride in each of 3 beakers. Draw into each beaker 50 to 60 c.c. of blood and immediately mix thoroughly and let stand. The magnesium and oxalate beakers will not coagulate even though they stand for days, but the sodium-chloride blood will clot in a few minutes.

The magnesium-sulphate blood will coagulate if diluted with a sufficient amount of distilled water or physiological saline solution. Make a series of dilutions and note when coagulation takes place. The sodium-oxalate blood will coagulate when a sufficient excess (1 per cent) of calcium chloride is added to neutralize the excess of sodium oxalate. Demonstrate this on a series of samples.

If a liter or so of magnesium or oxalate blood is secured and separated by a centrifuge, or by leaving stand for a sufficient time, a sample of salted plasma will be obtained. This sample will coagulate when it is treated as just described for salted blood, showing that the antecedents of fibrin are found in the plasma.

e. Action of Tissue Extracts on Coagulation. Wash out the blood of a small animal by circulating 0.9 per cent saline through the arteries until the outflowing fluid from the veins is clear. Take an organ, the liver for example, grind it up in a sausage mill by running it through the mill two or three times, then extract with 0.9 per cent physiological saline. The macerating mass should be shaken up at intervals, and may be kept from spoiling by adding an excess of chloroform or by keeping on ice. A few cubic centimeters of this fluid extract added to a sample of freshly drawn blood will very greatly hasten the rapidity of coagulation. This tissue ex-

tract is called *thrombokinase*, as it is an activator which hastens the formation of thrombin from thrombogen.

11. **The Chemistry of Blood-Plasma (or Serum).** The blood-plasma contains all the chemical substances which are utilized by the tissues in their nutrition or which are thrown off by the tissues as a result of their activity. It is therefore a very complex mixture. The serum contains the same substances in the same proportion, with the exception of the antecedents of fibrin. It may, therefore, be used as a substitute for plasma in most cases.

a. Proteids of Plasma. There are three principal proteids in blood-plasma: serum-albumin, serum-globulin, and *fibrinogen*. These may be isolated as follows: To a sample of blood-plasma add an equal quantity of sodium-chloride solution that has been saturated at 40° C. A white flocculent precipitate of *fibrinogen* comes down. Filter off, and add to the filtrate an equal volume of saturated ammonium sulphate. A second heavier precipitate of *serum-globulin* separates out. When this is separated, and crystals of ammonium sulphate are added to the filtrate to complete saturation at 40° C., a third precipitate of *serum-albumin* separates.

Each of these precipitates may be redissolved and purified by reprecipitation and can be tested by the characteristic proteid reactions, see page 96, which they all give.

b. Sugars of Blood-Plasma or Serum. If a quantity of blood-serum is diluted with about 5 to 10 times its volume of water, and the proteids are removed by slight acidulation with acetic acid and boiling and filtering, the filtrate will contain reducing sugar and the various solids of blood-plasma. To a concentrated sample of the filtrate add Fehling's solution and boil. A reddish precipitate indicates the presence of reducing sugar. If this experiment is done quantitatively, about from 0.1 to 0.2 per cent of sugar will be found.

c. The Salts of Blood-Plasma. The salts of blood-plasma are tested best by evaporating some of the blood serum to dryness, and burning the residue to oxidize the organic matter and dissolving the ash in water. Test as follows: To a sample add 1 per cent of silver nitrate; a white precipitate soluble in an excess of ammonia, but not soluble in nitric acid, indicates *chlorides*.

To a second sample add 1 per cent barium chloride. If *sulphates* are present there will be a white precipitate which settles out quickly.

Acidify a third sample with nitric acid and add ammonium molybdate and heat. A yellow precipitate indicates the presence of *phosphates*.

To the fourth sample add an excess of strong ammonia and 1 per cent ammonium oxalate, heat. A white precipitate indicates the presence of *calcium*.

12. **Blood-Corpuscles.** The characteristic substance in the composi-

tion of the corpuscles is the pigment known as *hemoglobin*, and this is the only chemical factor that will be considered in these experiments.

a. Hemoglobin Crystals. Take a sample of dog's blood, or if a centrifuge is available separate and wash the sample of blood-corpuscles, and mix with about three volumes of saturated ether water, or if blood is used dilute with two or three volumes of water and add about 10 per cent of pure ether and shake thoroughly. Crystals of oxyhemoglobin will be formed, and this can be mounted and examined with a microscope.

b. Spectrum of Hemoglobin and its Compounds.

1. *Oxyhemoglobin.* Dilute a sample of defibrinated blood with about ten volumes of distilled water. From this stock solution make five solutions all differing by $33\frac{1}{3}$ per cent. Examine these with a direct-vision spectroscope. Make a drawing showing the absorption spectrum of each sample as compared with the solar spectrum. Compare with the spectrum shown in the frontispiece.

2. *Hemoglobin.* The oxygen can be driven out from the hemoglobin by adding to the above samples a few drops of ammonium sulphide and gently warming. Re-examine with the direct-vision spectroscope and map as before.

3. *Carbon-Monoxide Hemoglobin.* Pass a stream of ordinary illuminating gas through the dilutions of hemoglobin. The carbon monoxide of the gas will form a compound with the hemoglobin, which now turns a bright scarlet color. When examined with the spectroscope, the absorption bands are found to be very similar to those of oxyhemoglobin. However, map the spectrum to the scale as usual. Add the reducing agent, warm, and shake vigorously and re-examine. It is very difficult to break up the combination of hemoglobin with carbon monoxide, hence the poisonous action of this gas.

CHAPTER V

THE CIRCULATION OF THE BLOOD

THE blood is contained in a system of closed vessels through which it is kept in circulation during the life of an individual. The energy to keep up this motion is supplied by the heart, which is a large muscular organ consisting of four great divisions, the right and left auricles and right and left ventricles. The right ventricle discharges its blood into the pulmonary artery,

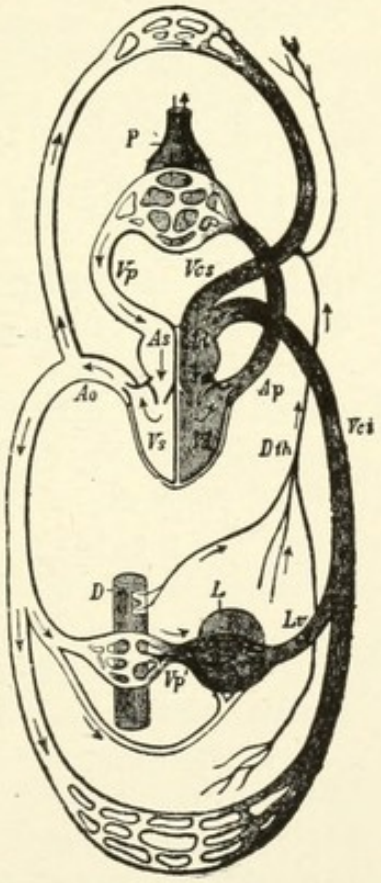


FIG. 133.—Diagram of the Circulation in an Animal with a Completely Separated Right and Left Ventricle and a Double Circulation. (After Huxley.) *Ad*, Right auricle receiving the superior and inferior venæ cavæ, *Vcs* and *Vci*; *Dth*, thoracic duct, the main trunk of the lymphatic system; *Ad*, right auricle; *Vd*, right ventricle; *Ap*, pulmonary artery; *P*, lung; *Vp*, pulmonary vein; *As*, left auricle; *Vs*, left ventricle; *Ao*, aorta; *D*, intestine; *L*, liver; *Vp*, portal vein; *Lv*, hepatic vein.

through which it passes to the lungs, returning through the pulmonary veins to the left auricle, and into the ventricle. From the left ventricle the blood is pumped into the great aorta, and through its branches distributed to the entire body. The terminal arteries are continuous with the general capillaries of the

body, and these in turn with the veins, which conduct the blood back to the right side of the heart again. It will be seen, therefore, that the circulatory apparatus consists of two great divisions, the *pulmonary* and the *systemic* circulation. This arrangement is illustrated by the accompanying figure. A study of this figure will show that in certain regions of the systematic circulation there are two capillary beds between the main arteries and the main veins. This subordinate stream through the liver is called the *portal* circulation, and the similar arrangement existing in the kidney is called the *renal* circulation. This, in general, is the outline of the course of the blood in its circulation.

To make a study of the various phenomena manifested in the physiology of the circulatory apparatus, it is obvious that we have to do with certain fundamental activities; first, the physiology of the pumping organ, the heart; second, the behavior of the blood in the arteries, capillaries, and veins; third, the coordination of these various divisions of the apparatus through the nervous system. To understand this it will be necessary to have in mind in detail the anatomical structure of the apparatus itself.

ANATOMICAL CONSIDERATIONS.

The Heart. The heart is contained in the chest or thorax, and lies between the right and left lungs, figure 134, enclosed in a membranous sac, the *pericardium*. The pericardium is made up of two distinct parts, an external fibrous membrane, and an internal serous layer, which not only lines the fibrous sac, but also is reflected on to the heart, which it completely invests. These form a closed sac, the cavity of which contains just enough fluid to lubricate the two surfaces, and thus to enable them to glide smoothly over each other during the movements of the heart. The vessels passing in and out of the heart receive investments from this sac to a greater or less degree.

The heart is situated in the chest behind the sternum and costal cartilages, being placed obliquely from right to left. It is of pyramidal shape, with the apex pointing downward, outward, and toward the left, and the base backward, inward, and toward the right. The heart is suspended in the chest by the large vessels which proceed from its base, but, excepting at the base, the organ itself hangs free within the sac of the pericardium. The part which rests upon the diaphragm is flattened, and is known as the *posterior* surface, while the free upper part is called the *anterior* surface.

On examination of the external surface, the division of the heart into parts which correspond to the chambers inside of it may be traced, for a deep transverse groove, called the *auriculo-ventricular groove*, divides the auricles from the ventricles; and the *interventricular groove* runs between the ventricles, both in front and in the back, separating the one from the other. The anterior groove is nearer the left margin, and the posterior nearer

the right, as the front surface of the heart is made up chiefly of the right ventricle and the posterior surface of the left ventricle. The coronary vessels which supply the tissue of the heart with blood run in the furrows or grooves; also the nerves and lymphatics, which are embedded in more or less fatty material, are found in this groove.

The Chambers of the Heart. The interior of the heart is divided by a longitudinal partition in such a manner as to form two chief chambers or cavities, the right and the left. Each of these chambers is again subdivided transversely into an upper and a lower portion, called respectively the auricle

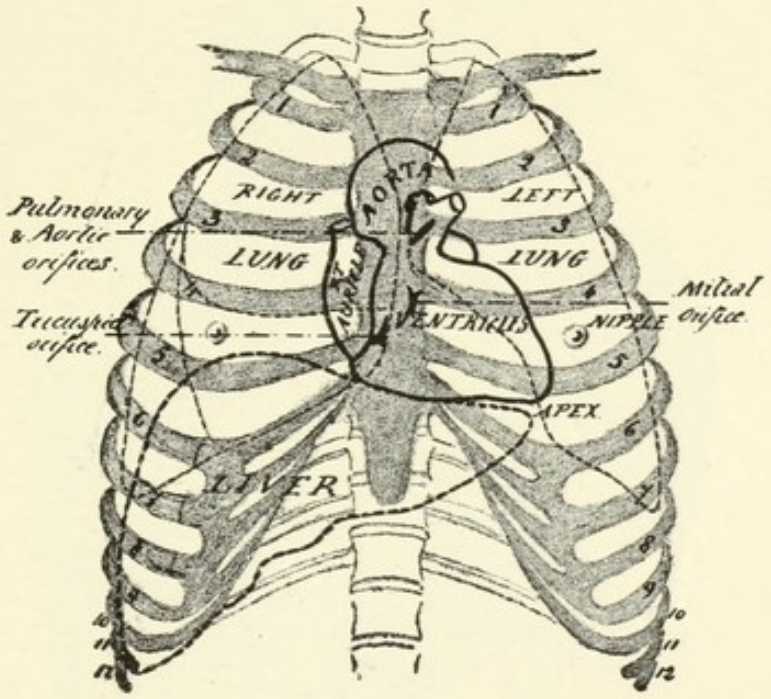


FIG. 134.—Outline of Heart, Lungs, and Liver to Show their Relations to each other and to the Chest Wall. (Heusman and Fisher's "Anatomical Outlines.")

and the ventricle, which freely communicate. The aperture of communication, however, is guarded by valves so disposed as to allow blood to pass freely from the auricle into the ventricle, but not in the opposite direction. There are thus four cavities in the heart, the auricle and ventricle of one side being quite separate from those on the other, figure 135.

The right auricle, the right part of the base of the heart as viewed from the front, is a thin-walled cavity of more or less quadrilateral shape, prolonged at one corner into a tongue-shaped portion, the right auricular appendix, which slightly overlaps the exit of the aorta from the left ventricle.

The interior of the auricle is smooth, being lined with the general lining membrane of the heart, the *endocardium*. The superior and inferior venæ cavæ open into the auricle. The opening of the inferior cava is protected and partly covered by a membrane called the *Eustachian valve*. In the posterior wall of the auricle is a slight depression called the *fossa ovalis*,

which corresponds to an opening between the right and left auricles, existing in fetal life. In the appendix are closely set elevations of the muscular tissue, covered with endocardium, and on the anterior wall of the auricle are similar elevations arranged parallel to one another, called *musculi pectinati.*

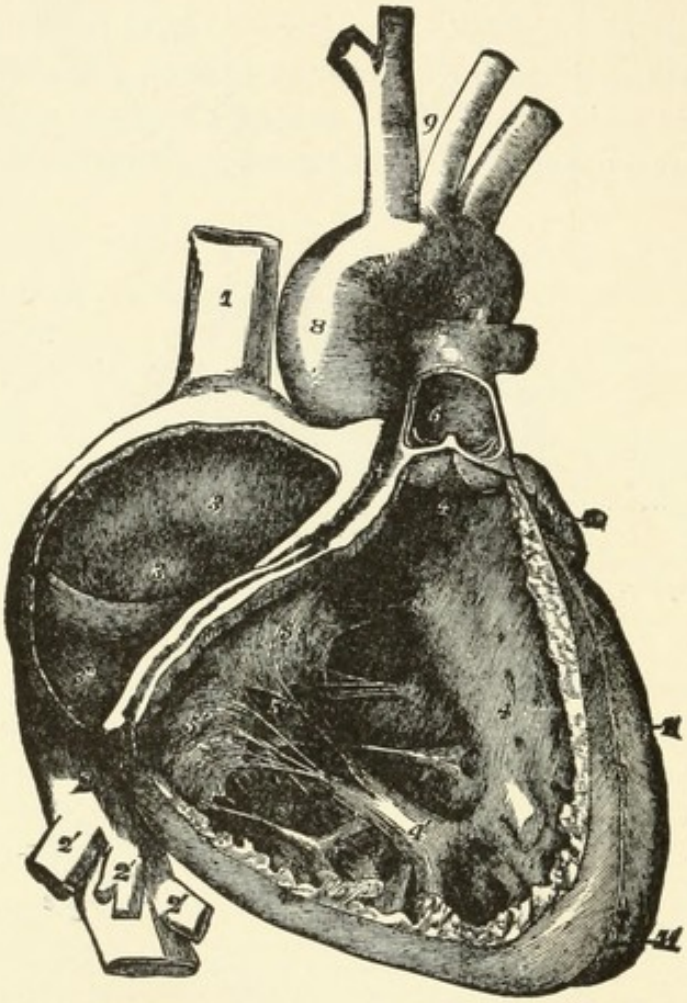


FIG. 135.—The Right Auricle and Ventricle Opened and a Part of their Right and Anterior Walls Removed so as to Show their Interior. 1, Superior vena cava; 2, inferior vena cava; 2′, hepatic veins cut short; 3, right auricle; 3′, placed in the fossa ovalis, below which is the Eustachian valve; 3″, is placed close to the aperture of the coronary vein; †, †, placed in the auriculo-ventricular groove, where a narrow portion of the adjacent walls of the auricle and ventricle has been preserved; 4, 4, cavity of the right ventricle, the upper figure is immediately below the semilunar valves; 4′, large columna carnea or musculus papillaris; 5, 5′, 5″, tricuspid valve; 6, placed in the interior of the pulmonary artery, a part of the anterior wall of that vessel having been removed and a narrow portion of it preserved at its commencement where the semilunar valves are attached; 7, concavity of the aortic arch close to the cord of the ductus arteriosus; 8, ascending part or sinus of the arch covered at its commencement by the auricular appendix and pulmonary artery; 9, placed between the innominate and left carotid arteries; 10, appendix of the left auricle; 11, 11, outside of the left ventricle the lower figure near the apex. (Allen Thomson.)

The right ventricle forms the right margin of the heart. It takes no part in the formation of the apex. On section its cavity is semilunar or crescentic, figure 137. Into it are two openings, the auriculo-ventricular orifice at the base, and the opening of the pulmonary artery, also at the base but more to the left. The part of the ventricle leading to the pulmonary artery is called the *conus arteriosus* or *infundibulum;* both orifices are guarded by valves, the former called the *tricuspid* and the latter the *semilunar.*

In this ventricle are also the projections of the muscular tissue called the *columnæ carneæ*.

The left auricle is situated at the left and posterior part of the base of the heart. The left auricle is only slightly thicker than the right and its

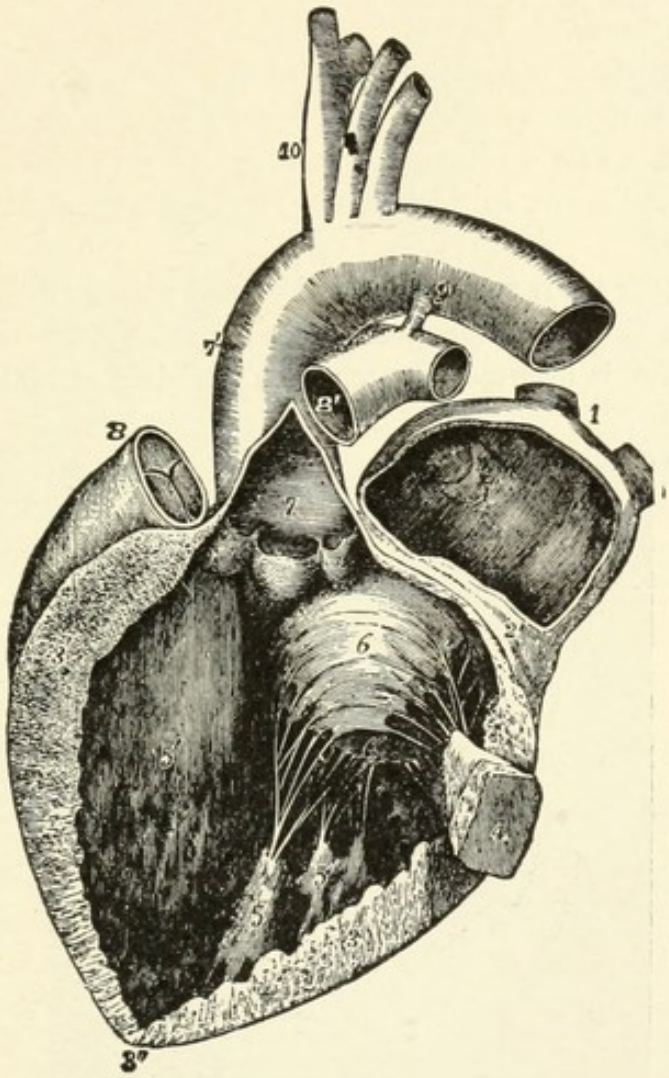


FIG. 136.—The Left Auricle and Ventricle Opened and a Part of Their Anterior and Left Walls Removed. Magnified ½. The pulmonary artery has been divided at its commencement; the opening into the left ventricle is carried a short distance into the aorta between two of the segments of the semilunar valves; and the left part of the auricle with its appendix has been removed. The right auricle is out of view. 1, The two right pulmonary veins cut short; their openings are seen within the auricle; 1′, placed within the cavity of the auricle on the left side of the septum and on the part which forms the remains of the valve of the foramen ovale, of which the crescentic fold is seen toward the left hand of 1′; 2, a narrow portion of the wall of the auricle and ventricle preserved round the auriculo-ventricular orifice; 3, 3′, the cut surface of the walls of the ventricle, seen to become very much thinner toward 3″, at the apex; 4, a small part of the anterior wall of the left ventricle which has been preserved with the principal anterior columna carnea or musculus papillaris attached to it; 5, 5, musculi papillares; 5′, the left side of the septum, between the two ventricles, within the cavity of the left ventricle; 6, 6′, the mitral valve; 7, placed in the interior of the aorta near its commencement and above the three segments of its semilunar valve which are hanging loosely together; 7′, the exterior of the great aortic sinus; 8, the root of the pulmonary artery and its semilunar valves; 8′, the separated portion of the pulmonary artery remaining attached to the aorta by 9, the cord of the ductus arteriosus; 10, the arteries rising from the summit of the aortic arch. (Allen Thomson.)

form and structure are the same as in the right. The left *auriculo-ventricular* orifice is oval and a little smaller than that on the right side of the heart. There is a slight vestige on the septum of the foramen between the auricles.

The left *ventricle* occupies the posterior and apical portion of the heart, and is connected directly with the great aorta. It is separated from the auricle by the *bicuspid* or *mitral* valves, and the opening into the great aorta is guarded by the semilunar valves. The walls of the left ventricle are two or three times as heavy as those of the right, and may be as much as half an inch in total thickness.

The left ventricle is capable of containing 90 to 120 c. c. of blood. The capacity of the auricles is considerably less after death owing to their contracted condition. The whole heart is about 12 cm. long by 8 cm. at its greatest width, and 6 cm. in thickness. The average weight in the adult is about 300 grams.

The walls of the heart are constructed almost entirely of layers of muscular fibers; but a ring of connective tissue, to which some of the muscular fibers are attached, is inserted between each auricle and ventricle and forms

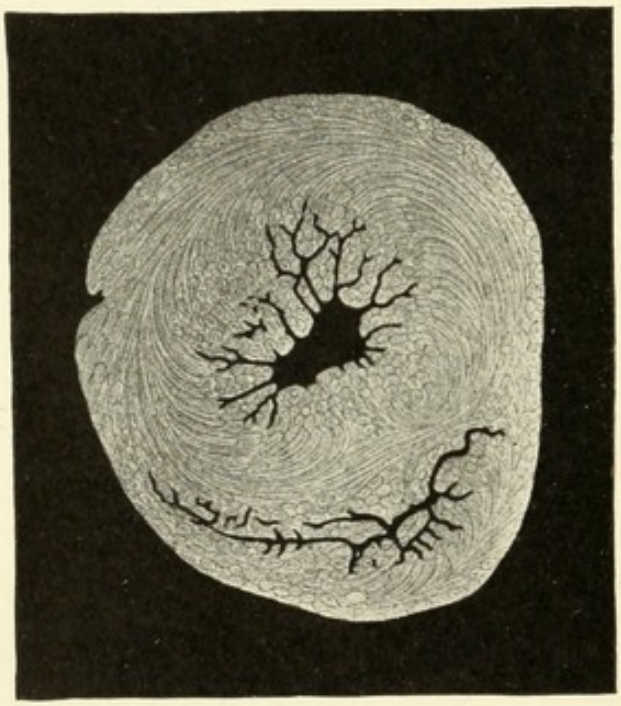


FIG. 137.—Cross-section of a Completely Contracted Human Heart, at the Level of the Lower and Middle Thirds. (According to Krehl.)

the boundary of the *auriculo-ventricular* opening. Fibrous tissue also exists at the origins of the pulmonary artery and aorta. The muscular fibers of each auricle are in part continuous with those of the other, and in part separate; and the same holds true for the ventricles. The fibers of the auricles are, however, quite separate from those of the ventricles, the bond of connection between them being the fibrous and the embryonic muscular tissue of the auriculo-ventricular rings and the bundle of His in the septum.

The development of the heart shows that it is derived from an embryonic tube, which in its growth becomes twisted upon itself and divided into the

two main divisions that we know in the adult. Anatomical dissections have shown that the muscles of the ventricles form spiral sheaths extending from

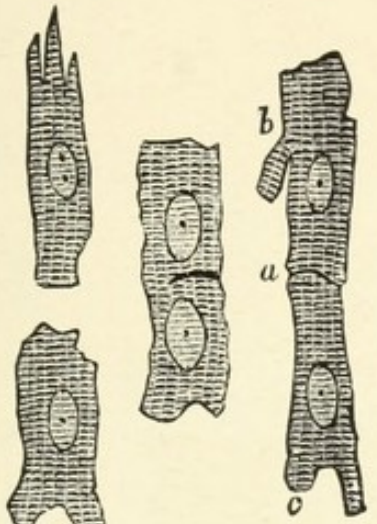


Fig. 138.

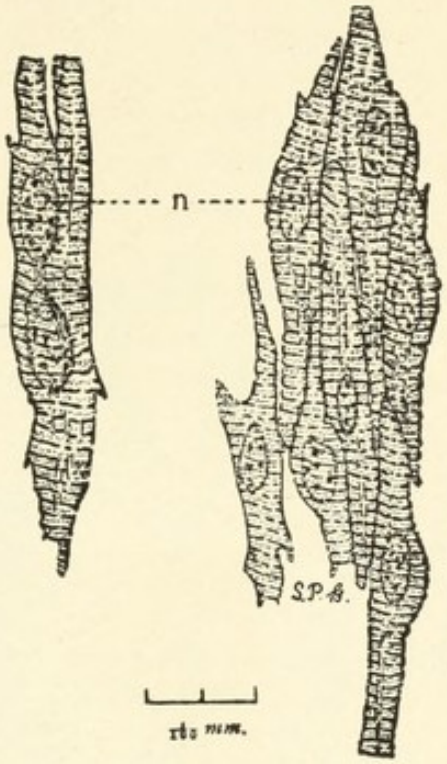


Fig. 139.

Fig. 138.—Cardiac Muscle Cells, Showing their Form, Branches, Nuclei, and Striæ. From the heart of a young rabbit. Magnified 425 diameters. (Schäfer.) *a*, Line of junction between the cells (intercellular cement); *b*, *c*, branches of the cells.

Fig. 139.—Cardiac Muscle Cells of the Left Ventricle of a Child at Birth (full term), to show the form of the cells, their structural details, their relations to one another, and their general agreement with those of cold-blooded vertebrates. *A*, Large cell with two nuclei; this cell has nearly the proportions of those of the adult; *B*, group of cells in their natural relation. At the right of the middle cell are two spaces or fissures. *n*, Nucleus. The transverse striations cross the nuclei in all the cells, and each nucleus possesses several nucleoli. (Gage.)

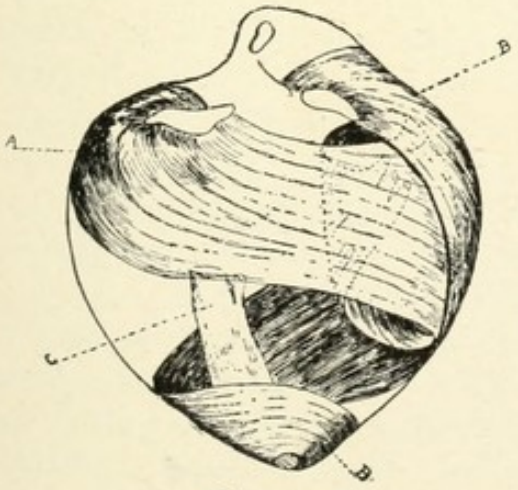


Fig. 140.

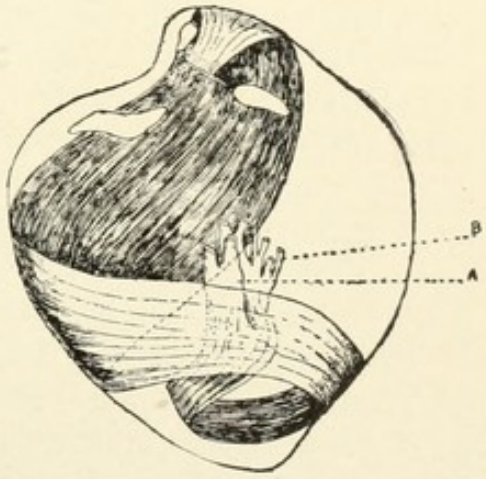


Fig. 141.

Fig. 140.—Diagram of the Course of the Superficial Muscle Layers Originating in the Right and Left Auriculo-ventricular Rings and in the Posterior Half of the Tendon of the Conus. (After MacCallum.) *C*, Anterior papillary muscle.

Fig. 141.—Diagram of the Course of the Superficial Muscle Layers Originating in the Anterior Half of the Tendon of the Conus. (After MacCallum.) *A*, Posterior papillary muscle; *B*, papillary muscle of the septum.

the base of the two ventricles in spiral bands toward the apex. These bands of muscle are wound about the surface of the ventricles in the right-to-left direction. At the apex they extend up into the deeper tissue. If the superficial muscles are dissected off, there is left a great central core of muscle,

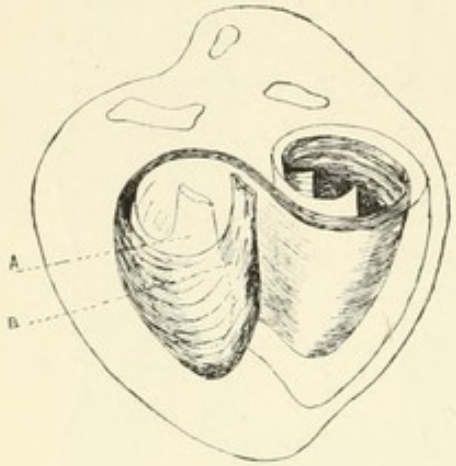


FIG. 142.

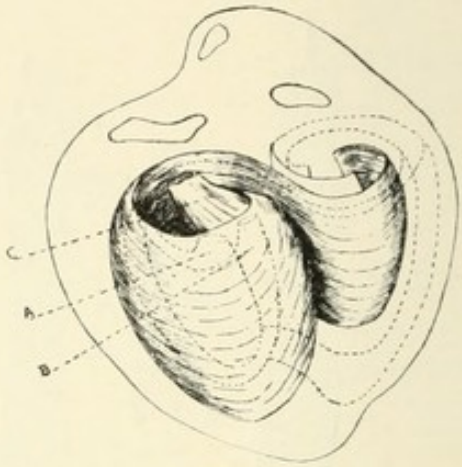


FIG. 143.

FIG. 142.—Diagram of the Course of the Layer Superficial to the Deepest Layer of the Muscle of the Left Ventricle, which is shown in outline. The deepest layer is also shown. (After MacCallum.) *A*, Posterior papillary muscle; *B*, papillary muscle of the septum.

FIG. 143.—Diagram of a Layer still more Superficial to that Shown in Fig. 142, and Ending in the Anterior Papillary Muscle. The deeper layers are represented in dotted lines. (After MacCallum.) *A*, Posterior papillary muscle; *B*, papillary muscle of septum; *C*, anterior papillary muscle.

which is described by MacCallum as running more transversely around the wall of one ventricle, then through the septum and around the other in a reverse scroll, figure 142.

The Valves of the Heart. The *valves* of the heart are arranged so that the blood can pass only in one direction. These are the *tricuspid valve*, between the right auricle and right ventricle, figure 135, and the *semilunar valves* of the pulmonary artery, the *mitral valve* between the left auricle and ventricle, and *semilunar valves* of the aorta. The bases of the tricuspid, figure 152, and mitral valves are attached to the walls of the auriculo-ventricular rings, respectively. Their ventricular surfaces and borders are fastened by slender tendinous fibers, the *chordæ tendineæ*, to the internal surface of the walls of the ventricles at points which project into the ventricular cavity in the form of bundles or columns, the *columnæ carneæ*.

The *semilunar valves* guard the orifices of the pulmonary artery and of the aorta. They are nearly alike on both sides of the heart, but the aortic valves are altogether thicker. Each valve consists of three parts which are of semilunar shape, the convex margin of each being attached to a fibrous ring at the place of junction of the artery to the ventricle, and the concave or nearly straight border being free, so as to form a little pouch like a pocket, 7, figure 136. In the center of each free edge of the valves which contains a fine cord of fibrous tissue, is a small fibrous nodule, the *corpus Arantii*.

The Arteries. The arterial system begins at the left ventricle in a single large trunk, the aorta, which, almost immediately after its origin, gives off in the thorax three large branches for the supply of the head, neck, and upper extremities; it then traverses the thorax and abdomen, giving off branches, some large and some small, for the supply of the various organs and tissues it passes on its way. In the abdomen it divides into two chief branches. The arterial branches, wherever given off, divide and subdivide until the caliber of each subdivision becomes very minute. These smallest arteries are called *arterioles*. These arterioles are continuous with the capillaries. Arteries frequently communicate or anastomose with other arteries. The arterial branches are usually given off at an acute angle, and the areas of the branches of an artery generally exceed that of the parent trunk, and,

Fig. 144.

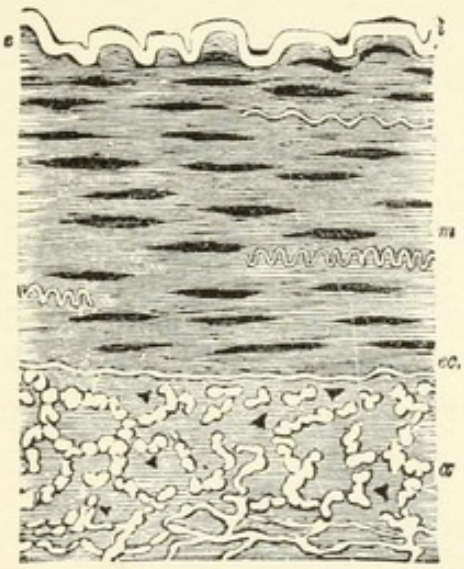


Fig. 145.

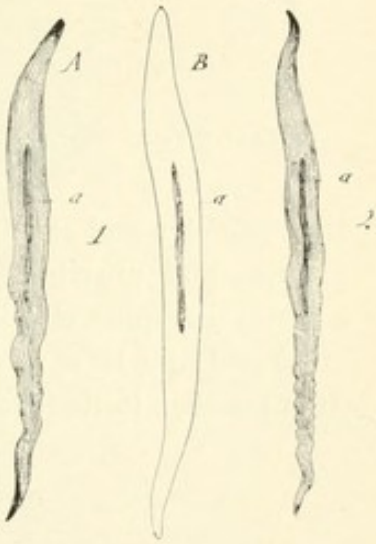


Fig. 146.

Fig. 144.—Minute Artery Viewed in Longitudinal Section. *e*, Nucleated endothelial membrane, with faint nuclei in lumen, looked at from above; *i*, thin elastic tunica intima; *m*, muscular coat or tunica media; *a*, tunica adventitia. (Klein and Noble Smith.)

Fig. 145.—Transverse Section through a Large Branch of the Inferior Mesenteric Artery of a Pig. *e*, Endothelial membrane; *i*, tunica elastica interna, no subendothelial layer is seen; *m*, muscular tunica media, containing only a few wavy elastic fibers; *e*, *c*, tunica elastica externa, dividing the media from the connective-tissue adventitia, *a*. (Klein and Noble Smith.) Magnification 350 diameters.

Fig. 146.—Muscular Fiber Cells from Human Arteries. Magnified 350 diameters. (Kolliker.) *a*, Nucleus; *B*, a fiber cell treated with acetic acid.

as the distance from the origin is increased, the area of the combined branches is increased also. As regards the arterial system of the lungs, the pulmonary artery and its subdivisions, they are distributed in much the same manner as the arteries belonging to the general systemic circulation.

The walls of the arteries are composed of three principal coats, the external or tunica adventitia, the middle or tunica media, and the internal or tunica intima. The *external coat*, figures 144 and 145, *a*, the strongest and toughest part of the wall of the artery, is formed of areolar tissue, with which is mingled throughout a network of elastic fibers. The *middle coat*, figure

145, *m*, is composed of both muscular and elastic fibers with a certain proportion of areolar tissue. In the larger arteries, figure 145, its thickness is comparatively as well as absolutely much greater than in the small arteries, constituting, as it does, the greater part of the arterial wall. The muscular fibers are unstriped, figure 146, and are arranged, for the most part, transversely to the long axis of the artery, figure 144, *m*, while the elastic element, taking also a transverse direction, is disposed in the form of closely interwoven and branching fibers intersecting in all parts the layers of muscular fiber. In arteries of various size there is a difference in the proportion of

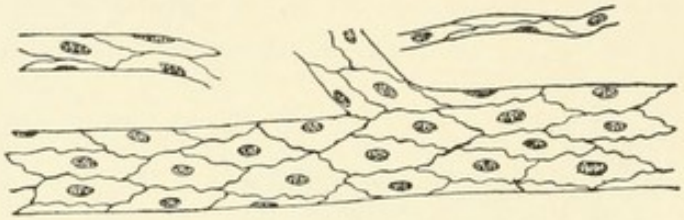


FIG. 147.—Vein and Capillaries. Silver-nitrate and hematoxylin stain, to show outlines of endothelial cells and their nuclei. (Bailey.)

the muscular and elastic element, elastic tissue preponderating in the largest arteries and unstriped muscle in those of medium and small size. The arteries are quite elastic in both large and small vessels. The *internal coat* is formed by a layer of elastic tissue, called the *fenestrated membrane* of Henle. It is peculiar in its tendency to curl up when peeled off from the artery, and

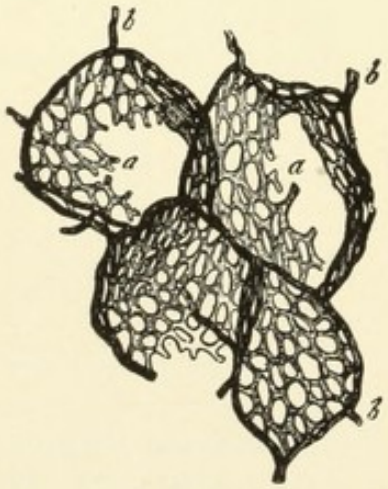


FIG. 148.—Network of Capillary Vessels of the Air Cells of the Horse's Lung Magnified. *a*, *a*, Capillaries proceeding from *b*, *b*, terminal branches of the pulmonary artery. (Frey.)

in the perforated and streaked appearance which it presents under the microscope. The inner surface of the artery is lined with a delicate layer of elongated endothelial cells, figure 145, *e*, which make it smooth and polished and furnish a nearly impermeable surface along which the blood may flow with the smallest possible amount of resistance from friction.

Nerves. Most of the arteries are surrounded by a plexus of nerves or nerve fibers, which twine around the vessel. The smaller arteries also have a delicate network of similar nerve fibers many of which appear to end near the nuclei of the transverse muscular fibers.

The Capillaries. In all vascular textures, except some parts of the corpora cavernosa of the penis, of the uterine placenta, and of the spleen,

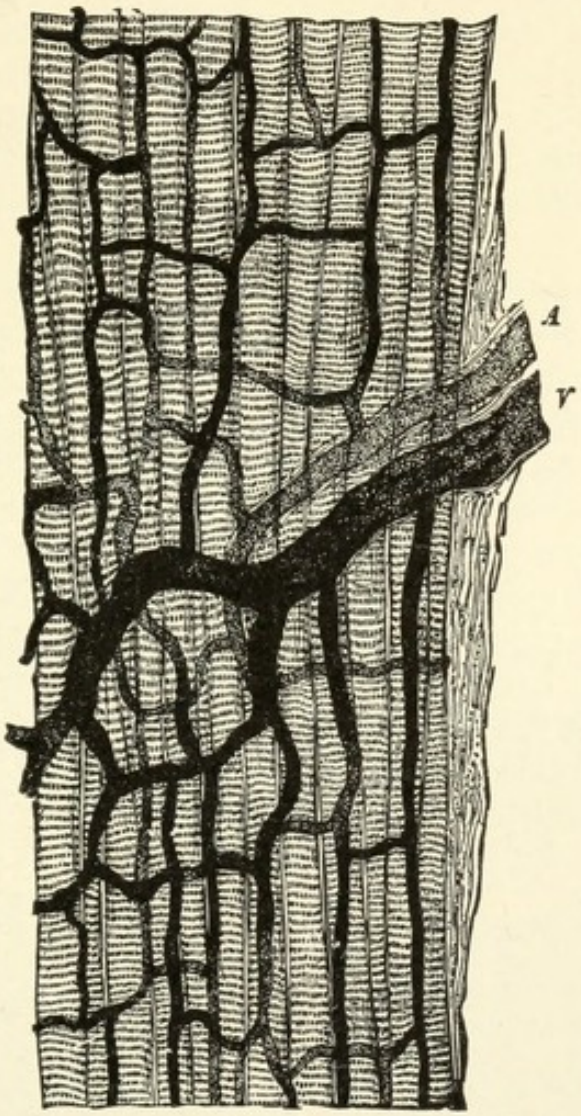


FIG. 149.—Capillaries of Striated Muscular Tissue. From a cat. Magnified 300 diameters. (Heitzmann.) *A*, Artery; *V*, vein.

the transmission of the blood from the minute branches of the arteries to the minute veins is effected through a network of capillaries. They may be seen in all minutely injected preparations.

The point at which the arteries terminate and the capillaries commence cannot be exactly defined, for the transition is gradual. The capillaries maintain essentially the same diameter throughout. The meshes of the network that they compose are more uniform in shape and size than those formed by the anastomoses of the minute arteries and veins.

The walls of the capillaries are composed of a single layer of elongated or radiate, flattened and nucleated endothelial cells, so joined and dovetailed together as to form a continuous transparent membrane, figure 147. Outside these cells in the larger capillaries there is a structureless supporting membrane on the inner surface of which they form a lining.

The diameter of the capillary vessels varies somewhat in the different textures of the body, the most common size being about 12 micromillimeters, $\frac{1}{3000}$ of an inch. Among the smallest may be mentioned those of the brain and of the follicles of the mucous membrane of the intestines; among the largest, those of the skin, and especially those of the medulla of the bones.

The form of the capillary network differs in the different organs of the body, but is usually adjusted to the structural arrangement of the cells of any given organ.

The capillary network is closest in the lungs and in the choroid coat of the eye. In the human liver the interspaces are of the same size, or even smaller than the capillary vessels themselves. In the human lung the spaces are smaller than the vessels; in the human kidney, and in the kidney of the dog, the diameter of the injected capillaries, compared with that of the interspaces, is in the proportion of one to four, or of one to three. The brain receives a very large quantity of blood; but its capillaries are very minute and are less numerous than in some other parts. In the mucous membranes, for example in the conjunctiva and in the cutis vera, the capillary vessels are much larger than in the brain and the interspaces narrower, namely, not more than three or four times wider than the vessels. In the periosteum and in the external coat of arteries the meshes are much larger, their width being about ten times that of the vessels. It may be held as a general rule that the more active the functions of an organ are, the more vascular it is.

The Veins. The venous system begins in small vessels which are slightly larger than the capillaries from which they spring. These vessels are gathered up into larger and larger trunks until they terminate in the two venæ cavæ and the coronary vein which enter the right auricle, and in four pulmonary veins which enter the left auricle. The total capacity of the veins diminishes as they approach the heart; but their capacity exceeds by two or three times that of their corresponding arteries. The pulmonary veins, however, are an exception to this rule. The veins are found after death more or less collapsed, and often contain blood. They are usually distributed in a superficial and a deep set which communicate frequently in their course.

The coats of veins bear a general resemblance to those of arteries, figure 150. Thus, they possess outer, middle, and inner coats. The *outer* coat is constructed of areolar tissue like that of the arteries, but is thicker. In some veins it contains muscular cells arranged longitudinally. The *middle* coat

is considerably thinner than that of the arteries; it contains circular unstriped muscular fibers mingled with a large proportion of yellow elastic and white fibrous connective tissue. In the large veins near the heart the middle

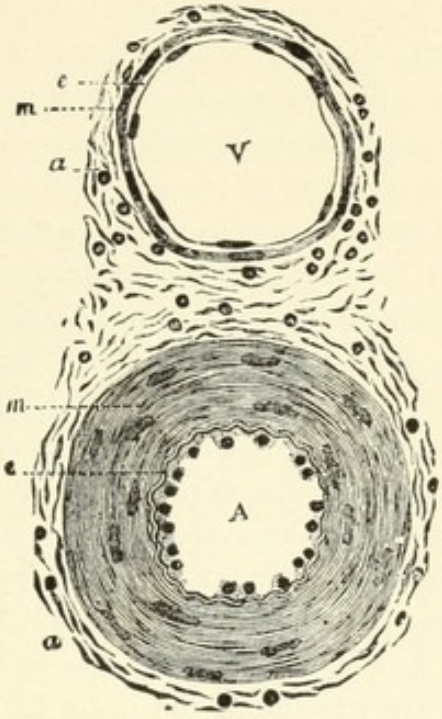
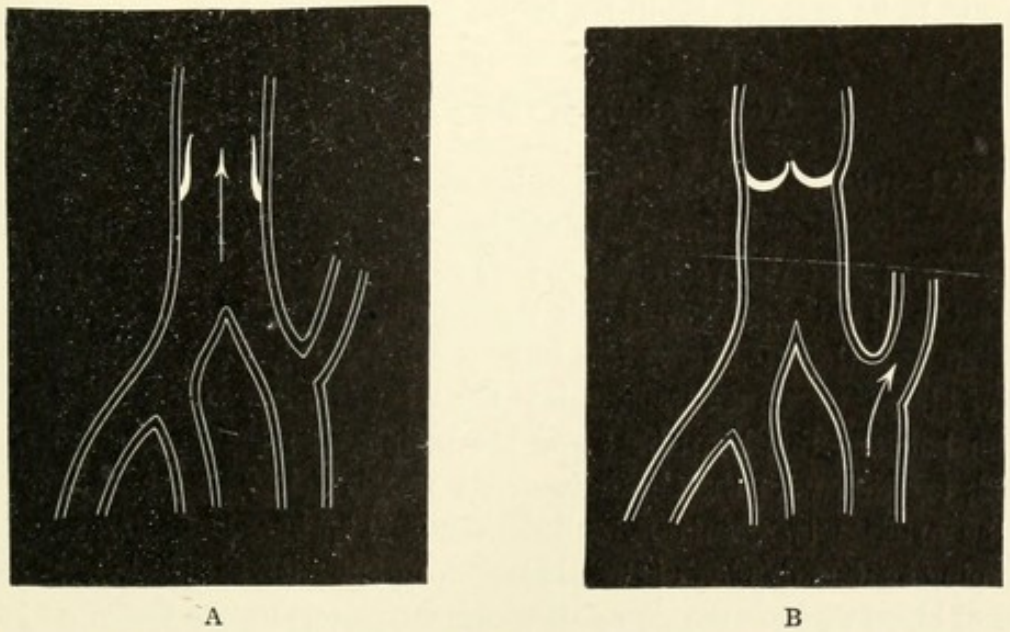


FIG. 150.—Transverse Section through a Small Artery and Vein of the Mucous Membrane of a Child's Epiglottis; the artery is thick-walled and the vein thin-walled. *A*, Artery; the letter is placed in the lumen of the vessel. *e*, Endothelial cells with nuclei clearly visible; these cells appear very thick from the contracted state of the vessel. Outside it a double wavy line marks the elastic tunica intima. *m*, Tunica media consisting of unstriped muscular fibers circularly arranged; their nuclei are well seen. *a*, Part of the tunica adventitia, showing bundles of connective-tissue fiber in section, with the circular nuclei of the connective-tissue corpuscles. This coat gradually merges into the surrounding connective tissue. *V*, The lumen of the vein. The other letters indicate the same as in the artery. The muscular coat of the vein, *m*, is seen to be much thinner than that of the artery. × 350. (Klein and Noble Smith.)



A B

FIG. 151.—*A*, Vein with valves open. *B*, vein with valves closed; stream of blood passing off by lateral channel. (Dalton.)

coat is replaced for some distance from the heart by circularly arranged striped muscular fibers continuous with those of the auricles. The *internal* coat of veins consists of a fenestrated membrane lined by endothelium. The fenestrated membrane may be absent in the smaller veins. The veins are supplied with valves in certain regions of the body, especially in the veins of the arms and legs. The general construction of these valves is similar to that of the semilunar valves of the aorta and pulmonary artery already described. Their free margins are turned in the direction *toward* the heart, so as to prevent any movement of blood backward. They are commonly placed in pairs, at various distances in different veins. In the smaller veins single valves are often met with, and three or four are sometimes placed together or near one another in the larger veins such as in the subclavians at their junction with the jugular veins. During the period of their inaction, when the venous blood is flowing in its proper direction, they lie by the sides of the walls of the veins; but when in action, they come together like valves of the arteries, figure 151. Their situation in the superficial veins of the forearm is readily discovered by pressing along its surface, in a direction opposite to the venous current, *i.e.*, from the elbow toward the wrist, when little swellings, figure 151, *B*, will appear in the position of each pair of valves.

Lymphatic spaces are present in the coats of both arteries and veins; but in the tunica adventitia or external coat of the large vessels they form a distinct plexus of more or less tubular vessels. In smaller vessels they appear as sinus spaces lined by endothelium. Sometimes, as in the arteries of the omentum, mesentery, and membranes of the brain, the pulmonary, hepatic, and splenic arteries, the spaces are continuous with vessels which distinctly ensheath them, *perivascular lymphatic sheaths*. Lymph channels are said to be present also in the tunica media.

THE ACTION OF THE HEART.

The heart's action in propelling the blood consists in the successive alternate contraction, *systole*, and relaxation, *diastole*, of the muscular walls of the auricles and the ventricles. This activity furnishes the power which keeps the blood moving through the arteries, capillaries, and veins. The heart in its activity is like a great force pump in that it injects a certain quantity of blood at each contraction into the great arteries. Owing to the interaction between this heart-beat and the peripheral resistance to the flow of blood, together with the elasticity of the vessels themselves, a high pressure in the arteries is maintained all the time. The heart's contractions then, pumping against this high arterial tension, are sufficient to maintain a constant flow of blood through the capillaries, and, therefore, through the active tissues.

The heart beats at an average rate of about 72 times per minute during

life. Each successive contraction really begins in the great veins, which are muscular, and extends over the auricles and ventricles in regular sequence. The contraction of each successive part is called its *systole* and the relaxation its *diastole*. The diastole covers the period of active relaxation of the muscle and the pause before beginning its next contraction. Each muscular chamber of the heart may, therefore, be said to have its systole and diastole. The whole series of events from the beginning of one contraction until the corresponding event in the next contraction is described as the *cardiac cycle*.

Action of the Auricles. The description of the action of the heart may be commenced at that period in each cycle in which the whole heart is at rest. The heart is then in a passive state. The auricles are gradually filling with the blood flowing into them from the veins, and a portion of this blood is passing at once through the auricles into the ventricles, the opening between the cavity of each auricle and that of its corresponding ventricle being free during the entire pause. The auricles, however, receiving more blood than at once passes through them to the ventricles, become, near the end of the pause, passively distended. At this moment a contraction wave begins on the bases of the venæ cavæ and, running down from the walls of the veins, passes to the muscular walls of the auricle. The contraction of the auricles, the right and left contracting at the same time, forces the blood into the ventricles.

The contraction of the muscular walls of the great veins maintains a condition of constriction of these veins during the time of the auricular contraction. This hinders the reflux of blood from the auricles into the veins during the auricular systole. Any slight regurgitation from the right auricle is limited by the valves at the junction of the subclavian and internal jugular veins beyond which the blood cannot move backward, and by the coronary vein which is supplied with a valve at its mouth. The force of the blood propelled into the ventricle at each auricular systole is transmitted in all directions, but, being insufficient to open the semilunar valves, it is expended in distending the walls of the ventricle.

Action of the Ventricles. The dilatation of the ventricles which occurs during the latter part of the diastole of the auricles, is completed by the forcible injection of the contents of the latter. The ventricles, now distended with blood, immediately begin to contract. The tricuspid valves are closed by the initial reflux of blood, or possibly by the currents of blood formed by the sudden injection of the ventricles by the auricular contraction. The ventricular systole follows the auricular systole so closely that it seems continuous with it. As a result of the ventricular systole sufficient pressure is produced on its contents to overcome the pressure against the semilunar valves of the aorta, and the pulmonary artery and the ventricles are thus emptied completely. After the whole of the blood has been expelled from the ventricles, the walls remain contracted for a brief period.

The form and position of the fleshy columns on the internal walls of the ventricles no doubt help to produce the obliteration of the ventricular cavity during contraction. The completeness of the closure may often be observed on making a transverse section of a heart shortly after death in any case in which *rigor mortis* is very marked, figure 137. In such a case only a central fissure may be discernible to the eye in the place of the cavity of each ventricle. The arrangement of the muscles of the heart, as described on page 148, is such as to expend the whole force of the contraction in diminishing the cavity of the ventricle, or, in other words, in expelling its contents.

On the conclusion of the systole the ventricular diastole begins. The muscular walls relax and, by virtue of their elasticity, a slight negative pressure is set up. This negative or suctional pressure on the left side of the heart is of importance in helping the pulmonary circulation. It is somewhat inconstant in appearance, but has been found to be equal to as much as 20 mm. of mercury, and is said to be quite independent of the aspiratory power of the thorax itself, which will be described in a later chapter. The ventricles now remain in a state of relaxation or rest until the next systole begins.

The duration of the ventricular systole and diastole has been variously estimated. A computation of the time of these two phases, for man, in figure 153, reproduced from Hürthle, gives for the systole 0.38 of a second, and for the diastole 0.4 of a second, with a total of 0.78 of a second. This is equivalent to a rate of 77 per minute. Variations in the time of the systole and the diastole of the ventricle falls chiefly on the pause of the diastole.

The ventricles undergo little or no change of shape in the unopened chest. At the moment in the systole when the ventricles begin to discharge their contents into the aorta and pulmonary arteries, respectively, there is a sharp decrease in size of the ventricles. This decrease takes place in all dimensions.

Action of the Valves. *The Auriculo-ventricular Valves.* During the diastole of both auricles and ventricles blood flows directly through the auricles into the ventricles, the auricles during this period acting as continuations of the large veins which empty into them. At the end of the period the ventricle on each side has already been filled and distended by the pressure of blood from the veins. The systole of the auricle completes this filling and slightly overdistends the ventricle. When the force of the auricular contraction is spent, the ventricular walls rebound slightly toward their former position and in so doing exert some pressure upon the ventricular side of the auriculo-ventricular valves which floats them upward toward the auricle. In this connection another force comes into play, viz., vortex or back currents resulting from the flow of blood into the ventricle under the pressure of the auricular systole. These currents aid in floating the valve leaflets into apposition. Thus, the auriculo-ventricular openings are closed at the end of the auricular systole, *i.e.*, the end of the ventricular diastole. The ventricular systole which follows simply serves to place the

valves under greater tension, thus closing them still more firmly. It should be recollected that the diminution in the breadth of the base of the heart in its transverse diameters during the ventricular systole is especially marked in the neighborhood of the auriculo-ventricular rings, and this aids in rendering the auriculo-ventricular valves competent to close the openings by greatly diminishing the diameter. The cusps of the auriculo-ventricular valves meet not by their edges only, but by the opposed surfaces of their thin outer borders. The margins of the valves are still more secured in apposition with one another by the simultaneous contraction of the muscular papillæ,

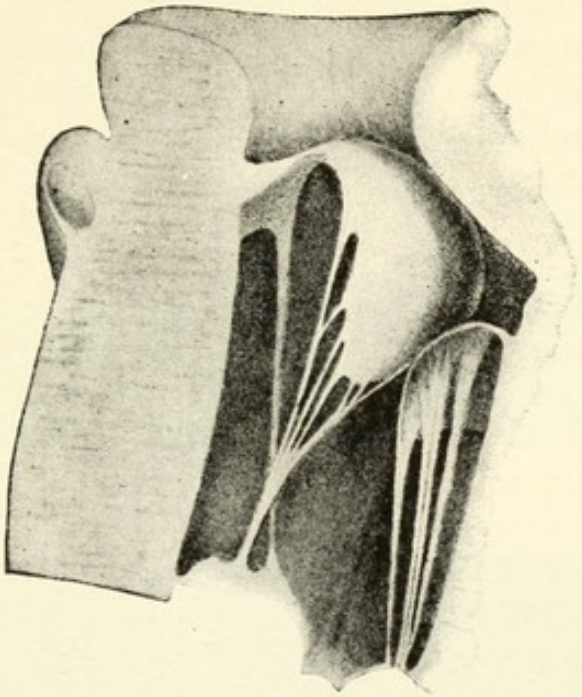


FIG. 152.—The Tricuspid Valves of the Ox, Closed. Vertical section. (Krehl.)

whose chordæ tendineæ have a special mode of attachment for this very object. They compensate for the shortening of the ventricular walls and thus prevent the valves from being everted into the auricle, an event that does occur in certain valvular lesions.

The actions of the tricuspid and mitral valves on the right and left sides of the heart are essentially the same.

The Semilunar Valves. The commencement of the ventricular systole precedes the opening of the semilunar valves by a fraction of a second. The intraventricular pressure increases with the progress of the systole until there is a distinct increase over the arterial pressure, then the opening of the valves takes place at once. They remain open as long as this difference continues. When the diastole of the ventricle begins and the arterial blood pressure exceeds the intraventricular pressure, there is an initial reflux of blood toward the heart which closes the semilunar valves.

The dilatation of the arteries is peculiarly adapted to bring this about. The lower borders of the semilunar valves are attached to the inner surface of the tendinous ring which bounds the orifice of the artery. The tissue of this ring is tough and inelastic and the valves are equally inextensible, being formed mainly of tough fibrous tissue with strong interwoven cords. The effect, therefore, of each propulsion of blood from the ventricle is to dilate the wall of the first portion of the artery in the three pouches behind the valves, while the free margins of the valves are drawn inward toward its center. This position of the valves and arterial walls is maintained while the ventricle continues in contraction; but as soon as it relaxes, and the dilated arterial walls can recoil by their elasticity, the blood is forced backward toward the ventricles and onward in the course of the circulation. Part of the blood thus forced back lies in the pouches (sinuses of Valsalva) between the valves and the arterial walls; and the valves are pressed together till their thin lunated margins meet in three lines radiating from the center to the circumference of the artery, 7 and 8, figure 136. The corpora Arantii at the middle of the free margins insure a more effective closure.

The Sounds of the Heart. When the ear is placed over the region of the heart, two *sounds* may be heard at every beat. They follow in quick succession, and are succeeded by a *pause* or period of silence. The *first* sound is dull and prolonged; its commencement coincides with the impulse of the heart against the chest wall, and just precedes the pulse at the wrist.

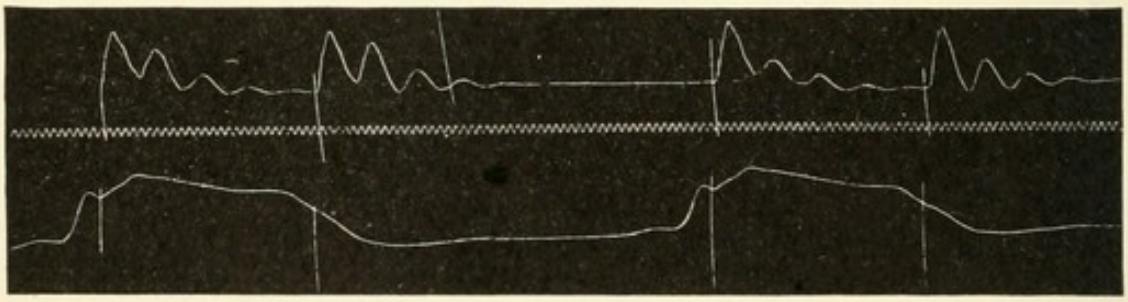


FIG. 153.—Simultaneous Tracings of the Cardiac Impact, or Cardiogram (lower), and the Heart Tones (upper), of Man. The cross strokes at the beginning of the cardiac sound tracing and on the cardiogram mark the synchronous events. (Hürthle.)

The *second* is shorter and sharper, with a somewhat flapping character. The periods of time occupied respectively by the two sounds taken together and by the pause between the second and the first are unequal. According to Foster, the interval of time between the beginning of the first sound and the second sound is 0.3 of a second, while between the second and the succeeding first it is nearly 0.5 of a second, see figures 153, 154, and 158. The relative length of time occupied by each sound, as compared with the other, may be best appreciated by considering the different forces concerned in the production of the two sounds. In one case there is a strong, comparatively slow contraction of a large mass of muscular fibers, urging forward

a certain quantity of fluid against considerable resistance; while in the other it is a strong but shorter and sharper recoil of the elastic coat of the large arteries—shorter because there is no resistance to the flapping back of the semilunar valves as there was to their opening. The sounds may be expressed by the words *lūbb—dŭp*. The beginning of the *first* sound corresponds in time with the beginning of the contraction of the ventricles, the closure of the auriculo-ventricular valves, and the first part of the dilatation of the auricles. The sound continues through a somewhat longer interval than the second sound. The second sound, in point of time, immediately

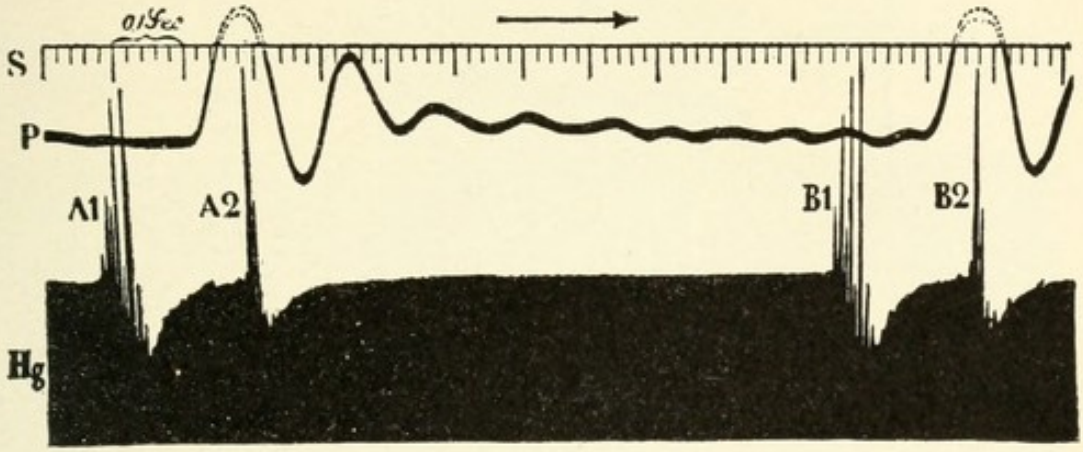


FIG. 154.—Simultaneous Tracings of the Heart Tone and Pulse of the Carotid in the Dog. *A* 1 and *A* 2, First and second sounds; *P*, pulse; *S*, time in tenths and fiftieths of a second. (Einthoven and Geluk.)

follows the cessation of the ventricular contraction, and corresponds with the commencing dilatation of the ventricles and the opening of the auriculo-ventricular valves, figure 154.

The exact cause of the first sound of the heart is not known. Two factors probably enter into it. First, the vibration of the auriculo-ventricular valves and of the chordæ tendineæ. Second, the vibration of the muscular mass of the ventricles themselves. The same mechanical conditions produce equal tension on the ventricular muscle itself and, according to the second view, this is sufficient to account for the first sound. Looking upon the contraction of the heart as a simple contraction and not as a series of contractions, or tetanus, it is at first sight difficult to see why there should be any muscular sound when the heart contracts.

The cause of the second sound is more simple and definite than that of the first. It is entirely due to the vibration consequent on the sudden closure of the semilunar valves when they are pressed down across the orifices of the aorta and pulmonary artery. The influence of these valves in producing the sound was first demonstrated by Hope who experimented with the hearts of calves. In these experiments two delicate curved needles were inserted, one into the aorta, and another into the pulmonary artery below the line of

attachment of the semilunar valves. After being carried upward about half an inch the needles were brought out again through the coats of the respective vessels, so that in each vessel one valve was held back against the arterial walls. Upon applying the stethoscope to the vessels it was found that after such an operation the second sound had ceased to be audible.

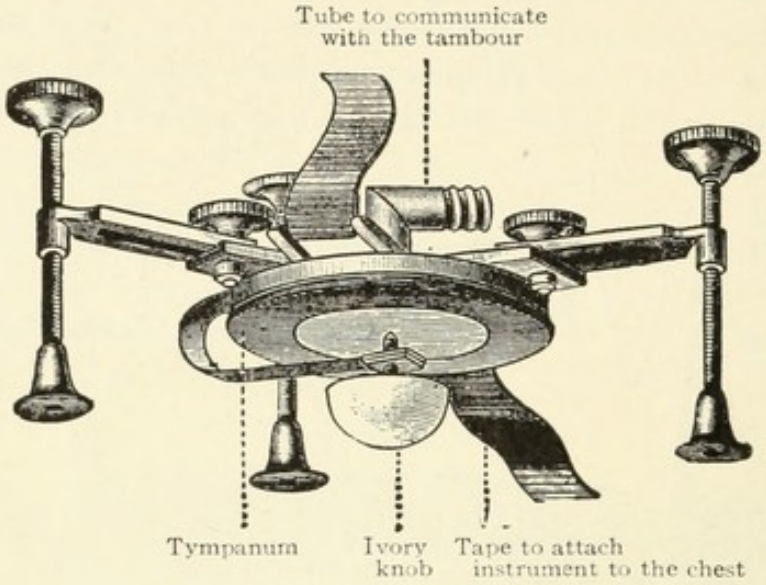


FIG. 155.—Cardiograph. (Sanderson's.)

Disease of these valves, when sufficient to interfere with their efficient action, also demonstrates the same fact by modifying the second sound or destroying its distinctness.

The Cardiac Impulse. The heart may be felt to beat with a slight shock or *impulse* against the walls of the chest at the level of the fifth inter-

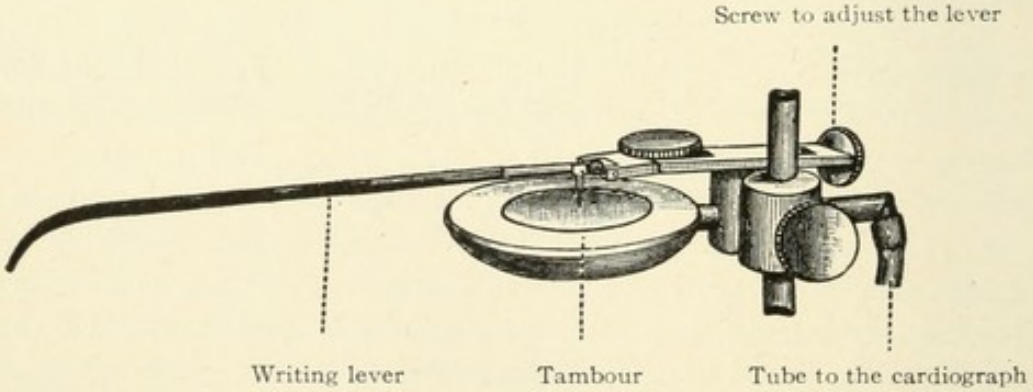


FIG. 156.—Marey's Tambour, to which the Movement of the Column of Air in the Cardiograph is Conducted by a Tube, and from which it is Communicated by the Lever to a Revolving Cylinder so that the tracing of the movement of the cardiac impulse is obtained.

costal space on the left side. Its extent and character vary in different individuals, a factor of considerable clinical significance, and therefore especially discussed in works on clinical diagnosis. The cause of the cardiac impulse has been variously described. It will be remembered that during

the period which precedes the ventricular systole the quiet heart rests with its apex against the wall of the chest. When the ventricles contract, their walls suddenly become firm and tense. Being firmly attached at the base the effect of the movement is to press the hardened ventricle against the chest wall. The discharge of the contents of the ventricle into the curved aorta intensifies this pressure by its mechanical effect in tending to straighten the curve of that vessel and thus holds the ventricle in firm contact with the chest. It is this sudden pressure of the contracting heart against the chest wall that is felt on the outside. The impact or shock is possibly more distinct because of the partial rotation of the whole heart toward the right and front along its long axis. The movement of the chest wall produced by the ventricular contraction against it may be registered by means of an instrument called the cardiograph; and the record or tracing, called a *cardiogram*, corresponds

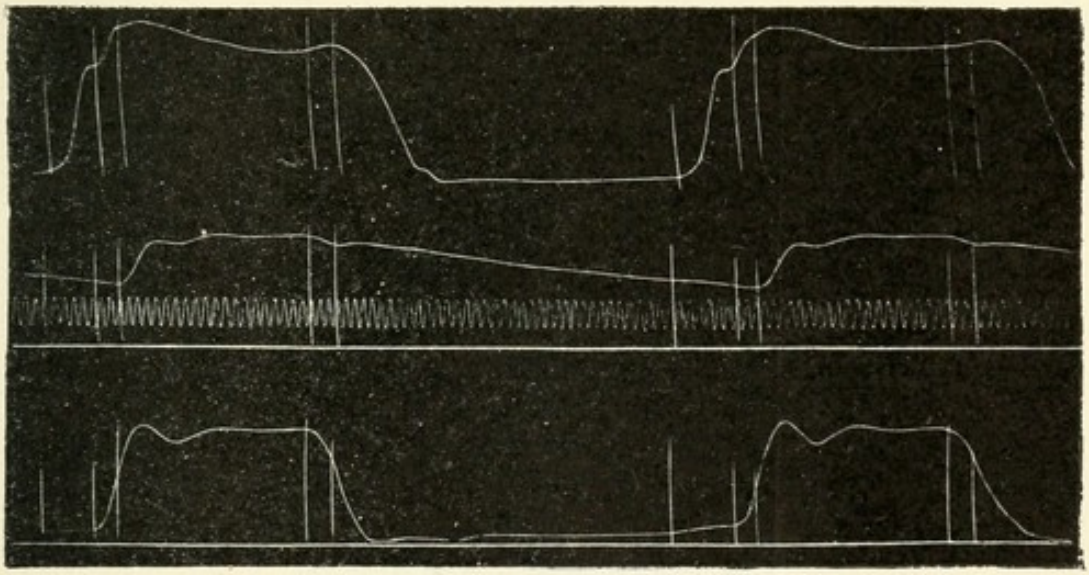


FIG. 157.—Typical Cardiogram (upper trace) from the Dog. Taken simultaneously with the aortic pressure (middle) and intraventricular pressure (lower) tracings. Time in 0.01 of a second. (Hürthle.)

almost exactly with a tracing obtained by an instrument applied over the contracting ventricle itself.

The *cardiograph*, figure 156, consists of a cup-shaped metal box over the open front of which is stretched an elastic India-rubber membrane upon which is fixed a small knob of hard wood or ivory. This knob, however, may be attached, as in the figure, to the side of the box by means of a spring, and may be made to act upon a metal disc attached to the elastic membrane.

The knob is for application to the chest wall over the place of the greatest impulse of the heart. The box or tambour communicates by means of an air-tight tube with the interior of a second or recording tambour supplied with a long and light writing lever. The shock of the heart's impulse being communicated to the ivory knob, and through it to the first tambour, the effect is, of course, at once transmitted by the column of air in the elastic

tube to the interior of the second recording tambour, also closed, and through the elastic and movable disc of the latter to the writing lever which is adjusted to a registering apparatus. This latter generally consists of a cylinder or drum covered with smoked paper and revolving by clock-work with a definite velocity. The point of the lever writing upon the paper produces a tracing of the heart's impulse or *cardiogram*.

Endocardiac Pressure. The effect of the muscular contractions and relaxations of the walls of the heart during its systole and diastole is to

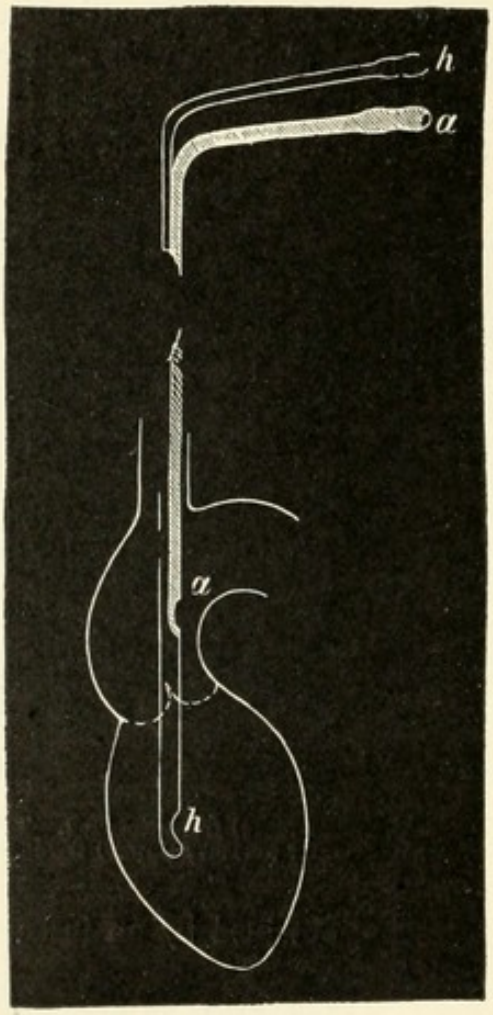


FIG. 158.—Double Cardiac Sound for Simultaneous Registration of the Blood Pressure in the Right Auricle and Ventricle, or in the Aorta and Left Ventricle. (Hürthle.)

produce varying changes of pressure on its content of blood. When this pressure is measured by the proper instrument it is found that the pressure in the left ventricle varies between wide ranges. With the beginning of the muscular contraction, the pressure rises till it slightly exceeds that of the pressure of the aorta, remains high for a brief interval of time, then slowly and quietly decreases to less than that of atmospheric pressure and remains low until the beginning of the next systole. For the right ventricle the events and variations are relatively the same.

In order to determine the endocardiac pressure communication must be established with the cavities of the heart. This is accomplished by a tube known as a *sound*, which is introduced into the left ventricle by passing

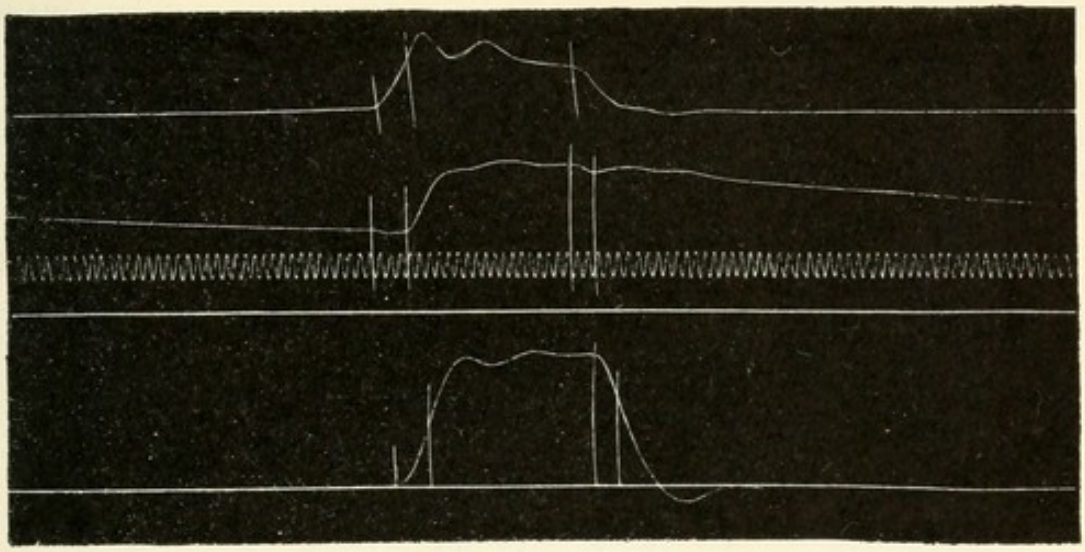


FIG. 159.—Simultaneous Registration of Curves of the Left Intraventricular Pressure (lower), the Aortic Pressure (middle), and the Cardiac Impact (upper). Time 0.01 of a second. (Hürthle.)

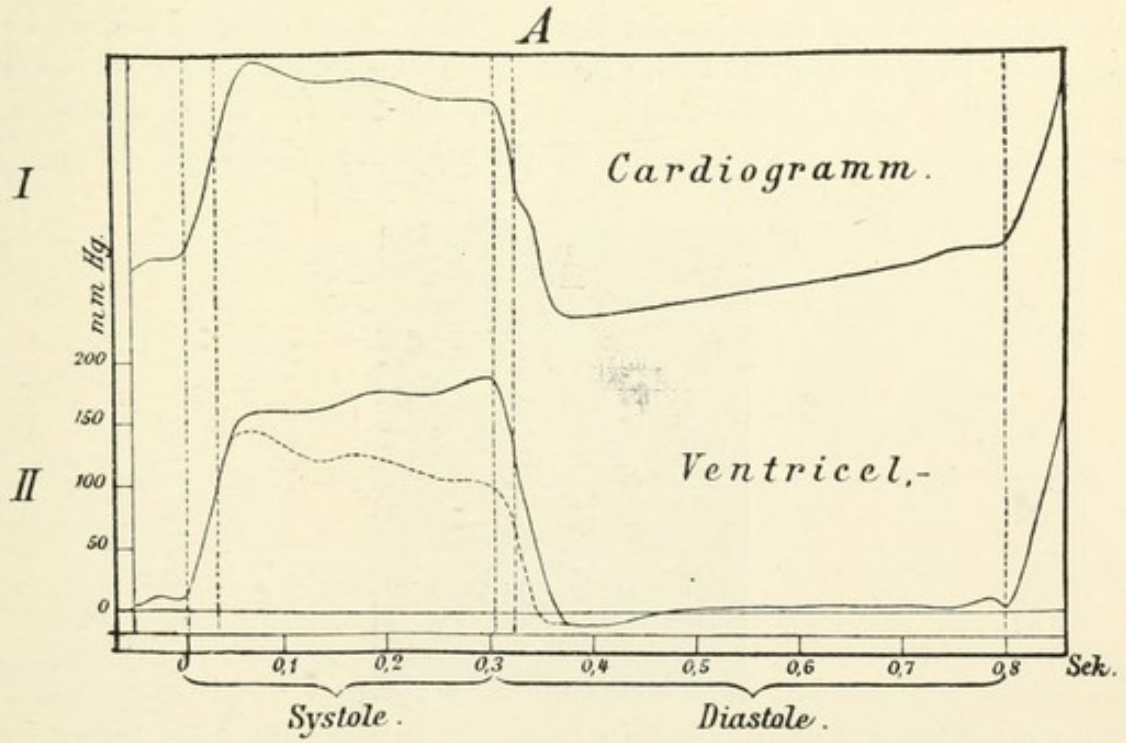


FIG. 160.—Schematic Cardiogram I, and Intraventricular Pressure Curves from the Dog. (Hürthle.) The ventricular pressure curve of the descending type is represented by the dotted line. Pressure in millimeters of mercury, time in tenths of a second.

it down the common carotid artery, or into the right auricle and ventricle through the jugular vein. When such tubes are introduced and connected with some form of pressure-recording apparatus, accurate tracings of the variations in pressure during the heart-beat are obtained.

Chauveau and Marey have been able to record and measure with much accuracy the variations of the endocardiac pressure and the comparative duration of the contractions of the auricles and ventricles. They placed three small India-rubber air-bags or *sounds* in the interior, respectively, of the right auricle, the right ventricle, and in an intercostal space in front of

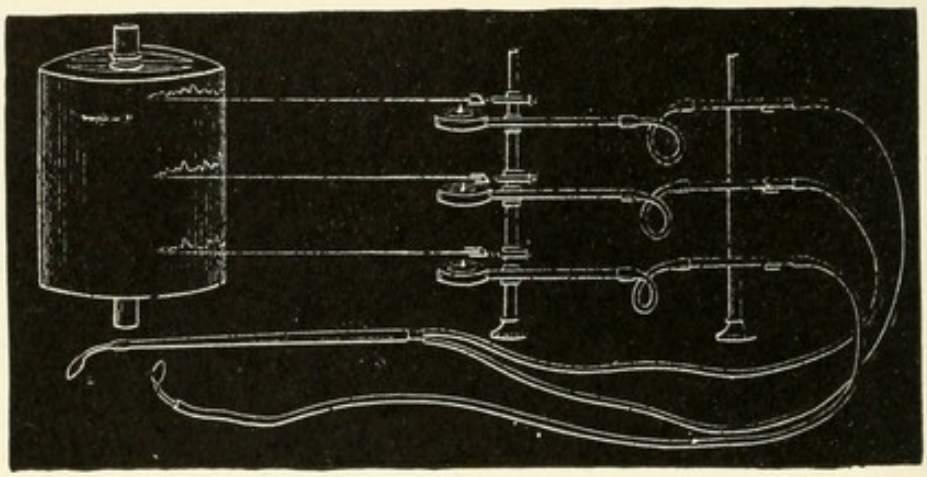


FIG. 161.—Apparatus of MM. Chauveau and Marey for Estimating the Variations of Endocardiac Pressure, and Production of the Impulse of the Heart.

the heart of living animals—the horse. These bags were connected by means of long narrow tubes with three levers arranged one over the other in connection with a registering apparatus, figure 161. The synchronism of the impulse with the contraction of the ventricles is also well shown by

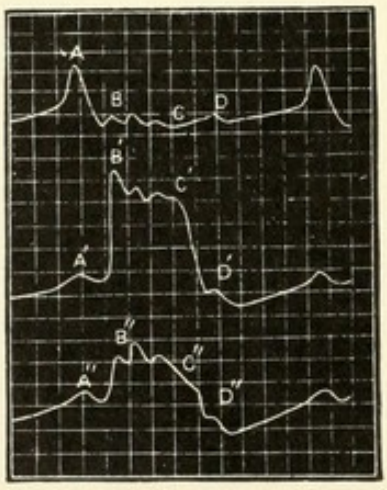


FIG. 162.—Tracings of 1, Intra-auricular; 2, Intraventricular Pressures; and 3, of the Cardiac Impulse of the Heart. To be read from left to right. Obtained by Chauveau and Marey.

means of the same apparatus, and the causes of the several vibrations of which it is really composed have been demonstrated.

In the tracing, figure 162, the intervals between the vertical lines represent periods of a tenth of a second. The parts on which any given vertical line falls represent simultaneous events. It will be nees that the contraction

of the auricle, indicated by the marked curve at *A* in the first tracing, causes a slight increase of pressure in the ventricle which is shown at *A′* in the second tracing, and produces also a slight impulse, which is indicated by *A″* in the third tracing. The closure of the semilunar valves causes a momentarily increased pressure in the ventricle at *D′*, affects the pressure in the auricle *D*, and is also shown in the tracing of the cardiac impulse *D″*.

The large curve of the ventricular and the impulse tracings, between *A′* and *D′*, and *A″* and *D″*, are caused by the ventricular contraction, while the smaller undulations, between *B* and *C*, *B′* and *C′*, *B″* and *C″*, are caused

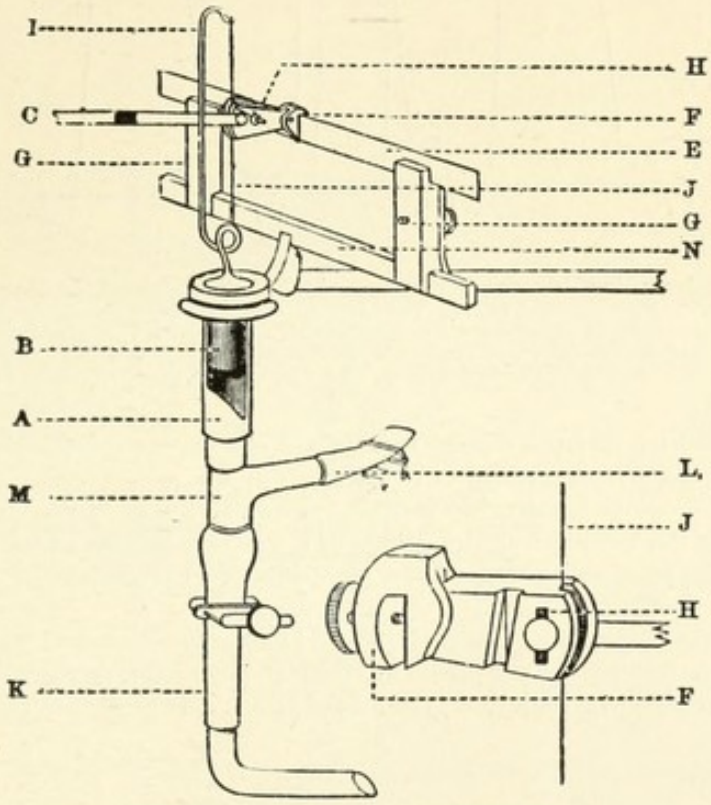


FIG. 163.—Apparatus for Recording the Endocardiac Pressure. (Rolleston.)

by the vibrations consequent on the tightening and closure of the auriculo-ventricular valves.

It seems by no means certain that Marey's curves properly represent the variations in intraventricular pressure. Objection has been taken to his method of investigation: First, because his tambour arrangement does not admit of both positive and negative pressure being simultaneously recorded; second, because the method is applicable only to large animals, such as the horse; third, because the intraventricular changes of pressure are communicated to the recording tambour by a long elastic column of air; and fourth, because the tambour arrangement has a tendency to record inertia vibrations. H. D. Rolleston, who has pointed out the above imperfections of Marey's method, has reinvestigated the subject with a more suitable apparatus.

The method adopted by Rolleston is as follows:

A window is made in the chest of an anesthetized and curarized animal, and an appropriately curved glass cannula introduced through an opening in the auricular appendix. The cannula is then passed through the auriculo-ventricular orifice without causing any appreciable regurgitation, into the auricle, or it may be introduced into the cavity of the right or left ventricle by an opening made in the apex of the heart. In some experiments the trocar is pushed through the chest wall into the ventricular cavity. His apparatus

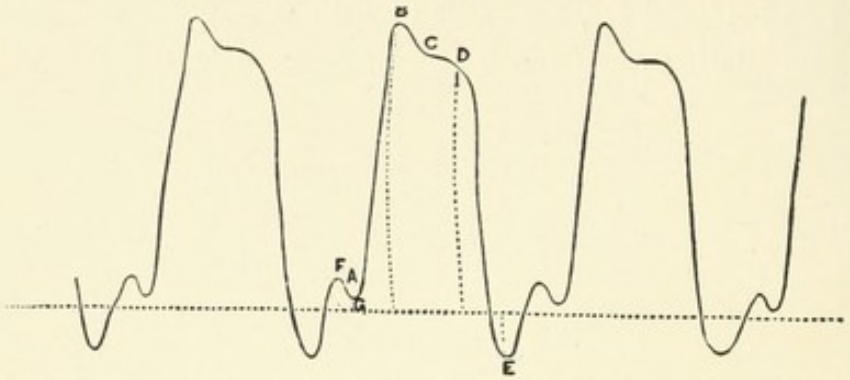


FIG. 164.—Endocardiac Pressure Curve from the Left Ventricle of the Dog. The thorax was opened and a cannula introduced through the apex of the ventricle; the abscissa is the line of atmospheric pressure. *G* to *D* represents the ventricular contraction; from *D* to the next rise at *G* represents the ventricular diastole. The notch, at the top of which is *F*, is a post-ventricular rise in pressure from below that of the atmosphere, and not a presystolic or auricular rise in pressure.

is filled with a solution of leech extract in 0.75 per cent saline solution, or with a solution of sodium bicarbonate of specific gravity 1083.

The animals employed were chiefly dogs. The movement of the column of blood is communicated to the writing lever by means of a vulcanite piston which moves with little friction in a brass tube connected with a glass cannula by means of a short connecting tube.

When the lower part of the tube, *A*, is placed in communication with one of the cavities of the heart, the movements of the piston are recorded by means of the lever, *C*. Attached to the lever is a section of a pulley, *H*, the axis of which coincides with that of the steel rib-

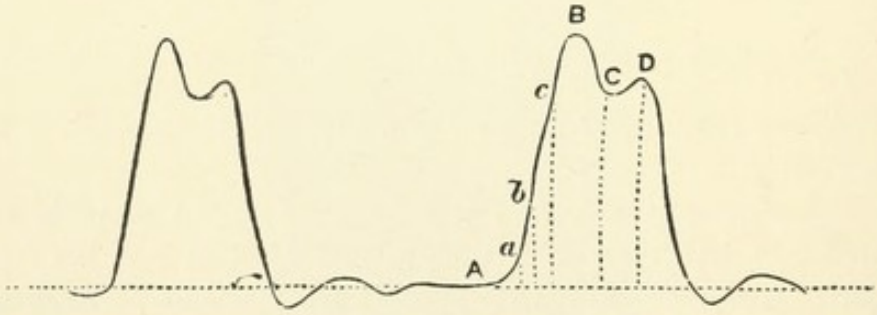


FIG. 165.—Curve with a Dicrotic Summit from the Left Ventricle; the Abscissa Shows the Atmospheric Pressure.

bon, *E*; while, firmly fixed to the piston, is the curved steel piston rod, *l*, from the top of which a strong silk thread, *J*, passes downward into the groove on the pulley.

This thread, *J*, after being twisted several times round a small pin at the side of the lever, enters the groove in the pulley from above downward, and then passes to be fixed to the lower part of the curve on the piston rod as shown in the smaller figure.

The movement of the lever, *C*, is controlled by the resistance to torsion of the steel ribbon, *E*, to the middle of which one end of the lever is securely fixed by a light screw clamp, *F*. At some distance from this clamp, the distance varying with the degree of re-

sistance which it is desired to give to the movements of the lever, are two holders, G, G', which securely clamp the steel ribbon.

As the torsion of a steel wire or strip follows Hooke's law, the torsion being proportional to the twisting force, the movements of the lever point are proportional to the force employed to twist the steel strip of ribbon—in other words to the pressures which act on the piston, B. To make it possible to record satisfactorily the very varying ventricular and auricular pressures, the resistance to torsion of a steel ribbon adapts itself very conveniently.

This resistance can be varied in two ways, 1st, by using one or more pieces of steel ribbon or by using strips of different thicknesses; or, 2d, by varying the distance between the holders, G, G', and the central part of the steel ribbon to which the lever is attached.

Rolleston's conclusions are: That there is no distinct and separate auricular contraction marked in the pressure curves obtained from the right or the left ventricle, the auricular and ventricular rises of pressure being merged into one continuous rise. He concludes that the auriculo-ventricular

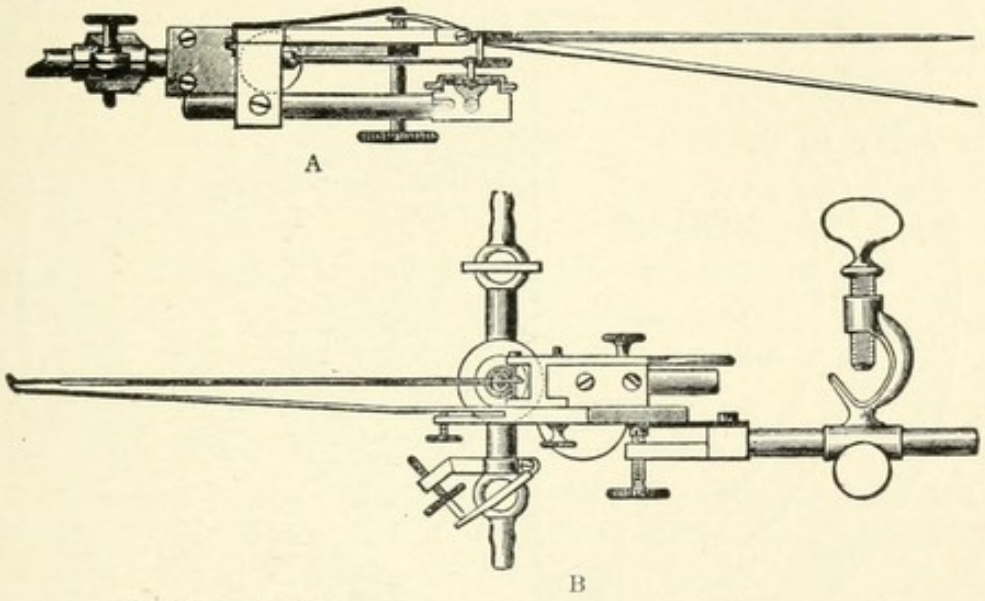


FIG. 166.—Hürthle's Spring Manometer. A, Viewed from the side; B, viewed from the top.

valves are closed before any great rise of pressure within the ventricle above that which results from the auricular systole, a, figure 165. The closure of the valve occurs probably in the lower third of the rise AB, figure 165, and does not produce any notch or wave. It is shown that the semilunar valves open at the point in the ventricular systole, situated at C, about or a little above the junction of the middle and upper thirds of the ascending line AB, and the closure about or a little before the shoulder, D. The figures show, finally, that the minimum pressure in the ventricle may fall below that of the atmosphere, but that the amount varies considerably.

On the whole, the most satisfactory recording instrument for the measurement of endocardiac pressures is the membrane manometer devised by Hürthle. This instrument avoids mechanical errors in a most satisfactory manner. By simultaneous tracings of the pressure in the ventricle and in the aorta by Hürthle's differential manometer, the exact moment of the

opening and closing of the semilunar valves has been determined. By similar methods we have been able to fix synchronism between other events occurring during the beat. These we will summarize in the following section.

Cardiac Cycle. The entire series of occurrences in a single heart-beat is called the *Cardiac Cycle.* If the condition of the heart is considered at that moment when its muscular walls are at rest it will be found that the auriculo-ventricular valves are open, that the blood is flowing from the great

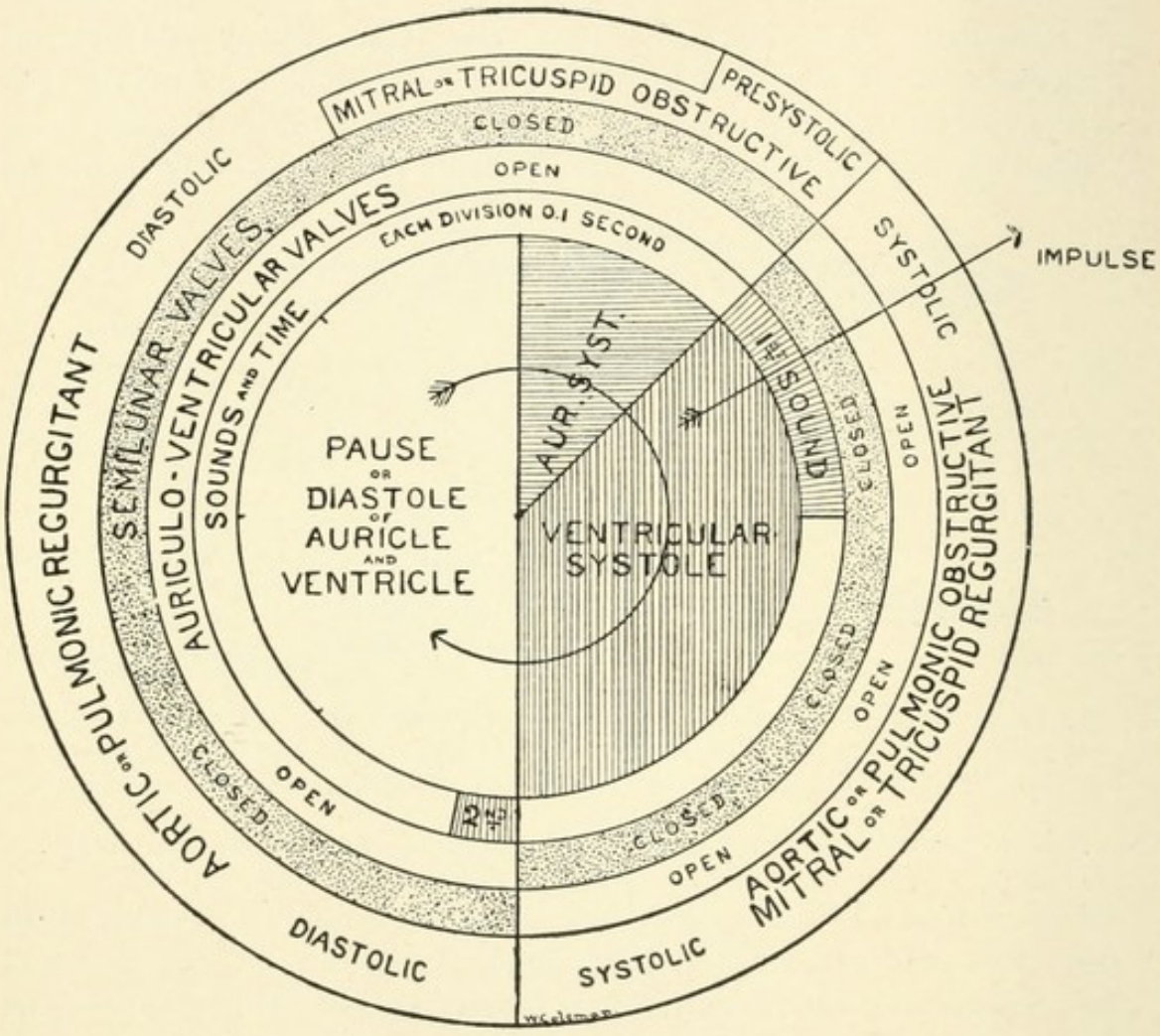


FIG. 167.—Diagrammatic Representation of the Events of the Cardiac Cycle. For events which occur in sequence, read in the direction of the curved arrow; for synchronous events, read from the center to the periphery in any direction. (Coleman.)

veins into the auricle and ventricle, which form a continuous cavity, and that the pressure is about that of the atmosphere, but slowly rising. Now a wave of contraction begins on the great veins and extends toward the auricles, which immediately contract and discharge their blood into the ventricles, somewhat distending their walls. At this moment the ventricular systole begins, the tricuspid (and mitral) valves are closed, the flow of blood into the ventricles is checked, and the first heart sound is heard. The contraction of the ventricles produces a rapidly rising pressure on the enclosed

contents until the pressure exceeds that in the pulmonary artery (and aorta), the semilunar valves open, and the blood is discharged into the arteries. The ventricles ordinarily remain contracted for a brief moment after their contents are emptied.

The ventricular diastole begins next and with the initial relaxation, and the first slight fall of the intraventricular pressure below that of the aorta, the semilunar valves close and the second sound is heard. The relaxation rapidly proceeds and the intraventricular pressure drops to below atmospheric pressure, the auriculo-ventricular valves fall open, the blood that has been accumulating in the auricles flows into the ventricles, and the whole heart is in the state of pause described as the point of beginning.

The duration of the cardiac cycle varies with the heart rate. With a rate of 75 per minute, the cardiac cycle will take 0.8 of a second. In round numbers the systole of the auricle takes 0.1 of a second with a diastole of 0.7 of a second, 0.6 of which is in the pause or rest period. The ventricle requires about 0.3 of a second for the systole, 0.5 of a second for the diastole, with 0.2 to 0.3 of this for the pause. It is evident that the whole heart is at rest at the same instant for from 0.1 to 0.2 of a second.

The relations of the cardiac sounds to the systole and the diastole have been graphically recorded by Hürthle, figure 153, page 158, and by Einthoven and Geluk, figure 154, page 159. The former found that in a heart-beat lasting 0.76 of a second the interval of time between the beginning of the first and second sounds was 0.25 of a second, and that the sounds occur just at the beginning of the ventricular systole and diastole respectively.

During the cardiac cycle the ventricles are completely closed from the moment of the beginning of the ventricular systole until the pressure amounts to a little greater than the pressure in the corresponding arteries, which takes about 0.2 of a second. From the opening of the semilunar valves until the closure of those valves, about 0.15 of a second, the ventricular cavity is in open communication with the arteries. There is, during the diastole, a second moment of complete closure of the ventricles, from the time of the closing of the semilunar valves until the ventricular pressure falls below the auricular pressure which permits the auriculo-ventricular valves to open.

The Force of the Cardiac Action. In estimating the amount of work done by a machine it is usual to express it in terms of work units. A convenient work unit for this purpose is the amount of energy required to lift a unit of weight, *i.e.*, 1 gram or 1 kilogram, through a unit of height, *i.e.*, 1 centimeter or 1 meter, the work required being 1 gramcentimeter for small units, and 1 kilogrammeter for large units, respectively. The average work done by the heart at each contraction can be readily computed by multiplying the weight of blood expelled by the ventricle by the height through which it would have to be lifted to overcome the resistance to its discharge from the cavities into the arteries.

The quantity of blood expelled and the pressure of the arteries can only be estimated for man. But the computations from indirect observations on other mammals indicate that the quantity of blood discharged from each ventricle at a single contraction is from 80 to 100 c.c. The pressure of the aorta, see page 192, is an average of say 150 mm. of mercury, or 200 cm. of blood. The pressure in the pulmonary artery is much less, say 30 mm. (20 to 40), of mercury or 40 cm. of blood. Collecting these facts we have the following computation:

	Blood Discharged.	Against Pressure Column of Blood.	Work in Gramcentimeters.
The left ventricle	90 c.c.	200 cm.	18,000
The right ventricle	90 c.c.	40 cm.	3,600
Total	90 c.c.	240 cm.	21,600

This computation shows that each heart-beat expends 21,600 gramcentimeters (21.6 grammeters) of work. The amount of energy developed in the contractions of the auricles may be ignored in this calculation, which is at best only of relative value. Calculations based on the determinations of Vierordt, also other earlier determinations, give much higher figures than are presented here.

The Properties of the Heart Muscle. It is evident that if we are to arrive at any adequate explanation of the action of the heart, one of the first questions that must be considered is, what are the fundamental properties of heart muscle, as such?

It has already been shown, page 61, that the muscular fibers of the heart differ in structure from skeletal muscle fibers on the one hand, and from unstriped muscle on the other, occupying an intermediate position between the two varieties. The heart muscle, however, possesses a property which is not possessed by skeletal muscle, or by unstriped muscle to such a degree, namely, the property of contracting rhythmically.

Rhythmicity. The property of rhythmic contraction is shown by the action of the heart within the body; its systole is followed by its diastole in regular sequence throughout the life of the individual. The force and frequency of the systole may vary from time to time as occasion requires, but there is no interruption to the action of the normal heart or any interference with its rhythmical contractions. Further, in an animal rapidly bled to death, the heart continues to beat for a time, varying in duration with the kind of animal experimentally dealt with and depending on whether or not there is entire absence of blood within the heart chambers. Furthermore, if the heart of an animal be removed from the body, it still continues, for a varying time, its alternate systolic and diastolic movements. Thus we see that the power of rhythmic contraction depends neither upon connection with the central nervous system nor yet upon the stimulation produced by

the presence of blood within its chambers. Whether or not rhythmicity is a property of heart muscle, as such, was conclusively settled by Gaskell and by numerous later investigators by a very simple process. Gaskell cut thin

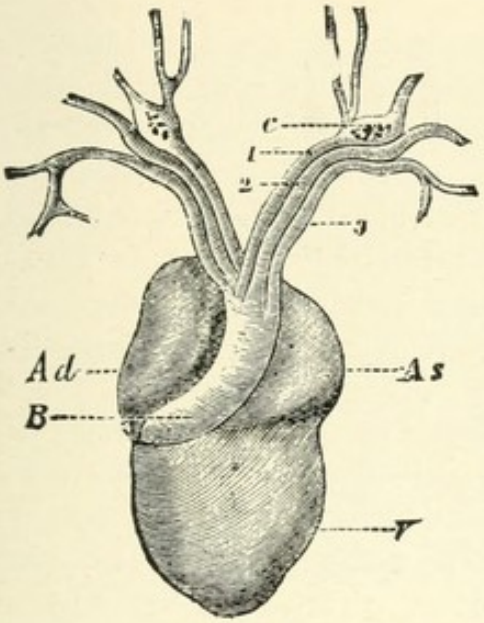


FIG. 168.

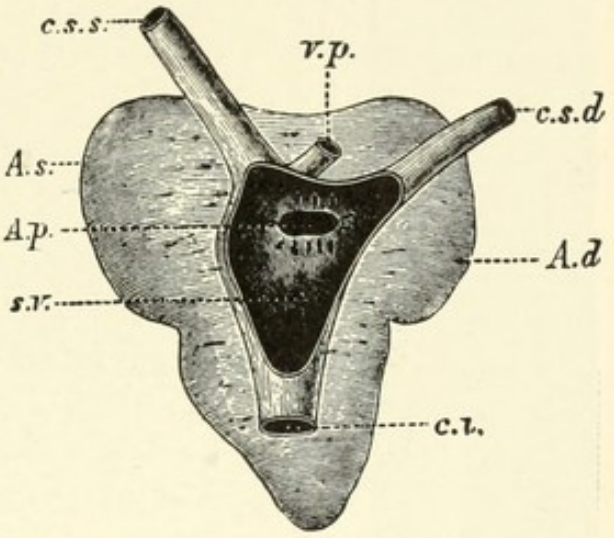


FIG. 169.

FIG. 168.—The Heart of a Frog (*Rana esculenta*), from the Front. *V*, Ventricle; *Ad*, right auricle; *As*, left auricle; *B*, bulbus arteriosus, dividing into right and left aortæ. (Ecker.)

FIG. 169.—The Heart of a Frog (*Rana esculenta*), from the Back. *s. v.*, Sinus venosus opened; *c. s. s.*, left vena cava superior; *c. s. d.*, right vena cava superior; *c. i.*, vena cava inferior; *v. p.*, vena pulmonales; *A. d.*, right auricle; *A. s.* left auricle; *A. p.*, opening of communication between the right auricle and the sinus venosus. × 2½–3. (Ecker.)

strips of the apex of the ventricle of the terrapin, which is free from the nerve cells, at least nerve ganglia, and found that they contracted rhythmically for hours. This experiment has become a classic one for the study of the car-

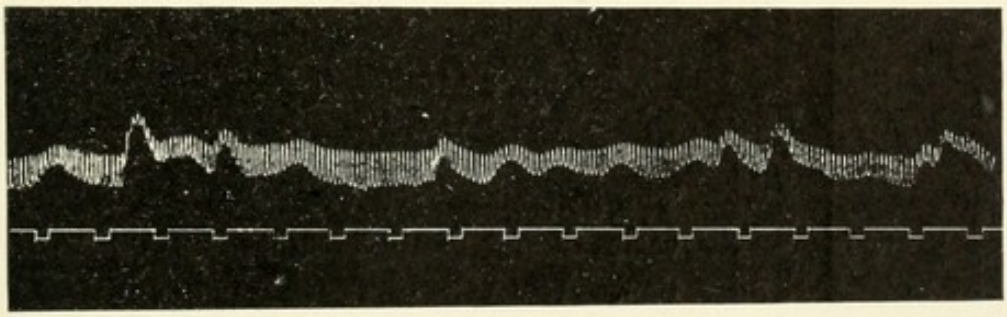


FIG. 170.—Automatic Contractions of Sinus Muscle from the Terrapin's Heart in 0.7 per cent Sodium Chloride. Time in minutes. (New figure by L. Frazier.)

diac muscular tissue. Strips of cardiac muscle cut from the auricle and from the contractile walls of the venæ cavæ, or sinus venosus, of the terrapin also contract rhythmically. If the strips of muscle are kept moist with the same blood or serum, then the rhythm of the sinus is greater than that of the

auricle, and that of the auricle greater than that of the ventricle, a difference that is based on a physiological differentiation of the tissue. The sinus muscle is also more delicately responsive to stimuli than is the ventricular muscle, *i.e.*, it is more irritable.

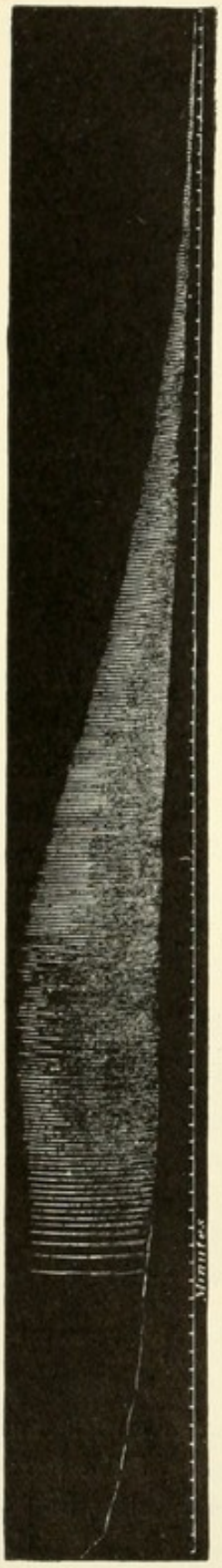


FIG. 171.—Contractions of a Strip of Muscle from the Apex of the Terrapin's Ventricle in 0.7 per cent Sodium Chloride. The muscle seems to grow weaker after a time, but it immediately gives strong contractions if changed to a solution containing the amount of calcium and sodium found in the blood. Time in minutes. (Greene.)

Porter has performed the more difficult experiment of isolating a small disc of muscle from the ventricle of the dog, leaving only the delicate nutrient artery through which the muscle was fed with defibrinated blood. This isolated small piece of ventricle contracted vigorously for many minutes. We may conclude, then, that the mammalian heart muscle is also automatically rhythmic.

Tonicity. Cardiac muscle is characterized by its maintaining a constant degree of partial contraction described as muscle *tone*, or *tonicity*. This property is possessed by all parts of the heart. In the auricle, however, and especially in the muscular walls of the sinus and veins, there is considerable variation in tonicity. Botazzi showed that in the auricle of the toad the variations of tone were wave-like and periodic, even though the auricle were contracting with its ordinary fundamental rhythm. Howell has published numerous experiments showing tone waves in auricular and sinus muscle of the terrapin, in which muscle there may or may not be occurring at the same time the ordinary fundamental rhythmic contractions, figure 170.

Irritability of Heart Muscle. Mention was made above of the difference in irritability of heart muscle chosen from different parts of the heart. The irritability of the muscle of each part also varies during the different stages of the contraction. When a contraction occurs, experiment shows that the muscle is not irritable to a special stimulus applied at any time from the beginning of the contraction until the summit of the contraction is reached. This is called the *refractory period*. From the summit, through the relaxation and succeeding pause, the irritability rapidly increases until the beginning of the next contraction.

Considering the automatically contracting muscle, the point in which the automatic contraction is released, *i.e.*, begins, is the point of maximal irritability. It is the moment when the irritability is so great that the muscular equilibrium is no longer stable, and the physiological contraction results.

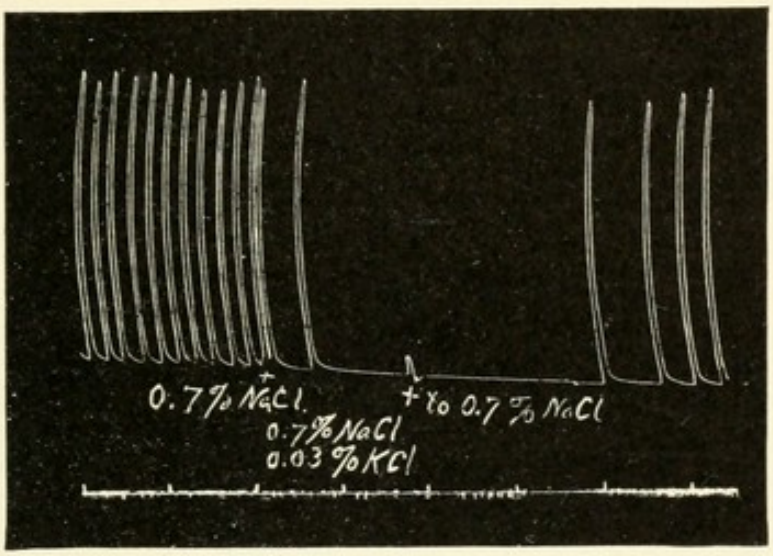


FIG. 172.—Automatic Contractions of a Strip of Ventricular Muscle from the Apex of the Terrapin's Heart contracting in 0.7 per cent Sodium Chloride; from + to + 0.03 per cent Potassium Chloride is added to the Sodium Chloride. The rhythm is recovered very slowly when the muscle is returned to 0.7-per-cent sodium chloride. Time in minutes (upper) and seconds (lower stroke). (New figure by Watkins and Elliott.)

The irritability of heart muscle is very sharply influenced by its condition of nutrition, especially by the inorganic salts present in the blood and lymph, see page 178. The salt content of the blood comprises about 0.7 per cent sodium

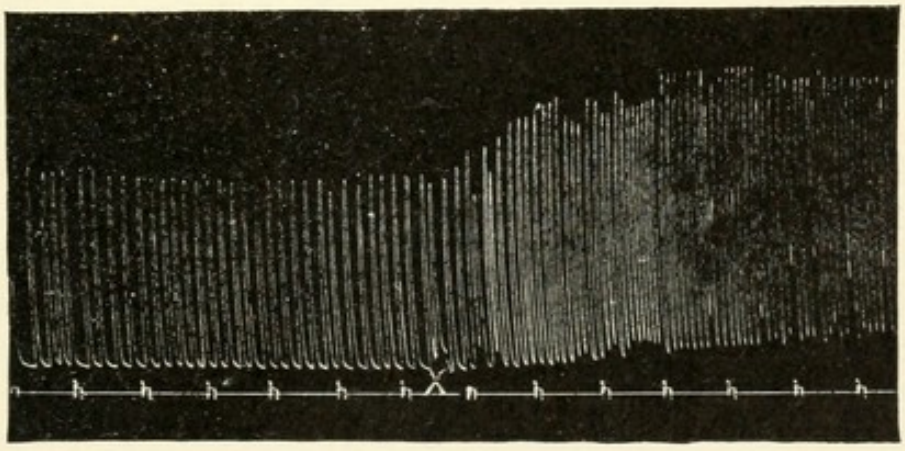


FIG. 173.—Automatic Contractions of a Strip of Ventricular Muscle from the Apex of the Terrapin's Heart. *a*, Contracting in 0.7 per cent sodium chloride; *b*, when 0.03 per cent calcium-chloride solution is added. Time in minutes. (New figure by L. Frazier.)

chloride, 0.03 per cent potassium chloride, and 0.025 to 0.03 per cent calcium (phosphate probably), as well as traces of other metal bases. The heart muscle has been shown by numerous investigators to be delicately

responsive to the proportions of these salts in the blood, or in any artificial solution which may be substituted for blood. If the rhythm is to be taken as an index of the irritability, then an increase of sodium and calcium salts increases the irritability (rhythm), while the influence of an increase in potassium is to depress the irritability (rhythm).

Cardiac Contractions Always Maximal. The heart muscle exhibits another property which distinguishes it from ordinary skeletal muscle, viz., the way in which it reacts to stimuli. The latter, Chapter XIII, reacts slightly to a stimulus little above the minimal, and with an increase of the strength of the stimulus will give contractions of increasing amplitude until the maximum contraction is reached. In the case of the heart-beats this is not so,

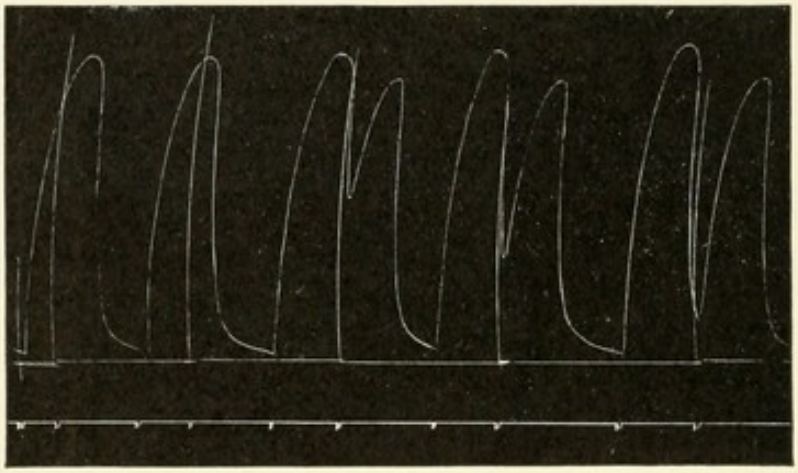


FIG. 174.—Refractory Period in the Ventricular Strip of the Terrapin.

since the *minimal stimulus which has any effect is followed by the maximum contraction;* in other words, the weakest effectual stimulus brings out as great a contraction as the strongest. If a contraction is induced earlier than it would automatically occur, then the succeeding pause is longer, *i.e.*, there is a *compensatory pause.* Also the contraction induced is smaller and the one following the compensatory pause is proportionately larger. This observation can easily be demonstrated on the heart strip, see figure 174, or on the whole ventricle of the frog, which was originally used by Bowditch.

Nerve influence, nutrition, temperature, etc., will of course affect the extent of the contractions, but under a given set of conditions it is held that the contractions which occur are maximal for the particular state. This is more readily understood when taken in connection with the fact that when a contraction originates in a cardiac cell it is conducted throughout the extent of all the cells of the muscular mass.

Theories of the Heart-Beat. The cause of the rhythmic power of the heart as a whole has been the subject of much discussion and experimental observation. Two leading hypotheses have given inspiration to

investigators, and now one, now the other theory has attracted followers as new facts have been discovered. The hypotheses that have been advanced to explain the heart-beat are known as the *neurogenic theory* and the *myogenic theory*, respectively.

The heart has long been known to have the power of rhythmic contractions after removal from the body and after all connection with the central nervous system has been destroyed. The isolated heart, even of man, will contract with good rhythm when kept at the proper temperature and given the proper nutritive fluid.

The Neurogenic Theory. The neurogenic theory attributes the remarkable power of the heart to continue its contractions after removal from the body, and presumably while in the body, to the presence of the local collections of nerve cells. The local nervous mechanism in the frog consists of

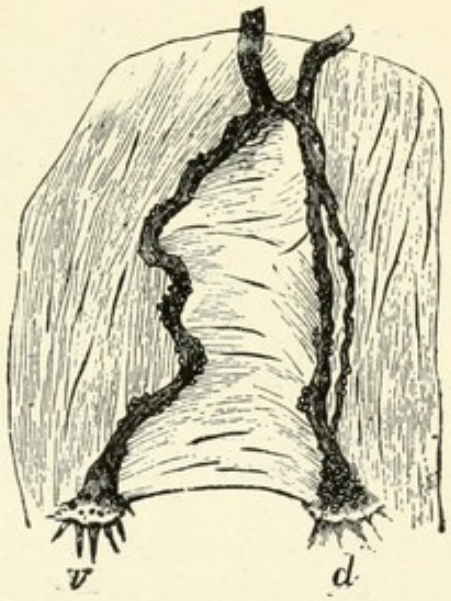


FIG. 175.—Course of the Nerves in the Auricular Partition, Heart of a Frog. *d*, Wall of the dorsal branch; *v*, ventral branch. (Ecker.)

three chief groups of cells or ganglia. The first group is situated in the wall of the sinus venosus at the junction of the sinus with the right auricle, *Remak's* ganglia; the second group is placed near the junction between the auricles and ventricles, *Bidder's* ganglia; and the third in the septum between the auricles, *von Bezold's* ganglia. Small ganglia have been described for the base of the ventricle, but no ganglia are present in the apical part of the ventricles, though isolated cells have been found. The nerve-cells of which these ganglia are composed are generally unipolar, seldom bipolar. Sometimes two cells are said to exist in the same envelope, constituting the twin cells of Dogiel. The cells are large, and have very large round nuclei and nucleoli, figure 176. As regards the automatic movements of the heart when removed from the body, our knowledge has been derived from the study of the hearts of the frog, tortoise, dog, cat, and rabbit.

If removed from the body entire, the frog's or terrapin's heart will continue to contract for many hours and even days, and the contraction has no apparent difference from the contraction of the heart before removal; it will take place, as we have mentioned, without the presence of blood or other fluid within its chambers. Not only is this the case, but the auricles and ventricle may be cut off from the sinus, and both parts continue to pulsate; and, further, the auricles may be divided from the ventricle, with the same result. If the heart be divided lengthwise, its parts will continue to pulsate rhythmically. The ventricle remains comparatively quiet, contractions occurring at longer intervals, if at all. However, the ventricle remains irritable so long as bathed in blood, and will contract upon receiving a slight stimulus; in fact a single stimulus will often call forth a series of contractions of the ventricle. The frog's ventricle, when its muscular and nervous con-

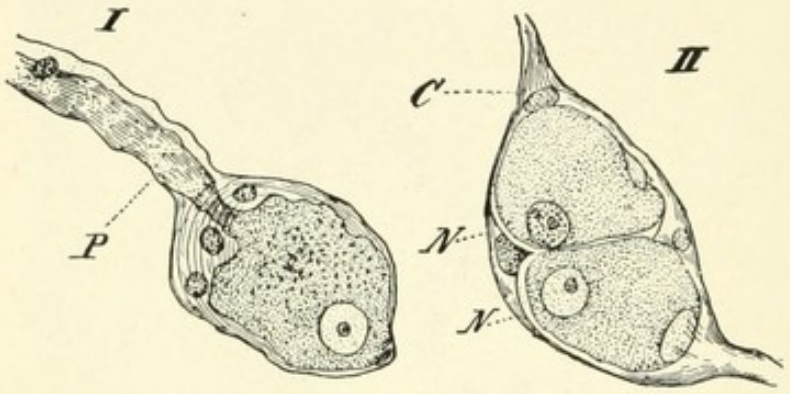


FIG. 176.—Isolated Nerve Cells from the Frog's Heart. *I*, Usual form; *II*, twin cell; *C*, capsule; *N*, nucleus; *P*, process. (From Ecker.)

nections with the auricle are physiologically severed, as by crushing, will remain quiet when fed by its own blood, but contracts rhythmically when fed with physiological salt-solution.

It will be thus seen that the rhythmical movements appear to be more marked in the parts supplied by the ganglia, that ventricular pieces contract when still connected with the auricles, and that rhythmic contractions of the ventricles do not readily occur in the ordinary condition when irrigated with blood. These are regarded as facts peculiarly in favor of the neurogenic theory.

The Myogenic Theory. In the myogenic theory the heart's rhythmical contractions are explained as due to the inherent property of the cardiac muscle itself. Most convincing facts in support of this theory have been arrived at by a study of cardiac muscle, as such, and by studies on the whole heart, particularly by Gaskell's method of blocking. The term blocking is explained as follows: It will be remembered that under normal conditions the wave of the contractions in the heart starts at the sinus and travels down over the auricles to the ventricles, the irritability of the muscle

and its power of rhythmic contractions being greatest in the sinus, less in the auricles, and least in the ventricles. By an arrangement of ligatures or by a system of clamps, one part of the heart may be more or less isolated from any other portion. With such a clamp the contraction waves can be more or less completely interrupted in their passage from the sinus end of the heart past the clamp toward the ventricular end. If the clamp is complete, so as to interrupt the physiological continuity between the parts, then any contractions in the apical portion will be entirely independent of those in the sino-auricular portion. If the blocking is partial only, then the ventricular end of the heart always contracts in unison with the sino-auricular, although its rate may be as 1 to 1, 1 to 2, 1 to 3, etc. In other words, only every second or every third sino-auricular contraction will be able to pass the block.

The effects of blocking are due to the interruption of muscle continuity rather than nerve continuity. This is beautifully demonstrated by an experiment of zigzag cutting of the ventricle in the terrapin, since it cannot be supposed that any nerves would pass through the ventricular mass by such a zigzag course. In this experiment the contraction wave passes down over the muscle and around the end of the cuts until it reaches the apex, and the apex contracts in sequence with the auricle and base of the ventricle. If the zigzag cuts are made almost complete so as to reduce to a minimum the muscular tissue which bridges from one cut to the next, then it happens that occasional contractions will be unable to pass and the apex contracts in the ratio of 1 to 2, or 1 to 3, etc., as described above. Thus, division of the muscle has the same effect as partial clamping in the same position.

It was thought for a long time that in the mammal there is no muscular continuity between the auricles and ventricles to conduct the contraction wave, but a well-marked muscular bridge, the bundle of His, has been shown to pass between these two parts. This fact has proven to be of strongest support to the myogenic theory. Erlanger has recently shown, by an ingenious device for partially clamping this muscular band, that even the mammalian ventricle exhibits the phenomenon of heart block. In his experiments the ventricle contracts in unison with every auricular contraction, or only every second or every third, according to the degree of blocking.

It was shown long ago that the isolated apex of the ventricle of the frog remains quiet when filled with blood, but readily gives good rhythmic contractions in physiological saline and other artificial solutions. The inactivity in blood is not necessarily, therefore, due to nervous isolation from the ganglionated parts of the heart. Contractions occur in the small bits of ventricular muscle as isolated by Gaskell, and these may continue for hours. It is well known also that the embryonic heart contracts rhythmically before nerve cells have reached the organ.

The phenomena of heart block, the contractions of the ventricular apex

when physiologically isolated from the parts of the heart which contain the ganglia, the behavior of isolated strips of the heart, especially of the ventricle, and the rhythm of the embryonic heart are all held to be in favor of the myogenic theory.

Automaticity of the Heart. Whether one adopts the neurogenic or myogenic theory of the heart's beat, he has still to explain the origin of the heart's rhythm. In the former case one must look to the nervous apparatus for the origin of the rhythm; in the latter case, the muscular apparatus, a fact to which Brown-Séquard long ago called attention. In the former view the problem is to explain not only the periodic origin of the nerve discharges from local cardiac ganglia, but also to explain the orderly discharge of nerve impulses which maintains the proper sequence between sinus, auricle, and ventricle.

To perhaps the majority of physiologists the facts are best explained by the myogenic theory. The origin of the rhythm is here supposed to be due to the automatic property of the muscle itself. The sequence is explained on the observed facts, first, that muscular contraction in cardiac muscle is conducted throughout the continuity of the mass, and second, the most highly rhythmic part of the muscular tissue of the heart, the sinus, sets the rhythm for the entire heart.

The function of the nervous system, by this view, is not to originate the rhythm, but to regulate it, the detail of which will be discussed below.

Relation of Rhythm to Nutrition. The whole heart, like the muscular parts of which it is composed, responds delicately to its condition of nutrition. In the frog's and turtle's hearts the muscular fibers are brought in intimate contact with the blood contained within its cavities. In the mammalian heart, on the other hand, a distinct system of vessels, the coronary vessels and the vessels of Thebesius, supply blood to the organ. If the heart is supplied with nutrient fluid similar to its normal blood, and with proper aeration to insure plenty of oxygen, it contracts with a strong rhythm for many hours. This rhythm, however, responds quickly to changes in the composition of the nutrient fluid. An abundant supply of oxygen is absolutely necessary to the maintenance of rhythm in the mammalian heart, though the heart, especially a cold-blooded heart, will contract for a time in an atmosphere of hydrogen. No doubt the organic constituents of blood are very essential to the prolonged maintenance of rhythm in the heart, but the heart is not dependent on these ingredients for its immediate reactions. The inorganic salts seem to be peculiarly closely related to the development and character of the cardiac rhythm, figures 172 and 173. Both the cold-blooded heart and the mammalian heart respond very quickly to the influence of these salts. The details of this influence have been discussed on page 173. It is somewhat surprising, however, that the highly organized mammalian heart will contract rhythmically for hours on purely inorganic

nutrient fluid, provided only that the oxygen be supplied in sufficient quantity and under high enough tension.

THE REGULATIVE INFLUENCE OF THE CENTRAL NERVOUS SYSTEM ON THE HEART.

The heart is capable of automatic rhythmic movement, yet while in the body its beats are under the constant control of the central nervous system. The influence which is exerted by the central nervous system is of two kinds: first, in the direction of *slowing* or *inhibiting* the beats, and, second, in the direction of *accelerating* or *augmenting* the beats. The influence of the first kind is brought to bear upon the heart through the fibers of the pneumogastric or vagus nerves, and that of the second kind through the sympathetic nerves.

The Inhibitory Nerves. It has long been known, indeed ever since the experiments of the Weber brothers in 1845, that stimulation of one or both vagi produces slowing of the rhythm of the heart. It has since been

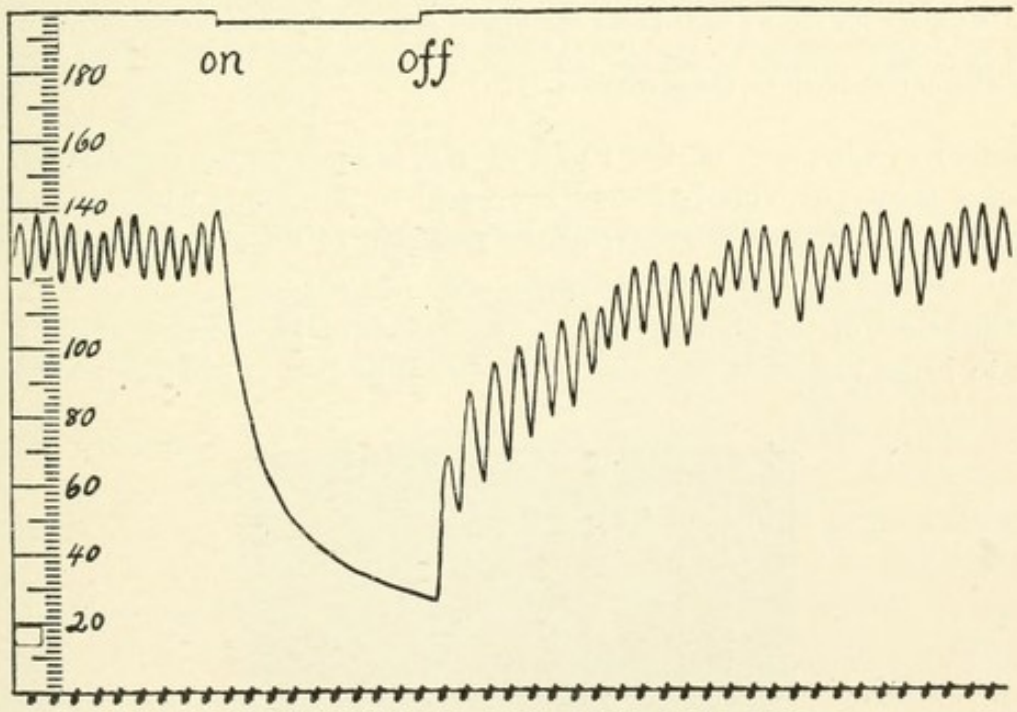


FIG. 177.—Effect on the Heart Rate and on the Arterial Blood Pressure of Stimulating the Right Vagus of the Dog. Stimulus applied at the mark "on" and removed at "off." Pressure in millimeters of mercury shown by the scale to the left. Time in seconds. (New figure by Hill and Chilton.)

shown, in all of the higher vertebrate animals experimented with, that this is the normal reaction to vagus stimulation. Moreover, a section of one vagus, or at any rate of both vagi, produces acceleration of the pulse; and stimulation of the distal or peripheral end of the divided nerve normally produces slowing or stopping of the heart's beats.

It appears that any kind of stimulus, either chemical, mechanical, electrical, or thermal, produces the same effect, but that of these the most potent is a rapidly interrupted induction current. A certain amount of confusion has arisen as to the effects of vagus stimulation in consequence of the fact that fibers of the sympathetic nerve run within the trunk of the vagus nerves of some animals.

The result of stimulation also depends, to some extent, upon the exact position of the application of the stimulus. Speaking generally, however,

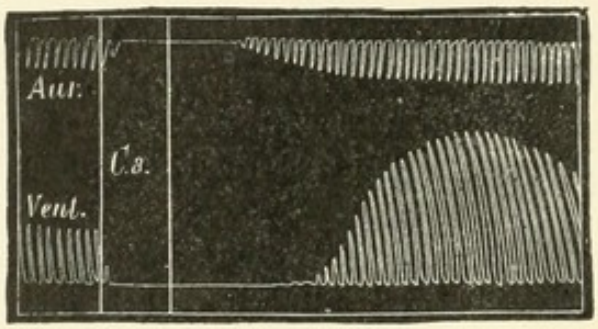


FIG. 178.—Tracing Showing Actions of the Vagus on the Heart of the Frog. *Aur*, Auricular; *vent*, ventricular tracing. The part between perpendicular lines indicates a period of vagus stimulation. *C.* 8 indicates that the secondary coil was 8 cm. from the primary. The part of tracing to the left shows the regular contractions of moderate height before stimulation. During stimulation, and for some time after, the beats of auricle and ventricle are arrested. After they commence again they are single at first, but soon acquire a much greater amplitude than before the application of the stimulus. (After Gaskell.)

excitation of any part of the trunk of the vagus produces inhibition, the stimulus being particularly potent if applied to the points where the nerves enter the substance of the heart at the situation of the sinus ganglia. The stimulus may be applied to either vagus with like effect.

The effect of the stimulus of the vagus is twofold—to slow the rate, or even to bring the heart to a complete standstill, and to produce a decrease

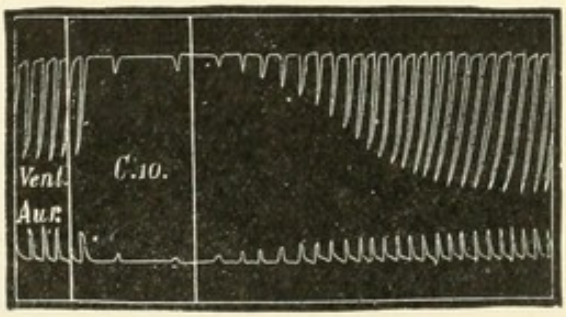


FIG. 179.—Tracing Showing Diminished Amplitude and Slowing of the Pulsations of the Auricle and Ventricle without Complete Stoppage during Stimulation of the Vagus. (After Gaskell.)

in the amplitude. The slowing does not take place until after the lapse of a short latent period during which one or more contractions may occur. The stoppage may be due either to prolongation of the diastole or to diminution of the systole. Vagus stimulation inhibits the spontaneous beats of the heart only, it does not entirely suppress the irritability of the heart-muscle,

since mechanical stimulation may bring out a beat during the pause caused by vagus stimulation. The inhibition of the beats varies in duration according to the strength of the stimulus and the animal stimulated. The heart of the terrapin can be completely inhibited for hours with a strong stimulus. The heart of a dog escapes from inhibition in a few seconds. When the beats reappear, the first few are usually feeble, and may be auricular only; after a time the contractions become more and more strong, and very soon exceed both in amplitude and frequency those which occurred before the application of the stimulus. This phenomenon is shown in figure 178, which illustrates the action of the vagus on the frog's heart.

The inhibitory fibers have their origin in nerve cells in the motor nucleus of the vagus and of the glosso-pharyngeal located in the floor of the fourth ventricle. These cells have not been exactly identified, but the center is

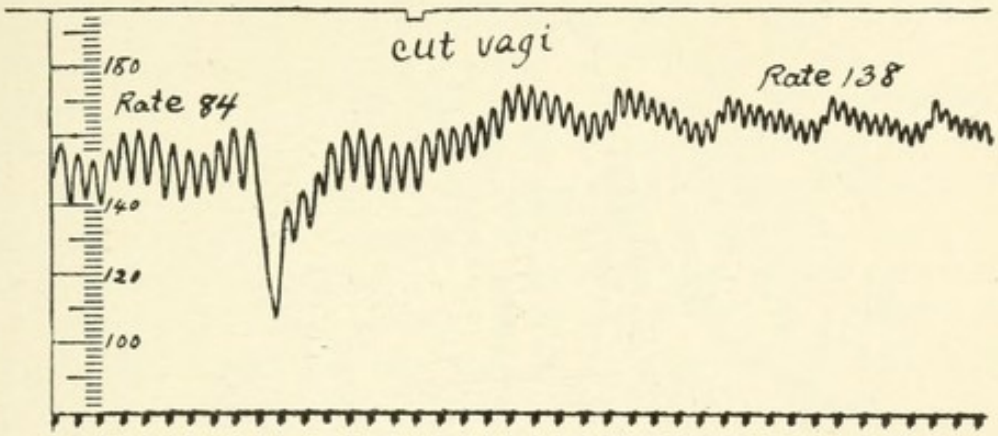


FIG. 180.—Arterial Blood Pressure of the Dog, Showing the Effect on the Heart Rate of Cutting both Vagus Nerves as marked. The scale to the left shows the pressure in millimeters of mercury. Time in seconds. The momentary inhibition just before the nerves were cut is probably due to mechanical stimulation of the nerves. (New figure by Hill and Chilton.)

called the *cardio-inhibitory center*. The center is a bilateral one and the fibers from it pass into the great vagus trunk to be distributed to the heart through superior and inferior cardiac branches which help to form the cardiac plexus. Within the heart the inhibitory fibers form synapses with cells whose axones reach the cardiac muscle cells. The cardiac-inhibitory center is in constant tonic activity, and the tonic influence is eliminated when both nerves are cut, figure 180.

The center is also influenced by afferent impulses which may reach it from the heart itself, by the depressor nerve, or from other parts of the body. These reflex stimulations of the heart through the vagus center are constantly occurring during our daily life and are the most potent factor in the coordinations going on between the heart and the rest of the body.

Rhythmical alterations of the heart rate occur in association with the effects of the mechanical variations of pressure of the thorax on the heart and blood-vessels. Apparently the cardio-inhibitory center is stimulated

during the fall of blood pressure. The activity of the center produces a slower rate of the heart during expiration, shown in figure 241. This variation in heart rate disappears when the vagi are cut off from the center.

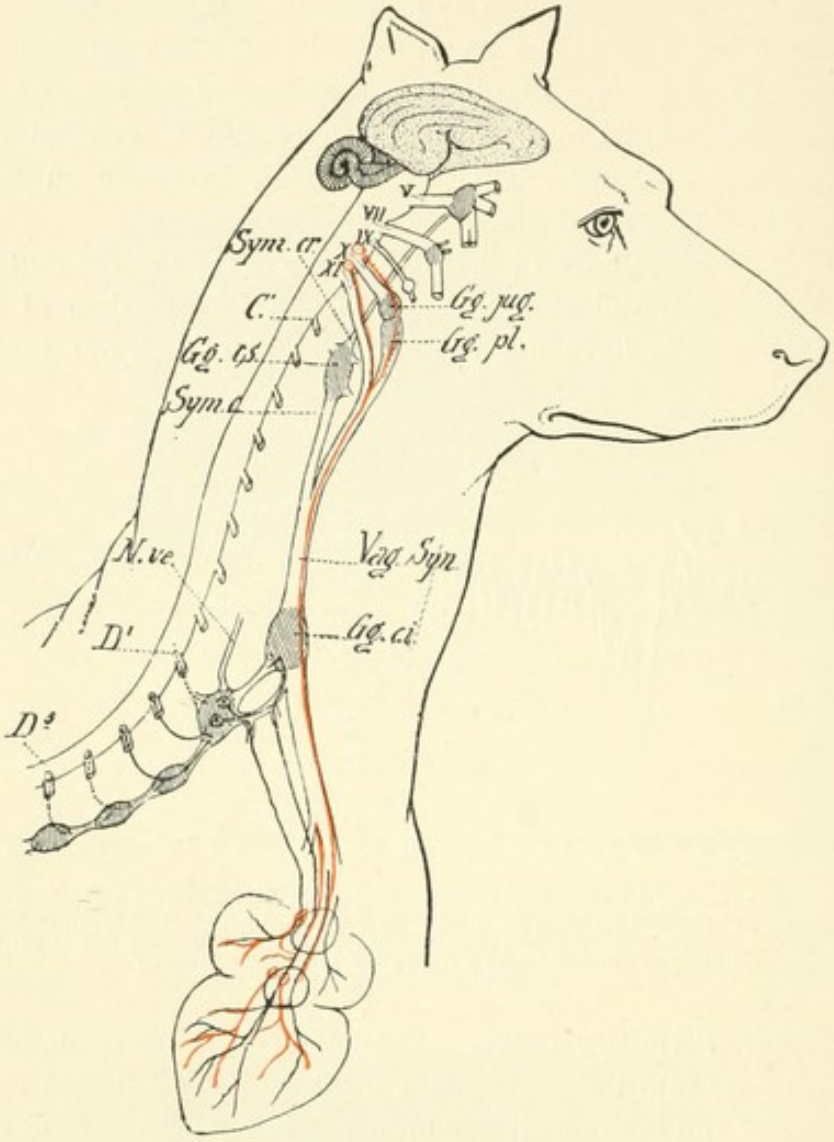


FIG. 181.—Diagrammatic Representation of the Origin and Course of the Cardiac Nerves in the Dog. *Vag. Syn*, Vago-sympathetic nerve; D^1, D^5, first to fifth dorsal spinal nerves. Inhibitory fibers in red, accelerators in black. (Modified from Moret.)

The Accelerator Nerves. The influence of the accelerator nerves reaching the heart through the sympathetic is the reverse of that of the vagus. Stimulation of the sympathetic, even of one side, produces acceleration of the rate of the heart-beats, and, according to certain observers, section of the nerve produces slowing. The acceleration produced by stimulation of the sympathetic fibers is accompanied by increased force, and so the action of the nerve is more properly termed *augmentor*. The sympathetic differs from the vagus in several particulars other than the augmentation which it produces; first, the stimulus required to produce any effect must be more

powerful than is the case with the vagus stimulation; second, a longer time elapses before the effect is manifest; and third, the augmentation is followed by exhaustion, the beats being after a time feeble and less frequent. The stimulation of the vago-sympathetic in the frog, which usually produces inhibition, will occasionally produce acceleration, especially if the heart is beating feebly at the time of the stimulation.

The fibers of the sympathetic system, which influence the heart-beat in the frog, leave the spinal cord by the anterior root of the third spinal nerve. They pass by the ramus communicans to the third sympathetic ganglion, thence to the second ganglion, the annulus of Vieussens (around the subclavian artery), through the first ganglion, and along the main trunk of the sympathetic to near the exit of the vagus from the cranium. There the two nerves join and run down to the heart within a common sheath, forming the vago-sympathetic trunk.

In the dog the augmentor fibers leave the cord by the anterior roots of the second and third dorsal nerves, and possibly also by the first, fourth, and fifth dorsal nerves. They pass by the rami communicantes to the ganglion stellatum, or first thoracic ganglion, around the annulus of Vieussens to the inferior cervical ganglion of the sympathetic. Fibers from the annulus or from the inferior cervical ganglion proceed to the heart, figure 181. The course of the augmentor fibers in the spinal cord is not so well known except that they originate in an augmentor center in the medulla. The circulation of venous blood appears to stimulate the augmentor center, and of highly oxygenated blood the inhibitory center.

The accelerator center, like the inhibitory, is in constant tonic activity; and the cardiac acceleration on cutting the vagi, shown in figure 180, is in part to be ascribed to this tone. When both nerves are stimulated together, the resulting rate is the algebraic sum of the opposed influences, according to Hunt. The accelerator center is influenced by afferent impulses arising throughout the body, and these reflexes contribute to the general coordination of the chest with the activities of the body.

In addition to direct and reflex stimulation, impulses passing down from the cerebrum may have a similar effect.

Other Influences Which Affect the Heart. A great variety of special conditions influence the heart's action in the normal body, conditions that are not discussed directly under any of the categories treated above. Of these may be mentioned the coronary circulation, temperature, mechanical tension, age, sex, etc.

The Coronary Circulation. The contractions of the heart cannot long be maintained without a due supply of blood or other nutrient fluid. The nutrient fluid for the heart of man and the mammals is supplied from the coronary arteries and the vessels of Thebesius. The coronary arteries arise from the base of the aorta, where they receive the benefit of the highest arterial

pressure. The coronary arteries are terminal arteries; that is, they do not permit the establishment of a collateral circulation when one of their branches is blocked. If the block be complete, that portion of the heart wall supplied by the branch dies. The immediate effect of the closure of a large coronary branch, in the dog, may be occasional and transient irregularity, or arrest of the ventricular contractions preceded by irregularities in the force of the contractions and a diminution in the amount of work performed. The force, rather than the rate, of the ventricular contractions is closely dependent upon the blood supply to the coronary arteries. Porter and others have shown that the pressure in the coronary vessels follows closely the pressure in the aorta and that there is not, as formerly claimed, a closure of these vessels by the pressure of the systole of the ventricle.

The vessels of Thebesius, which have been demonstrated to open both into the auricular and ventricular cavities, must now be looked upon, according to the investigations of Pratt, as an important source of cardiac nutrition. Blood may pass through them by way of connecting branches to the coronary arteries and veins. Pratt succeeded in maintaining cardiac contractions for several hours when the only source of nutrition was from these vessels. This source of nutrition may account for the survival of hearts for years where pronounced arterio-sclerosis of the coronary arteries exists.

Alteration of Temperature. The effect of cold is to slow the rate of the heart-beat, and if the heart of a frog be cooled down to 0° C. it will stop beating. It is said that the frog's heart may be frozen, and when thawed will renew its spontaneous beats. The effect of heat is to quicken and shorten the heart-beats, but at a moderate temperature, 20° C., the contractions are increased in force.

The isolated mammalian heart is influenced by temperature variations in much the same way as that of the frog. It will contract slowly in a low temperature and rapidly in a temperature higher than that normal to the body. The very rapid heart in some high fevers is in part due to the increase in temperatures which affects the heart directly.

Mechanical Tension. The mechanical factors produced by the heart beat are so prominent that it would be surprising indeed if there were no reaction of these mechanical conditions on the heart itself. The isolated cardiac muscle responds very quickly to variations in tension. Beginning with a low tension the activity of heart muscle is increased up to a certain optimum tension, after which further increase is unfavorable to the development of automatic rhythm. A quite strong stretching will paralyze the muscle.

Tension on the whole heart influences its activity, not only through the effects on the muscle, but indirectly through the nervous mechanism. High tension, such as contracting against a high aortic pressure, stimulates sensory nerves of the heart which, acting through the depressor nerve on the inhibitory

center, produce reflex slowing of the heart, as well as reflex vaso-dilatation, both of which relieve the high tension. This nerve reaction takes place with a tension which still mechanically stimulates the cardiac-muscle substance, and the inhibitory effects must therefore first overcome the direct stimulating effect of the tension on the muscle fibers.

Age, Sex, etc. The average heart rate for the normal adult man is 72 times a minute, but this rate will vary much in different individuals according to the age, sex, size, and personal equation. The frequency of the heart's action gradually diminishes from the commencement to near the end of life, but is said to increase again somewhat in extreme old age, thus:

Before birth the average number of pulsations per minute is	150
Just after birth	130 to 140
During the first year	115 to 130
During the second year	100 to 115
During the third year	90 to 100
About the seventh year	85 to 90
About the fourteenth year	80 to 85
In adult age	70 to 80
In old age	60 to 70
In decrepitude	65 to 75

The heart rate is greater in woman than in man. It is also greater in small than in large individuals. The rate varies from the type in certain individuals where no cause can be assigned other than personal equation.

Poisons and Other Chemical Substances. A large number of chemical substances have a distinct effect upon the cardiac contractions. Of these the most important are *atropine, muscarine, digitalis, barium,* etc.

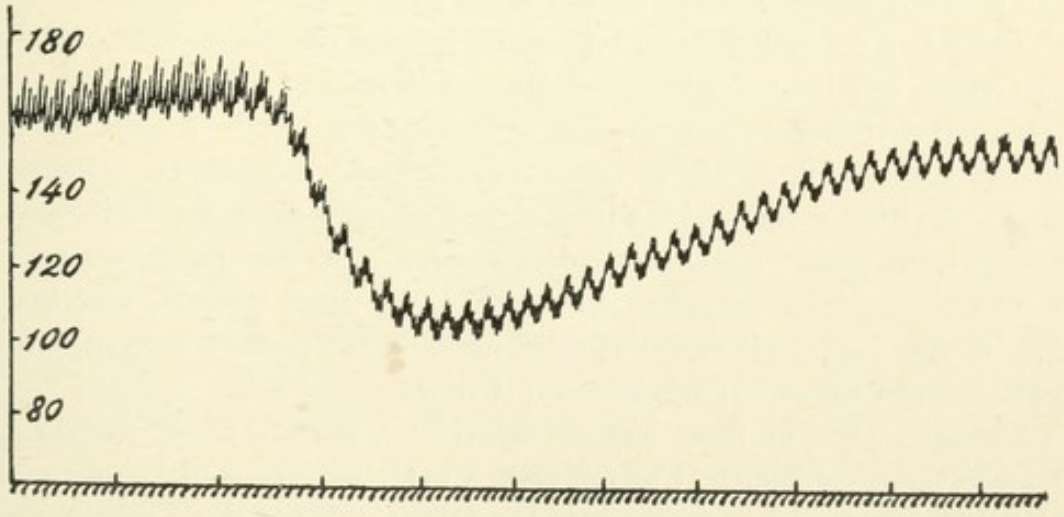


FIG. 182.—The Effect of an Intravenous Injection of Atropine on the Dog's Heart Rate Measured by Means of a Blood-Pressure Curve. (New figure by Dooley.)

Atropine produces considerable augmentation of the heart-rate, and when acting upon the heart prevents inhibition by vagus stimulation. Its effects are produced by poisoning the nerve endings of the vagus within

the heart. With these endings poisoned, stimuli arising in the inhibitory center of the medulla (tonic activity), or artifically applied to the vagus, cannot reach the heart muscle, and inhibition is impossible.

Muscarine, which is obtained from various species of poisonous fungi, produces marked slowing of the heart-beats, and, in larger doses, stoppage of the heart. It produces an effect similar to that of prolonged vagus stimulation. The effect can be removed by the action of atropine, hence is supposed to stimulate the nerve endings of the vagus.

Digitalis slows the heart by stimulating the vagi at their origin in the inhibitory center in the medulla. The heart muscle itself is also rendered more excitable.

Veratrine and *aconitine* have a somewhat similar effect.

THE CIRCULATION THROUGH THE BLOOD-VESSELS.

Blood Pressure. The subject of blood pressure has been already incidentally mentioned more than once in the preceding pages; the time has now arrived for it to receive more detailed consideration.

That the blood exercises pressure upon the walls of the vessels containing it is due to the following facts:

The heart at each contraction forcibly injects a considerable amount of blood, 80 to 100 c.c., suddenly and quickly into the arteries.

The arteries are highly distensible and stretch to accommodate the extra amount of blood forced into them. The arteries are already full of blood at the commencement of the ventricular systole, since there is not sufficient time between the heart-beats for the blood to pass into the veins.

There is a distinct resistance interposed to the passage of the blood from the arteries into the veins by the enormous number of minute vessels, small arteries (arterioles) and capillaries, into which the main artery has been ultimately broken up. The sectional area of the capillaries is several hundred times that of the aorta, and the friction generated by the passage of the blood through these minute channels opposes a considerable hindrance or resistance in its course. The resistance thus set up is called *peripheral resistance.* The friction is greater in the arterioles, where the current is comparatively rapid, than in the capillaries, where it is slow.

The interaction of these factors—heart-beat, elastic vessels, and peripheral resistance—is sufficient to maintain a continuous flow of blood through the entire circulatory system. It is the interrelation of these factors which maintains an even and steady flow through the capillaries and past the tissues, where it is desirable that the conditions of blood flow should be most constant. In fact, we shall find that it is through the interaction of this same group of factors, together with the possibility of variations through the regulation of their nerve-motor mechanisms, that we have the great variations

and adjustments of blood pressure, speed of flow, volume of flow, and the regulation of volume in particular parts of the body.

Arterial Blood Pressure. That the blood exerts considerable pressure upon the arterial walls in keeping them in a stretched or distended condition may be readily shown by puncturing any artery; the blood is instantly projected with great force through the opening, and the jet rises to a considerable height, the exact level of which varies with the size of the artery experimented upon. If a large artery be punctured the blood may be projected upward for several feet, whereas if it is a small artery the jet does not rise so high. Another characteristic of the jet of blood from a cut artery, particularly well marked if the vessel be a large one and near the heart, is the intermittent character of the outflow. If the artery be cut across, the jet issues with force, chiefly from the central end. If there is considerable anastomosis of vessels in the neighborhood the jet from the peripheral end may be as forcible and as intermittent as that from the central end. The intermittent flow in the arteries which is due to the action of the heart, and which represents the systolic and diastolic alterations of blood pressure, may be felt if the finger be placed upon a sufficiently superficial artery. The finger is apparently raised and lowered by the intermittent distention of the vessel occurring at each heart-beat. This intermittent distention of the artery is what is known as the *Pulse*, to the further consideration of which we shall presently return, but we may say here that in the normal condition the pulse is a characteristic of the arterial, and is absent from the venous, flow.

At the same time it must be recollected that in the veins also the blood exercises a pressure on its containing vessel which is small when compared with the arterial pressure. As might be expected, therefore, the blood is not expelled with so much force if a vein be punctured or cut. The flow from the cut vein is continuous and not intermittent, and the greater amount of blood comes from the peripheral and not from the central end, as is the case when an artery is severed.

Methods of Measuring Arterial Blood Pressure. The pressure in an artery may be measured by cutting the vessel and introducing into it a glass tube which has a tall vertical limb. A column of blood will rise in the tube at once to the height that can be supported by the pressure in that particular vessel. If the vessel be an artery, the blood will rise several feet, according to the distance of the vessel from the heart, and when it has reached its highest point it will be seen to oscillate with the heart-beats. This experiment shows that the pressure which the blood exerts upon the walls of the contained artery equals the pressure of a column of blood of a certain height. In the case of the rabbit's carotid it is equal to 90 to 120 cm. of blood, or rather more than the same height of water. In the case of the vein, if a similar experiment be performed, blood will rise in the tube only for 8 or 10 cm. or less.

The usual method of estimating the amount of blood pressure differs somewhat from the foregoing simple experiment. Instead of a simple straight tube of glass inserted into the vessel, a U-shaped tube containing mercury, the *mercurial manometer*, is employed. The artery is connected with the manometer by means of a small cannula which is inserted into the vessel, an arrangement being made whereby the cannula, tubes, etc., are filled with a saturated saline solution to prevent the clotting of blood when it is allowed

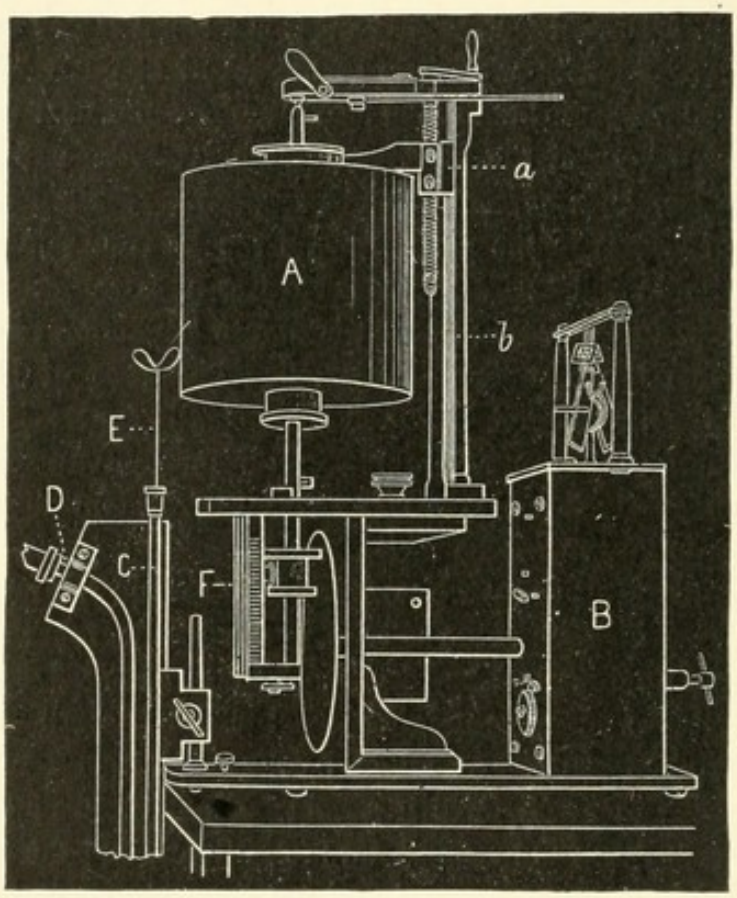


FIG. 183.—Diagram of Ludwig's Kymograph and Mercurial Manometer. *A*, Revolving cylinder, worked by a clock-work arrangement contained in the box (*B*), the speed being regulated by a fan above the box; cylinder supported by an upright (*b*), and capable of being raised or lowered by a screw (*a*), by a handle attached to it; *D*, *C*, *E*, represent a mercurial manometer, a somewhat different form of which is shown in the next figure.

to pass from the artery into the apparatus. The loss of blood is prevented during the preparation of the details of the experiment by a clamp or bull-dog forceps. The free end of the U-tube of mercury contains a very fine glass or metal rod with a bulb which floats upon the surface of the mercury and oscillates with the oscillations of the mercury. As soon as there is free communication between the artery and the tube of mercury, the blood rushes out and pushes before it the column of mercury. The mercury will therefore rise in the free limb of the tube, and will continue to do so until a point is reached which corresponds to the mean pressure of the blood-vessel used. The blood pressure is thus communicated to one limb of the mercurial column;

and the depth to which the latter sinks, added to the height to which it rises in the other limb, the weight of the saline solution being substracted, will give the height of the mercurial column which the blood pressure balances. For the estimation of the amount of blood pressure at any given moment, no further apparatus than this is necessary; but for accurately noting the *variations* of pressure in the arterial system, as well as its absolute amount, the instrument is usually combined with a recording apparatus, called a *kymograph*, figure 183, and permanent records are made of the observations.

The recording apparatus consists of a revolving cylinder, figure 183, *A*, which is moved by clock-work, and the speed of which is capable of regulation. The cylinder is covered with glazed paper, blackened in the flame of a lamp, and the mercurial manometer is so fixed, figure 183, *D*, that its

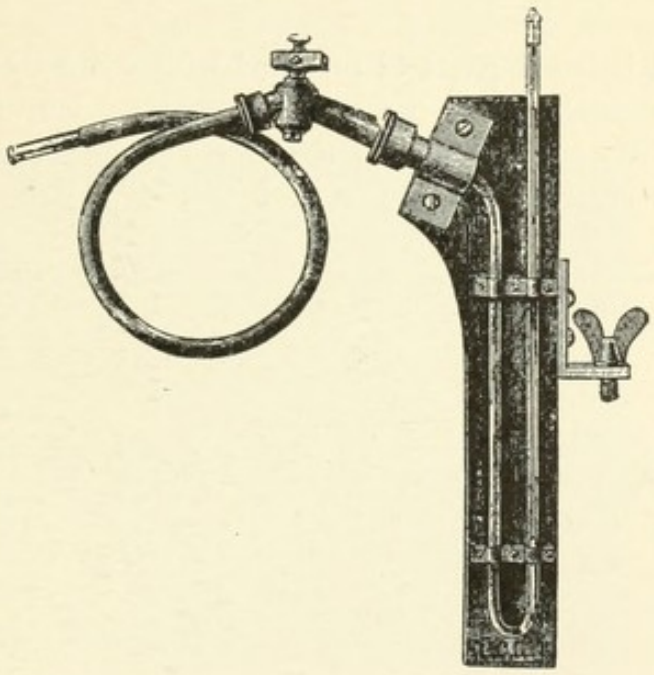


FIG. 184.—Ludwig's Mercury Manometer. The manometer is shown in figure 183, *D*, *C*, *E*. The mercury which partially fills the tube supports a float in the form of a piston, nearly filling the tube; a wire is fixed to the float, and the writing style or pen is guided by passing through the brass cap of the manometer tube; the pressure is communicated to the mercury by means of a flexible metal tube filled with fluid.

float, provided with a style, writes on the cylinder as it revolves. There are many ways in which the mercurial manometer may be varied; in figure 184 is seen a form which is known as Ludwig's. In order to obviate the necessity of a large quantity of blood entering the tube of the apparatus, it is usual to have some arrangement by means of which the mercury may be made to rise in the tube of the manometer to the level corresponding to approximately the mean pressure of the artery experimented with, so that the writing style simply records the variations of the blood pressure above and below the mean pressure. This is done by causing the saline solution, generally a saturated solution of sodium carbonate or a 10 per cent magnesium sul-

phate, to fill the apparatus from a bottle suspended at a height about that of the pressure to be measured, and capable of being raised or lowered as required for the purpose. The cannula inserted and tied into the artery may be of several different kinds. A glass T-tube with the end drawn out

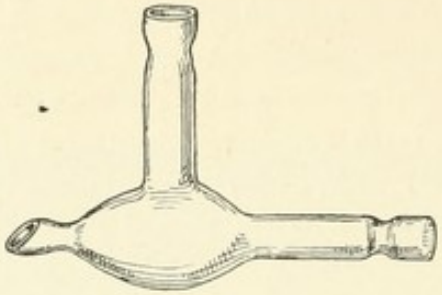


FIG. 185.—Arterial Cannula. T-form for convenience in washing out clots.

and cut so that it is oblique, and provided with a slightly constricted neck to prevent its coming out of the artery easily, is a very convenient form, figure 185. Of the two free ends of the T-cannula one is connected with the manometer, the other with the pressure bottle. The peripheral end of the

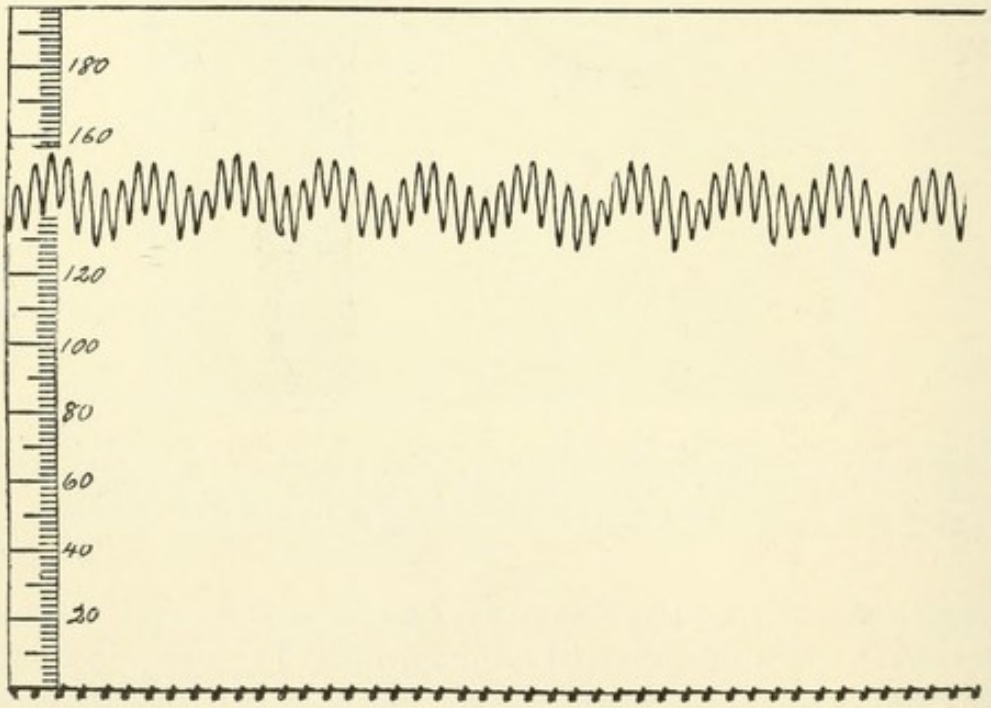


FIG. 186.—Tracing of Normal Arterial Pressure in the Dog, Obtained with the Mercurial Manometer. The smaller undulations correspond with the heart-beats; the larger curves with the respiratory movements. Pressure is in millimeters of mercury as shown by the scale to the left. Time in seconds. (New figure by March and Nugent.)

cut artery is tied to obviate the escape of blood. By this means, the pressure communicated to the column of mercury is the forward, and not the lateral, pressure of blood, but there is very little difference.

As soon as the experiment is begun, the writing float is seen to oscillate

in a regular manner, and a curve of blood pressure is traced upon the smoked paper by the style (or, if a continuous roll of unsmoked paper be used, the trace is made by an inked pen) when a figure similar to figure 186 will be obtained. This indicates two main variations of the blood pressure. The smaller excursions of the lever correspond with *the systole and diastole of the heart,* and the larger curves correspond with the respirations, being called the *respiratory undulations of blood pressure,* to which attention will be directed in the next chapter. Of course, the undulations spoken of are seen only in records of arterial blood pressure. They are more clearly marked in the arteries nearer the heart than in those more remote. The amount of the pressure in the smaller arteries as well as the indication of the systolic rise of pressure is, comparatively speaking, small.

In order to record the details of the undulations of arterial pressure, it is better for some purposes to use the Hürthle membrane manometer than the mercurial manometer. Two views of this instrument are shown in figure 166.

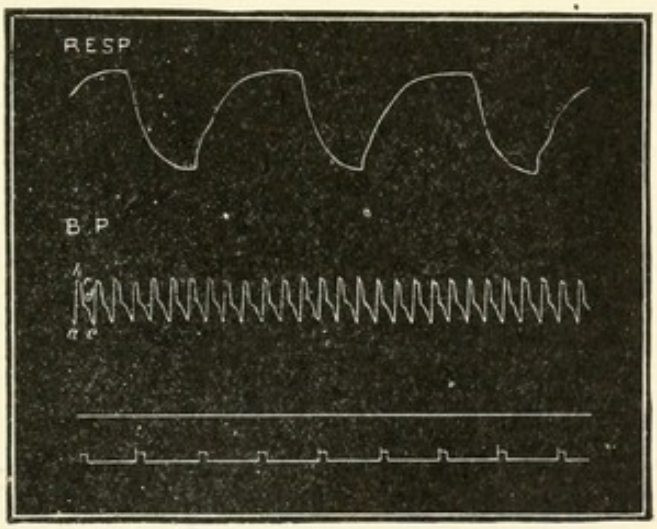


FIG. 187.—Tracing of Normal Arterial Pressure Taken from the Rabbit with a Hürthle Manometer. The horizontal lines show zero pressure. Time in seconds. (Dreyer.)

The instrument consists of a hollow tube and cup covered with rubber sheet against which a disc supported by a metal spring is adjusted. The apparatus is filled with fluid, the interior of which is connected with the artery by means of a metal tube and cannula. The pressure transmitted to the apparatus tends to stretch the rubber and bend the spring, and the movement thus produced is communicated by means of a lever to a writing style and so to a recording apparatus. This instrument obviates the errors which might be caused by the inertia of the mercury in the mercurial manometer; it also shows in more detail the variations of the blood pressure in the vessel during and after each individual beat of the heart.

As regards the actual amount of blood pressure, from observations which have been made by means of the mercurial manometer, it has been found

that the pressure of blood in the carotid of a rabbit is capable of supporting a column of 90 to 120 mm. of mercury; in the dog 100 to 175 mm.; in the horse 152 to 200 mm.; and in man the pressure is estimated to be about the same as in the horse. To measure the absolute amount of this pressure in any artery multiply the area of its transverse section by the height of the column of mercury which is already known to be supported by the blood pressure in any part of the arterial system. The weight of a column of mercury thus found will represent the absolute pressure of the blood. Calculated in this way, the blood pressure in the human aorta is equal to 1.93 kilogrammeters; that in the aorta of the horse being 5.2 kilogrammeters; and that in the radial artery at the human wrist only 0.08 kilogrammeter. Supposing the muscular power of the right ventricle to be only one-fourth that of the left, the blood pressure in the pulmonary artery will be only 0.5 kilogrammeter. The amounts above stated represent the arterial tension at the time of the ventricular contraction.

The arterial pressure is greatest at the beginning of the aorta, and decreases toward the capillaries. It is greatest in the arteries at the period of the ventricular systole, and least during the diastole. The blood pressure gradually lessens as we proceed from the arteries near the heart to those more remote, and again from these to the capillaries, as it does, also, from the capillaries along the veins to the right auricle.

Arterial Blood Pressure Measurements in Man. A number of instruments have been devised for estimating blood pressure in man for

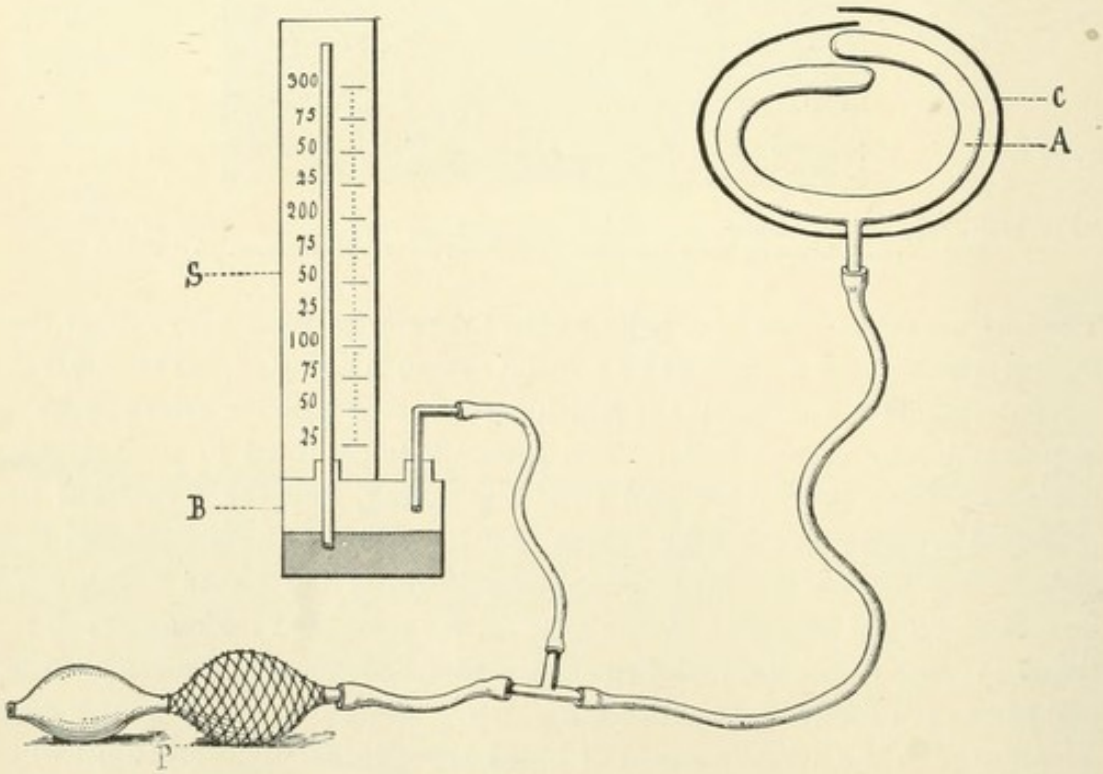


FIG. 188.—Riva-Rocci Apparatus (schematic) for Determining Blood Pressure in Man.

clinical purposes. Some of these, though excellent in principle, are too complicated for general use. The first simple and approximately accurate form of apparatus was that devised by Riva-Rocci in 1896. This has been modi-

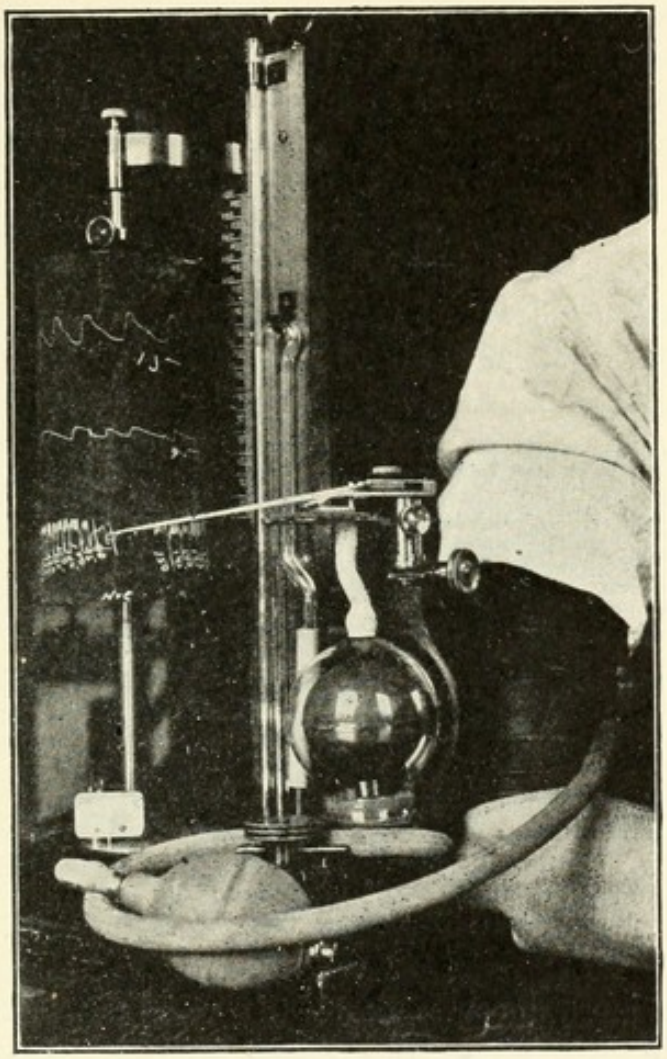


FIG. 189.—Erlanger's Sphygmomanometer, Shown with the Rubber Bag Attached to the Arm. The picture is taken at the end of an experiment after the pressure in the instrument is run up again to above the systolic pressure. The upper part of the cylinder shows a sphygmogram taken with the instrument. (Experiment and photo by Hill and Watkins.)

fied and improved in minor points since, but the principles of the original instrument remain practically the same.

In brief, the apparatus, figure 188, consists of an elastic tube ending in a rubber bag which can be adjusted about the arm or forearm, and a mercury manometer connected with this tube and also with some form of air pump used for inflating the tube about the arm and thus exerting pressure upon its blood-vessels. The elastic tube is covered by some inelastic tissue, usually a leather cuff, in order that the inflation of the bag may cause the full increase of pressure to be exerted upon the encased arm. By inflating the bag until the pulse at the wrist just disappears, and reading the height of the column of mercury in the manometer, the maximum or systolic pressure is obtained

in millimeters of mercury. If now the pressure on the arm is reduced until the widest oscillations of the mercury column are obtained, the lowest position of the mercury meniscus represents the diastolic pressure.

The apparatus depends on the principle that an external pressure just equal to the maximal pressure within an artery will hold the vessel in the collapsed condition, a fact that has been proven for vessels that are exposed. An external pressure that will just equal the minimal or diastolic pressure will cause a complete collapse of a vessel during diastole and will allow a complete expansion of an artery to its maximal limits during the systolic period of pressure. In other words, the mercury of the manometer will oscillate to its maximal. If the pressure is reduced to a still lower point, it will not be sufficient to compress the artery completely, and the mercury oscillations will again become smaller. In applying the instrument to the

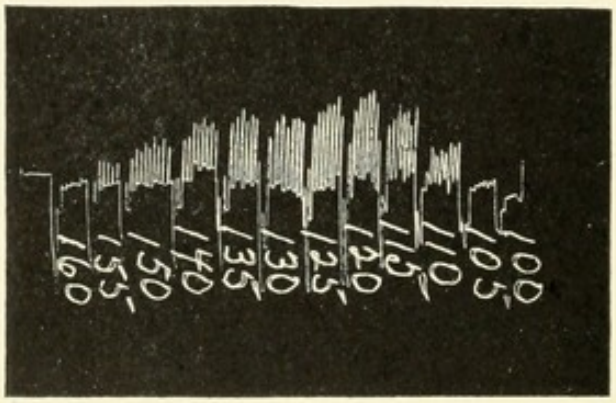


FIG. 190.—Tracing taken with Erlanger's Sphygmomanometer. The figures indicate pressure in millimeters of mercury. Systolic pressure, 160; diastolic pressure, 120. (New figure by Hill.)

brachial artery, one must, of course, deal with a vessel deeply buried in muscular and other tissues. These latter tissues probably consume a certain small percentage of the pressure, an error which may be ignored for all comparative purposes.

Erlanger has perfected a form of sphygmomanometer which contains a very ingenious and compactly arranged recording device, figure 189. This instrument has a mercury manometer from which the pressures are read off directly. On a side limb of the manometer there is a rubber bag enclosed in a glass bell. The cavity of the bell outside of the rubber bag is connected with a recording tambour, the entire apparatus being fully supplied with the necessary valves and adjusting devices which make it mechanically very perfect. The instrument is mounted on a stand with a small clock and recording cylinder adapting it to convenient clinical use.

The brachial arterial pressure of man when taken by this form of apparatus has been found to vary greatly, but Erlanger gives 110 mm. of mercury as the average of observations on young adults in the determination of the

systolic pressure, *i.e.*, the maximal arterial pressure. He gives for the diastolic pressure 40 to 45 mm. of mercury below the systolic pressure. Other observers using the same method find a somewhat higher average pressure, see figure 190, which represents a fair type of observation.

The Venous Blood Pressure and Capillary Pressure. The *blood pressure in the veins* is nowhere very great, but is greatest in the small veins, while in the large veins near the heart the pressure may become *negative*, or, in other words, when a vein is put in connection with a mercurial manometer the mercury may fall in the arm farthest away from the vein and will rise in the arm nearest the vein, the action being that of suction rather than pressure. In the large veins of the neck the tendency to suck in air is especially marked, and is the cause of death in some accidents or operations in that region. The amount of pressure in the brachial vein is said to support 9 mm. of mercury, whereas the pressure in the veins of the neck may fall to a negative pressure of from — 3 to — 8 mm.

The variations of venous pressure during systole and diastole of the heart are very slight, and a distinct pulse is never seen in veins except under extraordinary circumstances. In certain forms of cardiac valvular insufficiency there may be considerable regurgitation of the blood with a strong venous pulse.

Careful observations upon the web of the frog's foot, the tongue and mesentery of the frog, the tails of newts and small fishes, and upon the skin of the finger behind the nail (von Kries); as well as estimations of the amount of pressure required to empty the vessels of blood under various conditions, all indicate that *the capillary blood pressure* is subject to very great variations. Apparently the variations follow the variations of pressure in the arteries, though the measurements of the capillary pressure of the skin in man indicate that it is occasionally markedly influenced by the venous pressure variations.

The pulse in the arterioles, capillaries, and venules becomes more and more evident as the extravascular pressure is increased. The pressure in the web of the frog's foot has been found to be equal to about 14 to 20 mm. of mercury; in other capillary regions the pressure is found to be equal to from one-fifth to one-half of the ordinary arterial pressure.

General Variations in Blood Pressure. The arterial blood pressure may be made to vary by alterations in either of the chief factors upon which the pressure in the vessels depends, but primarily by the cardiac contractions and the peripheral resistance. Thus, increase of blood pressure may be brought about by either, 1, a more frequent or more forcible action of the heart, or, 2, by an increase of the peripheral resistance. On the other hand, diminution of the blood pressure may be produced, either by *a*, a diminished force or frequency of the contractions of the heart, or by *b*, a diminished peripheral resistance. These different factors, however, although

varying constantly, are so combined that the general arterial pressure remains fairly constant. For example, the heart may, by increased force or frequency of its contractions, distinctly increase the blood pressure, but this increased action is almost certainly followed by diminished peripheral resistance, and thus the two altered conditions may balance, with the result of bringing back the blood pressure to what it was before the heart began to beat more rapidly or more forcibly.

It will be clearly seen that the circulation of the blood within the blood vessels must depend upon the diminution of the pressure from the heart to the capillaries, and from the capillaries to the veins, the blood flowing in

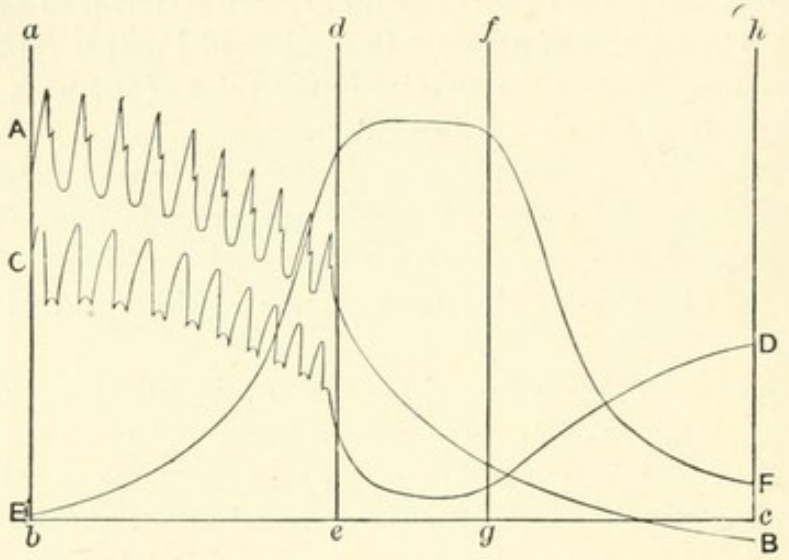


FIG. 191.—Schema Showing the Relation between Blood Pressure, Velocity of Flow, and Vascular Area, in the Arteries, Capillaries, and Veins. Ordinates represent height of pressure and speed of flow. The abscissa, *b-c*, represents zero pressure and speed. Space between lines *a-b* and *d-e* represents arterial system; between *d-e* and *f-g*, capillary system, and between *f-g* and *h-i*, the venous system. Line *A-B* equals pressure; line *C-D*, speed of flow; and line *E-F*, vascular area. (Modified from Gad.)

the direction of least resistance. We shall presently see further that the local flow also depends upon the relations between the heart's action and the peripheral resistance both general and local.

The Arterial Flow. The character of the flow of blood through the arterial system depends to a very considerable extent upon the structure of the arterial walls, and particularly upon the elastic tissue which is so highly developed in them.

The elastic tissue of the arteries, first of all, guards them from the suddenly exerted pressure to which they are subjected at each contraction of the ventricles. In every such contraction, as is above seen, the contents of the ventricles are forced into the arteries more quickly than they are discharged through the capillaries. The blood, therefore, being for an instant resisted in its onward course, a part of the force with which it is impelled is directed against the sides of the arteries; under this force their elastic walls dilate,

stretching enough to receive the blood, and becoming more tense and more resisting as they stretch. Thus by yielding they break the shock of the force impelling the blood. On the subsidence of the pressure, should the ventricles cease contracting, the arteries are able by the same elasticity to resume their former caliber.

The elastic tissue in the same way equalizes the current of blood by maintaining pressure on it in the arteries during the period at which the ventri-

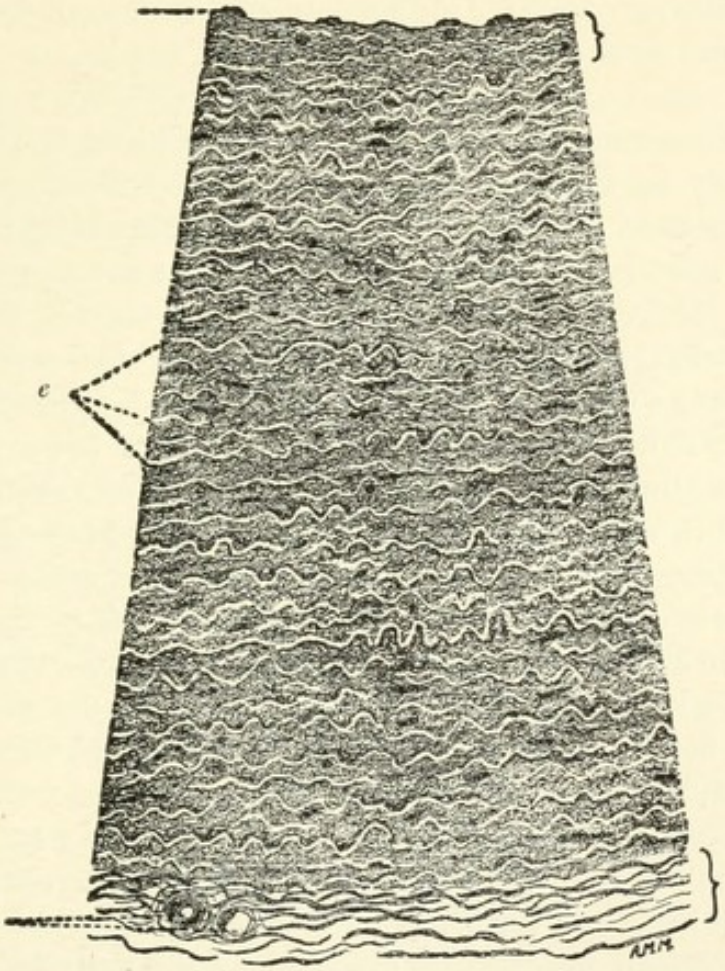


FIG. 192.—Cross Section of the Aorta to Show Elastic Tissue; *e*, elastic elements. (Bailey.)

cles are at rest or are dilating. If the arteries were rigid tubes, the blood, instead of flowing as it does in a constant stream, would be propelled through the arterial system in a series of spurts corresponding in time to the ventricular contractions and with intervals of almost complete rest during the inaction of the ventricles. But in the actual condition of the vessels, the force of the successive contractions of the ventricles is expended partly in the direct propulsion of the blood, and partly in the dilatation of the elastic arteries; and in the intervals between the contractions of the ventricles, the force of the recoil is employed in continuing the flow onward. Of course the pressure exercised is equally diffused in every direction, and the blood

tends to move backward as well as onward. All movement backward, however, is prevented by the closure of the semilunar valves, which takes place at the very commencement of the recoil of the arterial walls.

The Arterial Flow is Rhythmic. By the exercise of the elasticity of the arteries, all the force of the ventricles is expended upon the circulation. That part of the force which is used up or rendered potential in dilating the arteries is restored or made active or kinetic when they recoil. There is no loss of force, neither is there any gain; for the elastic walls of the artery cannot originate any force for the propulsion of the blood; they only restore that which they receive from the ventricles.

Since the ventricular discharge is intermittent, there will be intermittent accessions of pressure, and therefore the flow of blood in the arteries will be periodically accelerated. The volume of blood discharged from a cut artery increases and decreases with the systole and diastole of the ventricles, or with the systolic and diastolic pressures of the arteries themselves, see page 187.

This equalizing influence of the resistance of the successive arterial branches reacts so that at length the intermittent accelerations produced in the arterial flow by the discharge of the heart cease to be observable, and the jetting stream is converted into the continuous and even movement of the blood which we see in the capillaries and veins. In the production of a continuous stream of blood in the smaller arteries and capillaries, the resistance which is offered to the blood stream in these vessels is a necessary agent. Were there no greater obstacle to the *escape* of blood from the larger arteries than exists to its *entrance* into them from the heart, the stream would be intermittent, notwithstanding the elasticity of the walls of the arteries.

The muscular element of the middle coat cooperates with the elastic in adapting the caliber of the vessels to the quantity of blood which they contain; for the amount of fluid in the blood-vessels varies quite considerably even from hour to hour, and can never be quite constant; and were the elastic tissue only present, the pressure exercised by the walls of the containing vessels on the contained blood would be sometimes very small, and sometimes inordinately great. The presence of a muscular element, however, provides for a certain uniformity in the amount of pressure exercised; and it is by this adaptive, uniform, gentle muscular contraction that the normal tone of the blood-vessels is maintained. Deficiency of this tone is the cause of the soft and yielding arterial pulse, and the sluggish blood flow through the arterioles.

Incidentally it may be mentioned that the elastic and muscular contraction of an artery may also be regarded as fulfilling a natural purpose when, the artery being cut, the sudden contraction at first limits, and then, in conjunction with the coagulated fibrin, completely arrests, the flow of blood. It is only in consequence of such contraction and coagulation that we are

free from danger through even very slight wounds; for it is only when the artery is closed that the processes for the more permanent and secure prevention of bleeding are established.

The Velocity of the Arterial Blood Flow. The velocity of the blood current at any given point in the various divisions of the circulatory system is inversely proportional to their united sectional area at that point. If the united sectional area of all the branches of a vessel were always the same as that of the vessel from which they arise, and if the aggregate sectional area of the capillary vessels were equal to that of the aorta, the mean rapidity of the blood's motion in the small arteries and in the capillaries would be the same as in the aorta. If a similar correspondence of capacity existed in the veins there would be an equal correspondence in the rapidity of the circulation in them. But the arterial and venous systems may be represented by two truncated cones with their apices directed toward the heart; the area of their united bases, the sectional area of the capillaries, being four hundred to eight hundred times as great as that of the truncated apex representing the aorta. Thus the velocity of blood in the smallest arterioles and the capillaries is not more than one-four-hundredth of that in the aorta.

The velocity of the stream of blood is greatest in the neighborhood of the heart. The rate of movement is greatest during the ventricular systole and diminishes during the diastole. The rate of flow also decreases along the arterial system, becoming least in the parts of the system most distant from the heart. Chauveau has estimated the rapidity of the blood stream in the carotid of the horse at over 20 inches per second during the heart's systole, and nearly 6 inches during the diastole (520–150 mm.), see figure 191.

The Capillary Flow. It is in the capillaries that the chief resistance is offered to the progress of the blood; for in them the friction of the blood is greatly increased by the enormous multiplication of the surface with which it is brought in contact.

When the capillary circulation is examined in any transparent part of a full-grown living animal by means of the microscope, figures 193, 194, the blood is seen to flow with a constant equable motion; the red blood-corpuscles moving along, mostly in single file, and bending in various ways to accommodate themselves to the tortuous course of the capillary, but instantly recovering their normal outline on reaching a wider vessel,

At the circumference of the stream and adhering to the walls of the larger capillaries, but especially well marked in the small arteries and veins, there is a layer of plasma which appears to be motionless. The existence of this still layer, as it is termed, is inferred both from the general fact that such a one exists in all fine tubes traversed by fluid, and from what can be seen in watching the movements of the blood-corpuscles. The red corpuscles occupy the middle of the stream and move with comparative rapidity; the colorless corpuscles run much more slowly by the walls of the vessels; while next

to the wall there is a transparent space in which the fluid appears to be at rest; for if any of the corpuscles happen to be forced within it, they move more slowly than before, rolling lazily along the side of the vessel, and often adhering to its wall, figure 194. Part of this slow movement of the colorless corpuscles and their occasional stoppage may be due to their having a tendency to adhere to the walls of the vessels. Sometimes, indeed, when the motion of the blood is not strong, many of the white corpuscles collect in a capillary vessel, and for a time entirely prevent the passage of the red corpuscles.

When the peripheral resistance is greatly diminished by the dilatation of the small arteries and capillaries, so much blood passes on from the arteries into the capillaries at each stroke of the heart that there is not sufficient remaining in the arteries to distend them. Thus, the intermittent current of the ventricular systole is not always converted into a continuous stream by the elasticity of the arteries before the capillaries are reached; and so intermittency of the flow occurs both in capillaries and veins and a venous pulse is produced. The same phenomenon may occur when the arteries

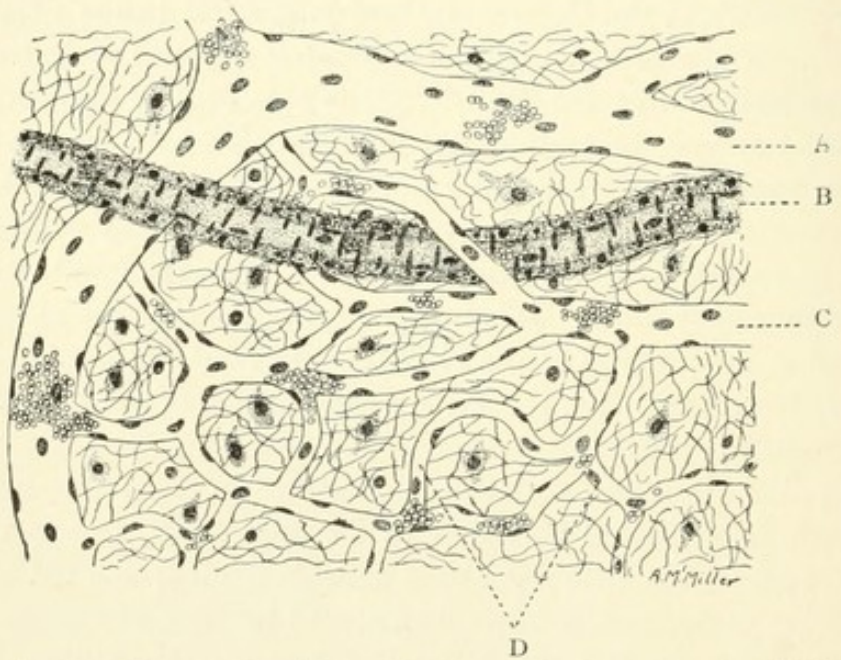


FIG. 193.—Capillary Network from Human Pia Mater, Showing also an Arteriole in "Optical Section"; and a Small Vein. × 350. *A*, Vein; *B*, arteriole; *C*, large capillary; *D*, small capillaries. (Bailey.)

become rigid from disease, and when the beat of the heart is so slow or so feeble that the blood at each cardiac systole has time to pass on to the capillaries before the next stroke occurs; the amount of blood sent at each stroke being insufficient properly to distend the elastic arteries.

It was formerly supposed that the occurrence of any transudation from the interior of the capillaries into the midst of the surrounding tissues was confined, in the absence of injury, strictly to the fluid part of the blood; in

other words, that the corpuscles could not escape from the circulating stream, unless the wall of the containing blood-vessel was ruptured. It is true that the English physiologist Augustus Waller affirmed in 1846 that he had seen blood-corpuscles, both red and white, pass bodily through the wall of the capillary vessel in which they were contained (thus confirming what had been stated a short time previously by Addison), and that as no opening could be seen before their escape, so none could be observed afterward, so rapidly was the part healed. But these observations did not attract much notice until the phenomenon of escape of the blood-corpuscles from the capillaries and minute veins, apart from mechanical injury, was rediscovered by Cohnheim in 1867.

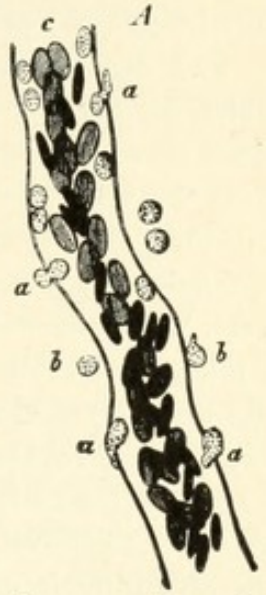


FIG. 194.—A Large Capillary from the Frog's Mesentery Eight Hours after Irritation had been set up, Showing Emigration of Leucocytes. *a*, Cells in the act of traversing the capillary wall; *b*, some already escaped. (Frey.)

Cohnheim's experiment demonstrating the passage of the corpuscles through the wall of the blood-vessel is performed in the following manner: A frog is curarized, that is to say paralysis is produced by injecting under the skin a minute quantity of the poison called curari. The abdomen is then opened, a portion of the small intestine is drawn out, and its transparent mesentery spread out under a microscope. After a variable time, occupied by dilatation following contraction of the minute vessels and the accompanying quickening of the blood stream, there ensues a retardation of the current and the red and white blood-corpuscles begin to make their way through the capillaries and small veins.

The white corpuscles pass through the capillary wall chiefly by the ameboid movement with which they are endowed. This migration occurs to a limited extent in health, but in inflammatory conditions is much increased.

The process of *diapedesis* of the red corpuscles, which occurs under circumstances of impeded venous circulation, and consequently increased blood pressure, resembles closely the migration of the leucocytes, with the exception that they are squeezed through the wall of the vessel, and do not, like the leucocytes, work their way through by ameboid movement.

Various explanations of these remarkable phenomena have been suggested. Some believe that pseudo-stomata between contiguous endothelial cells provide the means of escape for the blood-corpuscles. But the chief share in the process is probably due to mobility and contraction of the parts concerned, both of the corpuscles and of the capillary wall itself.

The Speed of the Blood in the Capillaries. The velocity of the blood through the capillaries must, of necessity, be largely influenced by that which occurs in the vessels on both sides of them, in the arteries and

the veins, their intermediate position causing them to respond at once to any alteration in the size or rate of the arterial or venous blood stream. Thus, the apparent contraction of the capillaries, on the application of certain irritating substances or during certain mental states, and their dilatation in blushing may be referred primarily to the corresponding action of the small arteries.

The Measurement of Velocity in the Capillaries. The observation of Hales, E. H. Weber, and Valentin agree very closely as to the rate of the blood current in the capillaries of the frog; and the mean of their estimates gives the velocity of the *systemic* capillary circulation at about 0.5 mm. per second. The velocity in the capillaries of warm-blooded animals is greater, in the dog 0.5 to 0.75 mm. per second. This may seem inconsistent with the facts, which show that the whole circulation is accomplished in about half a minute. But the whole length of capillary vessels, through which any given portion of blood has to pass, probably does not exceed 0.5 mm. Therefore the time required for each quantity of blood to traverse its own appointed portion of the general capillary system will scarcely amount to more than a second. This comparatively slow velocity is evidently favorable to the nutritive interchanges that go on through these thin-walled vessels between the blood within the capillaries and the outside active tissues.

The Venous Flow. The blood current in the veins is maintained, *a*, primarily by the contractions of the left ventricle; but very effectual assistance to the flow is afforded, *b*, by the action of the muscles capable of pressing on the veins with valves, and *c*, by the aspiration of the thorax and possibly, *d*, by the aspiration of the heart itself.

The effect of muscular pressure upon the circulation may be thus explained: When pressure is applied to any part of a vein, and the current of blood in it is obstructed, the portion behind the seat of pressure becomes swollen and distended as far back as the next pair of valves, which are in consequence closed. Thus, whatever force is exercised by the external pressure of the muscles on the veins, is distributed partly in pressing the blood onward in the proper course of the circulation, and partly in pressing it backward and closing the valves behind.

The circulation might lose as much as it gains by such an action, if it were not for the numerous communications, or venous anastomoses; for owing to these anastomoses the closing up of the venous channel by the backward pressure is prevented from being any serious hindrance to the circulation, since the blood which is arrested in its onward course by the closed valves can at once pass through some anastomosing channel, and proceed on its way by another vein. Thus the effect of muscular pressure upon veins which have valves is turned almost entirely to the advantage of the circulation; the pressure of the blood onward is all advantageous, and the pressure of the blood backward is prevented from being a hindrance by the closure of the valves and of the anastomoses of the veins.

The venous flow is also assisted by the aspiration of the thorax and to some extent by that of the heart, since at some time during every cardiac cycle the intraauricular and intraventricular pressure falls below that of the atmosphere. This activity will be considered more fully in the chapter on Respiration. In this connection it may be said, however, that the pressure in the great veins falls during inspiration and rises during expiration.

The Velocity in the Veins. The velocity of the blood is greater in the veins than in the capillaries, but less than in the arteries; this fact depending upon the relative capacities of the arterial and venous systems. If an accurate estimate of the proportionate areas of arteries and the veins corresponding to them could be made, we might, from the velocity of the arterial current, calculate that of the venous. The usual estimate is that the capacity of the veins is about two or three times as great as that of the arteries, and that the velocity of the blood's motion is, therefore, about one-half or one-third as great in the veins as in the arteries, *i.e.*, 200 mm. a second. The rate at which the blood moves in the smallest venules is only slightly greater than that in the capillaries, but the speed of flow gradually increases the nearer the vessel approaches to the heart, for the sectional area of the venous trunks, compared with that of the branches opening into them, becomes gradually smaller as the trunks advance toward the heart, figure 191.

The Velocity of the Circulation as a Whole. It would appear that a portion of blood can traverse the entire course of the circulation, in the horse, in half a minute. Of course it would require longer to traverse the vessels of the most distant part of the extremities than to go through those of the neck, but taking an average length of the vessels to be traversed it may be concluded that half a minute represents the average rate. Stewart estimated that the circulation time in man is probably not less than twelve nor more than fifteen seconds.

Satisfactory data for these estimates are afforded by the results of experiments to ascertain the rapidity with which chemicals introduced into the blood are transmitted from one part of the vascular system to another. The time required for the passage of solutions of potassium ferrocyanide, mixed with the blood, from one jugular vein, through the right side of the heart, the pulmonary vessels, the left cavities of the heart, and the general circulation, to the jugular vein of the opposite side, varies from twenty to thirty seconds in the dog. The same substance is transmitted from the jugular vein to the great saphenous vein in twenty seconds; from the jugular vein to the mesenteric artery in between fifteen and thirty seconds; to the facial artery, in one experiment, in between ten and fifteen seconds; in another experiment, in between twenty and twenty-five seconds; in its transit from the jugular vein to the metatarsal artery, it occupies between twenty and thirty seconds. The result is said to be nearly the same whatever the rate of the heart's action. In more recent methods some innocuous dye like methylene

blue is used, since it permits the determination without the loss of blood, the change in color being visible through the walls of the blood-vessels.

Stewart has made most accurate measurements of the circulation time by the electrical-resistance method. Strong salt solutions injected into the jugular vein on one side when they reach the other jugular (or any other vessel) are instantly detected by a decrease in the electrical resistance through the vessel when it is laid between the poles of the proper conductivity apparatus.

In all these experiments it is assumed that the substance injected moves with the blood and at the same rate, and does not move from one part of the organs of circulation to another by diffusing itself through the blood or tissues more quickly than the blood moves. The assumption may be accepted that the times above mentioned as occupied in the passage of the injected substances are the times in which the portion of blood itself is carried from one part to another of the vascular system.

Another mode of estimating the general velocity of the circulating blood is by calculating it from the quantity of blood supposed to be contained in the body, and from the quantity which can pass through the heart in each of its contractions. But the conclusions arrived at by this method are less satisfactory. For the total quantity of blood, and the capacity of the cavities of the heart, have as yet been only approximately ascertained. Still the most careful of the estimates thus made accord very nearly with those already mentioned; and it may be assumed that the blood may all pass through the heart in about twenty-five seconds.

THE PULSE.

The most characteristic feature of the arterial pressure and blood flow is its intermittency, and this intermittent flow is seen or felt as waves of change in diameter of the arteries, known as the *Pulse*.

The pulse is generally described as a wave-like expansion of the artery produced by the injection of blood at each ventricular systole into the already full aorta. The force of the left ventricle is expended in pressing the blood forward and in dilating the aorta. With the injection of each new quantity of blood into the aorta there is a wave of dilatation which passes on, expanding the arteries as it goes, running as it were over the more slowly traveling blood contained in them, and producing the pulse as it proceeds. A sharp distinction must be made between the passage of the pulse wave along an artery and the rate of flow of the blood in the vessel. The pulse produced by any given beat of the heart is not felt at the same moment in all parts of the body. Thus, it can be felt in the carotid a short time before it is perceptible in the radial artery, and in this vessel before it occurs in the dorsal artery of the foot. Careful measurements of the intervals between the time of the pulse

at the carotid and at the wrist shows that the delay in the beat is in proportion to the distance of the artery from the heart. The difference in time between the pulse of any two arteries probably never exceeds one-sixth to one-eighth of a second. The rate at which the pulse travels in the arteries is from five to ten meters per second.

The distention of each artery increases both its length and its diameter. In their elongation the arteries change their form, the straight ones becoming slightly curved, and those already curved becoming more so; but they recover their previous form as well as their diameter when the ventricular contraction ceases, and their elastic walls recoil. The increase of their curves which accompanies the distention of arteries, and the succeeding recoil, may be well seen in the prominent temporal artery of an old person. In feeling the pulse, the finger cannot distinguish the sensation produced by the dilatation from that produced by the elongation and curving. That which it perceives most plainly, however, is the dilatation and return more or less to the cylindrical form of the artery, which has been partially flattened by the finger.

The Sphygmograph. Much light has been thrown on what may be called the form of the pulse wave by an instrument called the sphygmo-

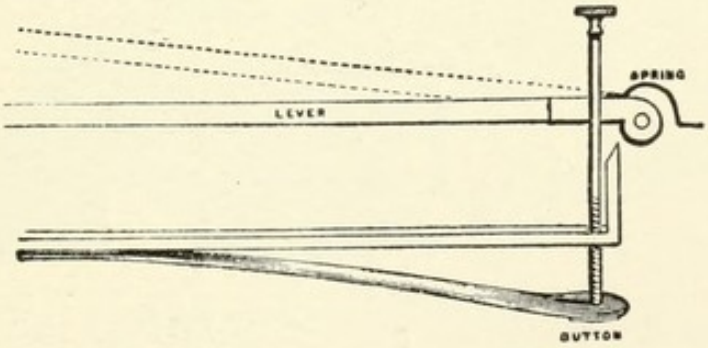


FIG. 195.—Diagram of the Lever of the Sphygmograph.

graph, figures 195 and 196. The principle on which it acts will be seen on reference to the figures.

A small button replaces the finger in the act of taking the pulse. This button is made to rest lightly on the artery the pulsations of which it is desired to investigate. The up-and-down movement of the button is communicated to the lever, to the hinder end of which is attached a light spring. The spring is adjusted to the proper tension to follow the movements of the artery wall during the pulse wave. The sphygmograph is bound on the wrist while taking a record.

It is evident that the beating of the pulse will cause an up-and-down movement of the lever, the pen of which will write the effect on a smoked card moved by the clock-work of the instrument.

Thus a tracing of the pulse is obtained, and in this way much more delicate changes can be seen than can be felt by the mere application of the finger.

The principle of the sphygmometer of Roy and Adami is shown in the diagram, figure 197.

The apparatus consists of a box, *a*, which is moulded to fit over the end of the radius so as to bridge over the radial artery. Within this is a flexible bag, *b*, filled with water, and connected by a T-tube with a rubber bag, *h*, and mercurial manometer. The fluid in the box may be raised to any desired pressure, and may then be shut off by tap, *c*. At the upper part of the box is a circular opening, and resting upon *b* is a flat button, *d*, which by means of a short light rod, *e*, communicates the movement of *b* to the lever, *f*. At the axis of rotation of this lever is a spiral watch-spring, *g*, which can be tightened at will, so that the lever can be made to take a vertical position at any desired hydrostatic

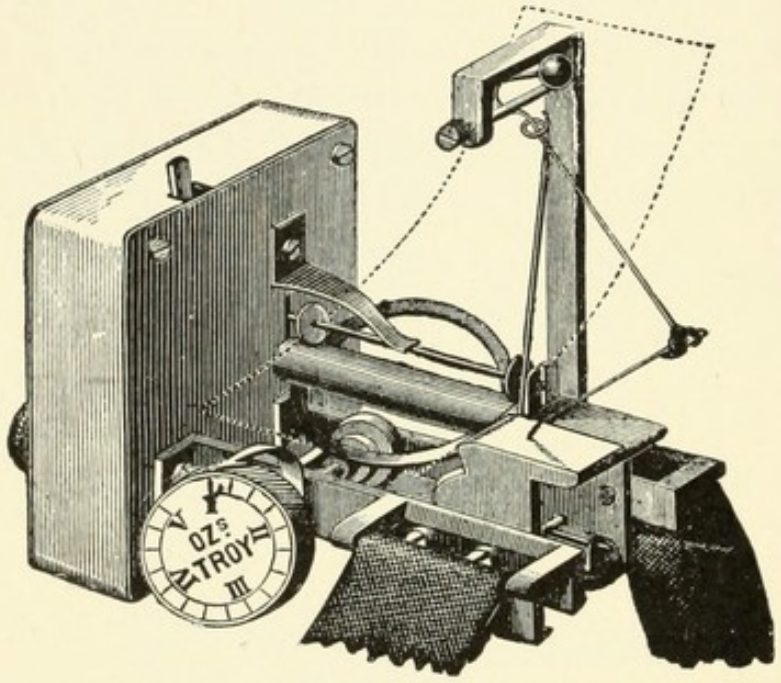


FIG. 196.—Dudgeon's Sphygmograph.

pressure within the box. The movements of the lever are recorded upon a piece of blackened glazed paper made to move in a vertical direction past it. When in use, the box is fixed upon the wrist by an appropriate holder, and the pressure is raised to any desired height to which the lever is adapted by tightening or slackening the spring; the tap, *c*, is then closed. The pressure within the box acts in all directions, and is correctly indicated by the manometer.

Sphygmogram. The tracing of the pulse obtained by the use of the sphygmograph, called a *sphygmogram*, differs somewhat according to the artery from which it is taken, but its general characters are much the same in all cases. It consists of a sudden upstroke, or *anacrotic* limb, figure 198, *A*, which is somewhat higher and more abrupt in the pulse of the carotid and of other arteries near the heart than in the radial and other arteries more remote; and a gradual decline or *catacrotic* limb, *B*, less abrupt, and taking a longer time than A. It is seldom, however, that the decline is an uninterrupted fall; it is usually marked about half-way by a distinct notch,

C, called the *dicrotic notch*, followed immediately by a second more or less marked ascent of the lever called the *dicrotic wave*, *D*. Not infrequently there is also at the beginning of the descent a slight wave previous to the dicrotic notch; this is called the *pre-dicrotic wave*, and in addition there may be one or more slight waves after the dicrotic, called *post-dicrotic*, *E*. The interruptions in the downstroke are called the *catacrotic* waves to distinguish them from an interruption in the upstroke, called the *anacrotic* wave, which is sometimes met with.

The explanation of these tracings presents some difficulties, not, however, as regards the two primary factors, viz., the upstroke and downstroke,

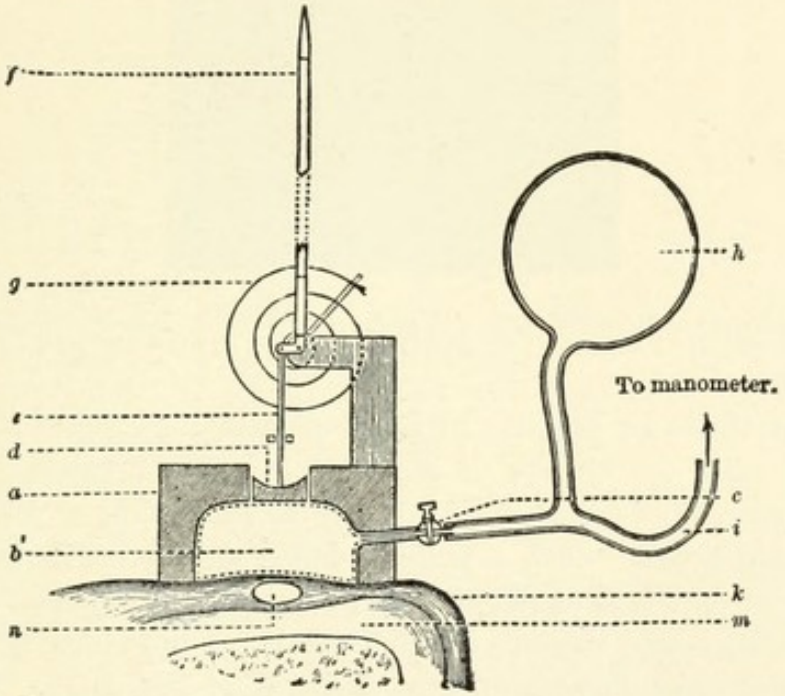


FIG. 197.—Diagrammatic Sectional Representation of the Sphygmometer. *a*, Box by which the portion of the artery is covered; *b*, thin-walled india-rubber bag filled with water, and communicating through tap, *c*, with the manometer and thick-walled rubber bag, *h*; *d*, piston connected by rod, *e*, with recording lever, *f*; *g*, spiral spring, attached to axis of lever, and by which the pressure in *b*, against the piston, *d*, is counterbalanced; *k*, skin and subcutaneous tissue; *m*, end of radius seen in section; *n*, radial artery seen in section. (Roy and Adami.)

because they are universally taken to mean the sudden injection of blood into the already distended arteries, and the gradual recovery of the arteries by their recoil. These points may be demonstrated on a system of elastic tubes, with a pump to inject water at regular intervals, just as well as on the radial artery, or on the *arterial schema*, a more complicated system of tubes in which the heart, the arteries, the capillaries and veins are represented. If we place two or more sphygmographs upon such a system of tubes at increasing distances from the pump, we may demonstrate, first, that the rise of the lever commences earliest in that nearest the pump, and, second, that it is higher and more sudden. So in the arteries of the body the wave gradually gets less and less as we approach the periphery of the arterial system, and is lost in the capillaries.

The origin of the secondary waves is to some extent a matter of uncertainty. The *anacrotic* wave occurs when the peripheral resistance is high; that is, when, for some time during the systole, the flow from the aorta toward the periphery is slower than the flow from the ventricle into the aorta. Thus it is seen in some cases of nephritis where the arteries ase rigid and the peripheral resistance is high.

The *dicrotic* wave is the most important of the secondary waves, and has been the subject of much discussion. It is constantly present in pulse-

FIG. 198.—Diagram of Pulse Tracing. *A*, upstroke or anacrotic limb; *B*, downstroke or katacrotic limb; *C*, pre-dicrotic wave; *D*, dicrotic; *E*, post-dicrotic wave.

tracings, but varies in height. In point of time the dicrotic wave occurs immediately after the closure of the aortic semilunar valves. In certain conditions, generally of disease, it becomes so marked as to be quite plain to the unaided finger. Such a pulse is called *dicrotic*. The generally accepted view of the cause of the dicrotic wave is that it represents a rebound from the closed aortic valves. During systole, as the blood is forcibly injected into the aorta, there is an overdistention of the artery. The systole suddenly ends, the aorta by reason of its elasticity tends to recover itself,

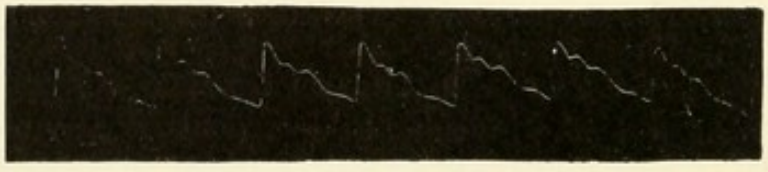


FIG. 199.—Sphygmogram from the Radial Artery Taken with Marey's Sphygmograph. (Langendorff.)

the blood is driven back against the semilunar valves, closing them and at the same time giving rise to a wave, the dicrotic wave, which begins at the heart and travels onward toward the periphery like the primary wave. According to Foster, the conditions favoring the development of dicrotism are: 1, a highly extensible and elastic arterial wall; 2, a comparatively low mean blood pressure, leaving the extensible reaction free scope to act; 3, a vigorous and rapid stroke of the ventricle discharging into the aorta a considerable

quantity of blood. The other secondary waves are probably due to the oscillations in the elastic recoil of the arteries, though some of them at least may be due to the inertia of the instruments used.

In the use of the sphygmograph care must be taken in the regulation of the pressure of the spring. If the pressure be too great, the characters of

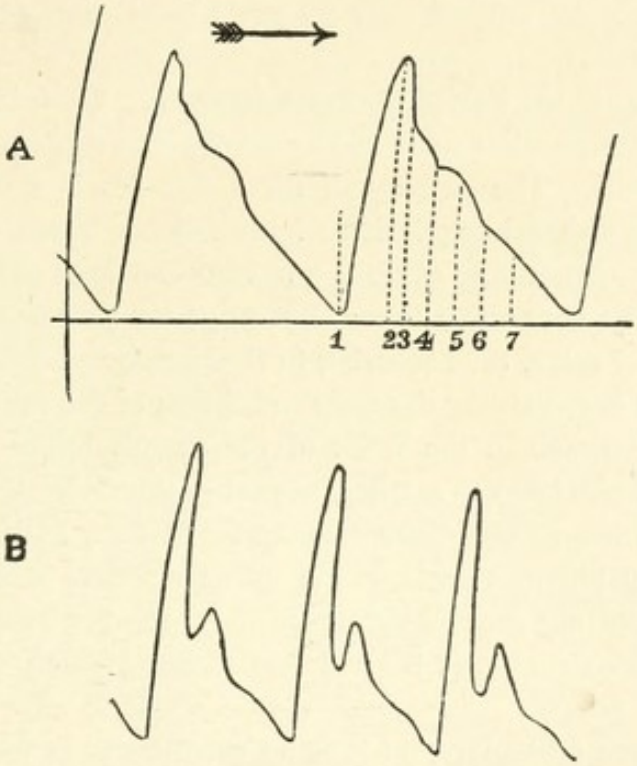


FIG. 200.—*A*, Normal Pulse-Tracing from Radial of Healthy Adult Obtained by the Sphygmometer; *B*, from same artery, with the same extra-arterial pressure, taken during acute nasal catarrh.

the pulse may be almost entirely obscured, or the artery may be completely obstructed and no tracing is obtained. On the other hand, if the pressure is too slight, a very small part of the characters may be represented on the tracing.

THE PERIPHERAL REGULATION OF THE FLOW OF BLOOD.

The flow of blood through the circulatory system depends on the interaction of several factors which have already been mentioned in another connection: The rate and volume of the heart-beat, the elasticity of the blood-vessels, the resistance of the microscopic peripheral vessels, and the volume of blood in the body. We have already learned, page 179, that both the rate and the volume of the contractions of the heart are under very minute and intimate regulation and control through the cardiac nervous mechanism. Also we have found that there is intimate coordination between the activity of the circulatory and the activity of all other parts of the body, a coordination accomplished through the nervous system. All regulation which affects

the heart must of necessity affect the general blood pressure and, therefore, not directly any particular part.

The general elasticity of the blood-vessels, and of the arteries in particular, which makes the general arterial pressure possible, is dependent primarily on the presence of a large amount of elastic connective tissue in the walls of the vessels. The elasticity of this tissue is a purely passive property which can be utilized only by some positive source of energy, in this instance the heart.

The Variations in Peripheral Resistance. Certain arteries and veins, especially the smallest ones, the arterioles, are supplied with muscular tissue in their walls. The activity of these muscles in the vascular complex makes the peripheral regulation of the flow of blood possible. They supply a tissue which not only exhibits a passive elasticity comparable to that of the yellow elastic connective tissue, but upon the proper stimulation they actively contract or relax, thus securing to the peripheral resistance an active adjustment to the ever-varying dynamic conditions of the vascular apparatus.

The muscular tissue in the walls of the vessels increases relatively in amount as the arteries become smaller, so that in the arterioles it is developed out of all proportion to the other elements. In fact, in passing from the arterioles to the capillary vessels, made up as we have seen of endothelial cells with a supporting ground substance only, the last change on the side of the arteries, which occurs as the vessels become smaller, is the disappearance of muscular fibers.

The office of the muscular coat is to adjust the size of the arterioles and, therefore, the flow of the blood, to regulate the quantity of blood to be received by each part or organ, and to adjust the quantity to the requirements of each, according to various circumstances, but chiefly according to the degree of activity which each organ at different times exhibits. The amount of work done by each organ of the body constantly varies, and the variations often quickly succeed each other, so that, as in the muscles for example, within the same hour a part may be now very active and now quite inactive. In all its active exercise of function, such an organ requires a larger supply of blood than is sufficient for it during the times when it is comparatively inactive.

It is evident that the heart cannot regulate the blood supply to each part of the body at different periods independently of the other parts. Neither could this be regulated by any general and uniform contraction of the arteries. But it may be regulated by the power which the arteries of each part have, through their muscular tissue, of contracting or relaxing so as to diminish or increase the supply of blood, according to the requirements of the particular part of the body to which the vessels are distributed. Thus, while the ventricles of the heart determine the total quantity of blood to be sent onward at each contraction, and the force of its propulsion, and while the

large and merely elastic arteries distribute the blood and equalize its stream, the smaller arteries by means of their muscular tissue regulate and determine the proportion of the whole quantity of blood which shall be distributed to each particular organ.

The variation of the size of arterioles and, therefore, of the resistance to the flow of the blood in them is secured by the muscular tissue, but the muscles are regulated in their contraction by the nervous system. The muscular tissue in the blood-vessels of the different organs of the body is also coordinated by the same regulative and controlling influence of the nervous system.

The Discovery of the Vaso-motor Nerves. More than half a century ago it was shown by Claude Bernard that if the cervical sympathetic nerve is divided, the blood-vessels of the corresponding side of the head and

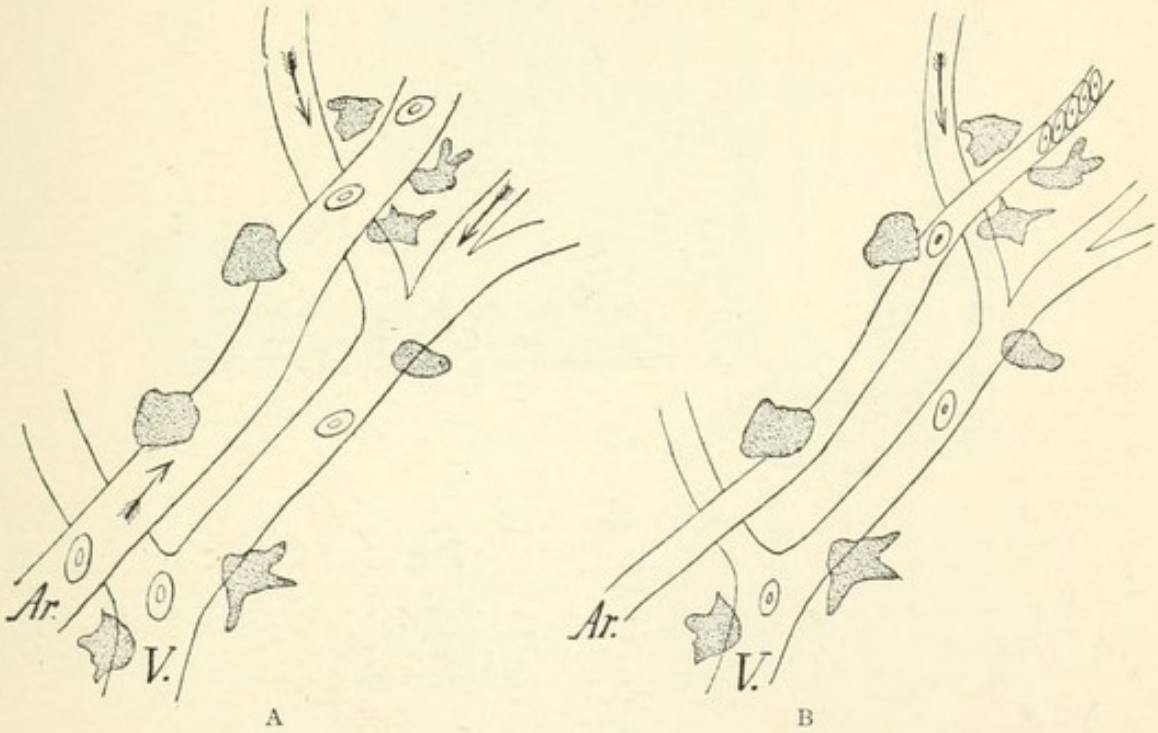


FIG. 201.—Small Artery and Vein of the Frog's Web. *A*, Under normal conditions; *B*, upon stimulation of the sciatic nerve; *Ar.*, artery; *V*, vein. In this experiment the vein also showed well-marked vaso-constriction. (New figure by Greene.)

neck become dilated. This effect is best seen in the ear, which if held up to the light is seen to become redder, and the arteries to become larger. The whole ear is distinctly warmer than the opposite one. This effect is produced by removing the arteries from the influence of the central nervous system, which influence normally passes along the course of the divided nerve.

If the peripheral end of the divided nerve be stimulated in its course toward the organ, *i.e.*, that farthest from the brain, the arteries which were before dilated return to their natural size, and the parts regain their former condition. And, besides, if the stimulus is very strong or very long continued,

the amount of normal constriction is passed and the vessels become much more contracted than before. The natural condition, which is midway between extreme contraction and extreme dilatation, is called the natural *tone* of an artery. If this is not maintained, the vessel is said to have lost

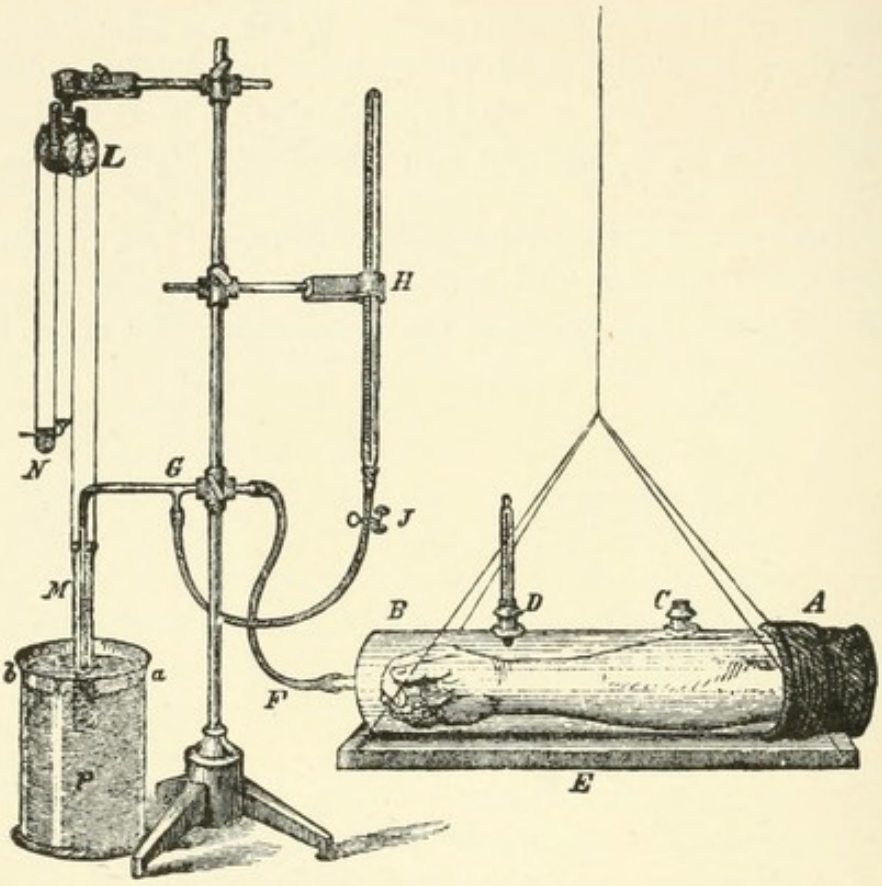


FIG. 202.—Arm Plethysmograph. Apparatus for measuring the change in volume in the arm due to variation in the blood supply. The arm is enclosed in a glass cylinder which is completely filled with fluid, the opening through which the arm is inserted being closed by a rubber sleeve, *A*. The cavity of the glass cylinder communicates through the tube, *F*, *G*, with the test tube *M*, which is supported in the jar, *P*. Any variation in volume in the arm will cause water to flow out or into the test tube, *M*, which is lowered as the tube fills, and raised as it empties. The rise and fall of the test tube, *M*, is communicated over the pulley, *L*, to the writing-pen, *N*, which records the movements on the smoked cylinder. Kymograph not shown. (Mosso.)

tone, or, if it is exaggerated, the tone is said to be too great. The effects described as having been produced by section of the cervical sympathetic and by subsequent stimulation are not peculiar to that nerve and the vessels to which it is distributed.

It has been found that for every part of the body, except the brain, there exists a nerve the division of which produces the same effects, viz., dilatation of the vessels. Such may be cited as the case with the sciatic, the splanchnic nerves, and the nerves of the brachial plexus; when these are divided, dilatation of the blood-vessels in the parts supplied by them takes place. It appears, therefore, that nerves exist which have a distinct control over the vascular supply of every part of the body. These are called *vaso-motor* or *vaso-constrictor* nerves. But the arterioles are also under the influence of

a second set of nerves, also discovered by Claude Bernard, which produce exactly the opposite influence, *i.e.*, dilatation. These nerves are called *vaso-dilator* nerves.

Mall has also shown that *veins*, at least the portal vein, possess a vaso-motor nerve supply as well as arteries.

Vaso-constrictor Nerves. The presence of vaso-constrictor nerves can be shown in several different ways, of which the most convincing is that of direct inspection. If a vascular membrane, like the web of the frog's foot or the bat's wing, be adjusted on the stage of a microscope for direct inspection, and the smaller arterioles are under observation, then upon the stimulation of the general nerve supplying the part these arterioles will sharply decrease in size. In fact the vaso-constriction is often so great as com-

FIG. 203.—Plethysmogram of the Hind Limb of a Cat, showing Vaso-constriction upon Stimulating the Sciatic 64 times per second. To be read from right to left. (Bowditch and Warren.)

pletely to occlude the vessel. Very soon after the stimulation the vessel again dilates to its normal size.

The presence and course of the vaso-constrictor nerve supply to the organs of the body have been demonstrated not by direct inspection, but by the use of various forms of the plethysmograph. A plethysmograph is an instrument designed to measure the variations in the volume of an organ. If the finger, the whole hand, the spleen, or the kidney be placed in such an instrument and the proper steps be taken to record the volume changes, it will be found that the volume of the enclosed organ is constantly changing with every variation of the blood pressure. If the nerves to the organ are stimulated by the usual rapidly interrupted induction current, for example, the splanchnics to the kidney, then there is a decrease in the volume of the organ. This decrease takes place even when there is a simultaneous increase of the arterial blood pressure, a result that can be explained only on the assumption of vascular decrease in the organ. The decrease in the flow of blood to the specific organ can be induced only by a great decrease in the size of the arterioles produced by contractions of the circular muscles of their walls.

Vaso-motor Tone. Vaso-constrictor changes are constantly occurring in the blood-vessels of the organs of the body, a fact that has been abundantly demonstrated by the plethysmographic experiments just mentioned. Direct inspection of the ear of an albino rabbit will show that the arteries, and veins as well, are now full and large and red, and the interspaces filled with blood, and now pale and constricted, and the interspaces apparently bloodless. If the cervical sympathetic is cut as in Bernard's experiment, then the ear vessels remain dilated, that is, they lose their tone, showing that the condition is dependent primarily on the constant discharges of nerve impulses from the nervous system. It is said that the vessels regain their tone after a time when the nerves are cut. The regained power may be ascribed to the muscle fibers themselves.

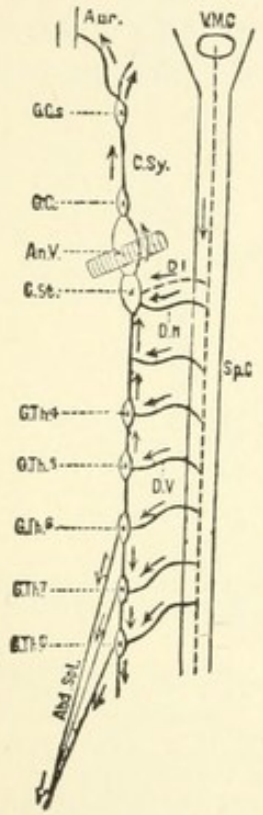


FIG. 204.—Diagram Showing the Paths of the Vaso-constrictor Fibers along the Cervical Sympathetic and the Abdominal Splanchnic. *Aur*, Artery of ear; *G.Cs*, superior cervical ganglion; *An. V*, annulus of Vieussens; *G.St.* stellate ganglion; *D.I*, *D.II*, *D.V*, thoracic spinal nerves; *Abd. Spl.* abdominal splanchnic. The arrows indicate the direction of vaso-constrictor impulse.

Vaso-constrictor Center. When the tonic influence exerted by the nerve-fibers on the arterioles is traced back into the central nervous system, it is found to be associated with the activity of certain groups of nerve-cells, or centers, which are called the *vaso-constrictor centers*. This determination is made in part by the method of sectioning. A lesion of the cerebro-spinal axis below the corpora quadrigemina is followed by partial or complete general dilatation of the blood-vessels and great fall of blood pressure. This is due to the isolation of the vaso-constrictor center, which lies in the floor of the fourth ventricle, a millimeter or two caudal to the corpora quadrigemina, and extends longitudinally over an area of about three millimeters. Owsjannikow has shown that the center is composed of two halves, each half lying in the lateral column to the side of the median line. This center is in constant action during life, and its discharges are responsible for the vascular tone described in the previous paragraph. The vaso-constrictor center varies in its activity, sometimes producing wave-like contractions with relaxations of the arterial walls, producing variations in the blood pressure known as Traube-Hering waves. They are more often observed in mammalian blood-pressure experiments after prolonged operations, when the center may be supposed to be itself in a weakened condition.

Secondary vaso-motor centers are present in the spinal cord as proven by Goltz. Under normal conditions they do not act independently of the medullary center; but when the function of the latter has been interrupted

by section of the cord, then after a few days the spinal cells below the section take on central functions and bring about a re-establishment of the lost vascular tone. If these centers be destroyed by the destruction of the cord, then the tone of the vessels immediately disappears but is regained after the lapse of a much longer time. This can be ascribed to the presence of possible sympathetic constrictor centers or more probably to a fundamental property of the muscles themselves. This experiment was carried out by Goltz and Oswald, who found that after destruction of the lower part of the spinal cord, the tone of the vessels of the hind limbs, lost as a result of the operation, was later re-established.

Vaso-constrictor Reflexes. Under normal conditions the medullary center responds to afferent stimuli by vaso-motor reflexes. The secondary vaso-motor centers in the spinal cord, when removed from the influence of the bulbar center, can and do respond to afferent impulses by similar vaso-motor action.

The afferent impulses which excite reflex vaso-motor action may proceed from the terminations of sensory nerves in general, or possibly from the blood-vessels themselves, and the constriction which follows generally occurs in the area whence the impulses arise. Yet the reflex may appear elsewhere. Impulses proceeding to the vaso-motor center from the cerebrum may cause vaso-dilatation, as in *blushing*, or vaso-constriction, as in the *pallor* of fear or of anger.

Afferent influence upon the vaso-motor centers is well shown by the action of the *depressor* nerve, the existence of which was demonstrated by Cyon and Ludwig. The depressor is a small afferent nerve which passes up to the medulla from the heart, in which it takes its origin. It runs upward in the sheath of the vagus or in the superior laryngeal branch of the vagus or as an independent branch, as in the rabbit, communicating by filaments with the inferior cervical ganglion as it proceeds from the heart. If, in a rabbit, this nerve be divided and the central end stimulated during a blood-pressure observation, a remarkable fall of blood pressure takes place, figure 205.

The cause of the fall of blood pressure is found to proceed primarily from the dilatation of the vascular district within the abdomen supplied by the splanchnic nerves, in consequence of which the vessels hold a much larger quantity of blood than usual. The engorgement of the splanchnic area very greatly diminishes the amount of blood in the vessels elsewhere, and so materially diminishes the blood pressure. The function of the depressor nerve is that of conveying to the vaso-motor center afferent nerve impulses from the heart, which produces an inhibition of the tonic activity of the vaso-motor center and, therefore, a diminution of the tension in the blood-vessels, thus relieving the heart from the overstrain of propelling blood into the already too full or too tense arteries. It has been shown by Porter and Beyer that the fall in blood pressure, following stimulation of the depres-

sor nerve, will still occur, even when the abdominal vaso-constriction is kept constant by a simultaneous stimulation of the splanchnics. It is therefore evident that the inhibitory effect of depressor-nerve stimulation is a general one and not confined to the splanchnic area alone.

The action of the depressor nerve in causing an inhibition of the vaso-motor center illustrates the more unusual effect of afferent impulses, that is, inhibition of the vaso-constrictor tone. As a rule, the stimulation of the central end of an afferent nerve, such as the sciatic or the internal saphenous, produces the reverse, *i.e.*, a *pressor* effect, and increases the tonic influence

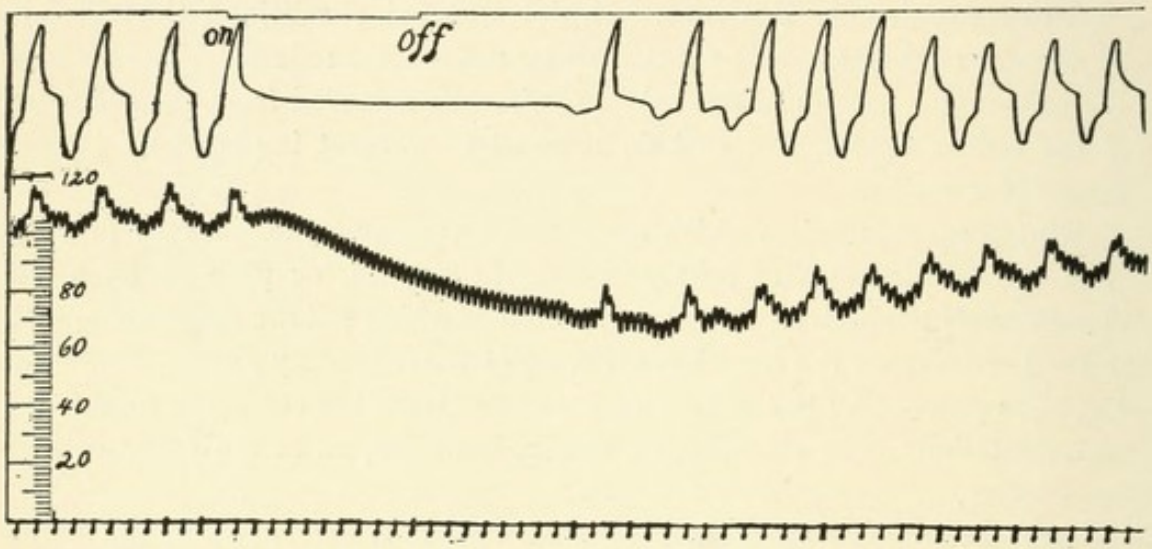


FIG. 205.—Blood-Pressure Record (lower) and Respiratory Record (upper) Obtained from a Dog upon Stimulating the Central End of the Divided Vagus, Both Vagi being Cut. The marked fall in blood pressure is due to the effect of stimulating the depressor fibers contained in the vagus trunk of the dog. (New figure by Dooley and Dandy.)

of the center which by causing constriction of the arterioles raises the blood pressure. Thus the effect of stimulating an afferent nerve may be either to constrict or to dilate the arteries. These reflexes may be general enough to influence the general blood pressure, but the local effects are the all-important ones, since by these the local regulation of the blood flow is accomplished.

Traube-Hering Curves. The *vaso-motor center* sends out rhythmical impulses by which undulations of blood pressure of a large and sweeping character are produced, quite independent of the so-called respiratory undulations. The action of this center in producing such undulations is demonstrated in the following observations. In an animal under the influence of curari and with both vagi cut, and a record of whose blood pressure is being taken, if artificial respiration be stopped, the blood pressure rises sharply at first. After a time the rhythmical undulations shown in figure 206 occur. These variations are called *Traube's* or *Traube-Hering curves.* There may be upward of ten of the respiratory undulations in one Traube-

Hering curve. They continue until the vaso-motor center is asphyxiated and the heart exhausted, when the pressure falls. The undulations cannot depend upon anything but the vaso-motor center, as the mechanical effects of respiration have been eliminated by the curari and by the cessation of artificial respiration, and the effect of the cardio-inhibitory center has been removed by the division of the vagi. The rhythmic rise of blood pressure is most likely due to a rhythmic constriction of the arterioles followed by a

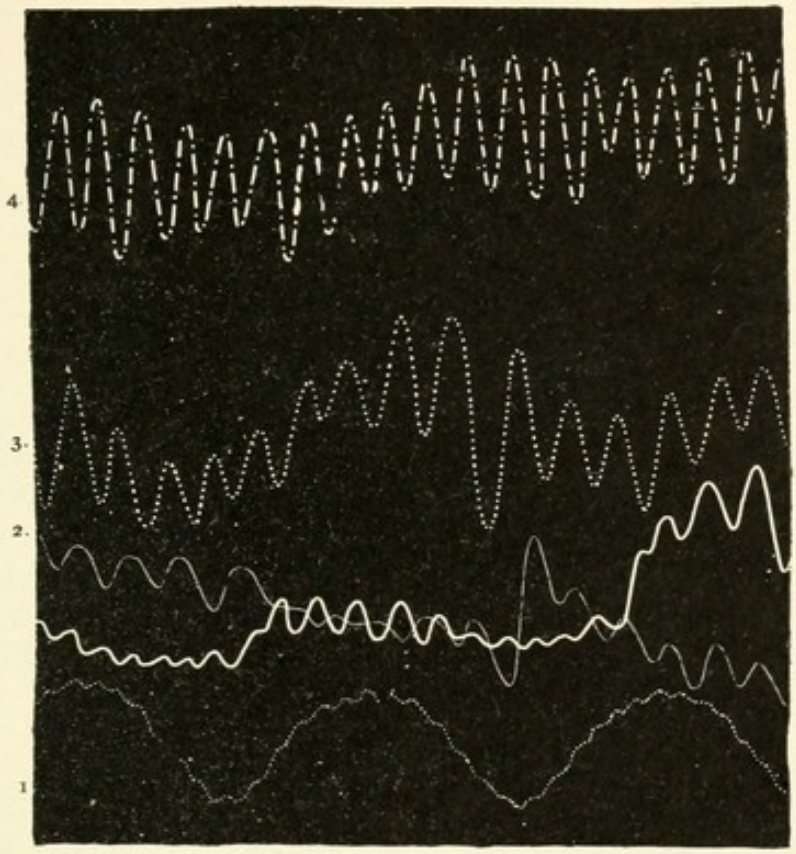


FIG. 206.—Traube-Hering's Curves. (To be read from left to right.) The curves 1, 2, 3, 4, and 5 are portions selected from one continuous tracing forming the record of a prolonged observation, so that the several curves represent successive stages of the same experiment. Each curve is placed in its proper position relative to the base line, which is omitted; the blood pressure rises in stages from 1 to 2, 3, and 4, but falls again in stage 5. Curve 1 is taken from a period when artificial respiration was being kept up, but, the vagi having been divided, the pulsations on the ascent and descent of the undulations do not differ; when artificial respiration ceased, these undulations for a while disappeared, and the blood pressure rose steadily while the heart-beats became slower. Soon, as at 2, new undulations appeared; a little later, the blood pressure was still rising, the heart-beats still slower, but the undulations still more obvious (3); still later (4), the pressure was still higher, but the heart-beats were quicker, and the undulations flatter; the pressure then began to fall rapidly (5), and continued to fall until some time after artificial respiration was resumed. (M. Foster.)

rhythmic fall of pressure and relaxation, both being due to the action of the vaso-motor center. The vaso-motor center, therefore, is capable of producing rhythmical undulations of blood pressure.

Vaso-dilator Nerves. Claude Bernard discovered that the blood flow was increased through the salivary glands by stimulation of the nerves (the chorda tympani for the submaxillary, and the tympanic branch of the glossopharyngeal for the parotid), thus proving that the arteries have not

only vaso-constrictors, but also *vaso-dilator nerves*. Vaso-dilator nerves have been described for most parts of the body. In general they are distributed in the same nerve trunks which bear the vaso-constrictors.

It is not supposed that the vaso-dilators produce widening of the arterioles by stimulation to active muscular contraction; in fact the circular arrangement of the muscle fibers would seem to exclude such a deduction. It is probable that there is local inhibition of the tonic contraction of the muscles, thus allowing the mechanical factor of the general blood pressure to dilate

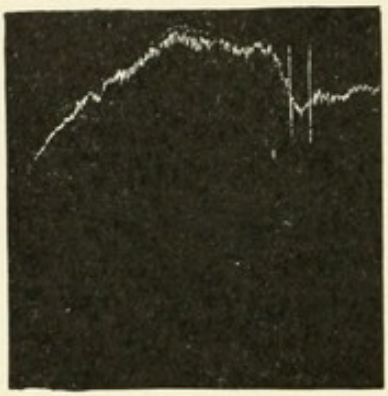


FIG. 207.—Plethysmogram of the Hind Limb of a Cat, Showing Vaso-dilatation upon Stimulating the Sciatic Once per Second. To be read from right to left. (Bowditch and Warren.)

the vessels. The vaso-dilator nerves are characterized by their response to slowly developed stimuli, shown by Bowditch and Warren, and by the retention of irritability after degeneration of the constrictors has taken place, see figure 207.

Vaso-dilator Centers. No distinct medullary center has yet been shown to regulate the vaso-dilator nerve activity. Such centers, if they exist, should be influenced by isolating them from their efferent paths, on the one hand, or by stimulation by afferent channels, on the other. The former method of study has revealed nothing that can be compared to the tonic activity of the constrictor center. Efferent dilator-nerve impulses can be reflexly produced by sensory stimulation. The isolated lumbar cord of a dog is capable of reflex vaso-dilator activity, since stimulation of the skin of the penis leads to reflex vaso-dilatation, indicating the presence of local vaso-dilator centers in this portion of the spinal cord.

Vaso-dilator Reflexes. Perhaps the only unquestioned case of reflex vaso-dilatation is that of the lumbar cord just mentioned. It is true that many apparent reflexes can be noted, for example the increased flow of blood in the salivary glands under gustatory reflexes, the blushing of the skin on exposure to sudden warmth, or even the blushing of emotional origin, which on first thought might be regarded as vaso-dilator reflexes. But each of these instances can be just as readily explained as inhibitions of the vaso-constrictor tonic activity. This double explanation can, as a matter of fact,

be applied to the action of the depressor nerve described above, page 217. On the whole, however, while we cannot directly and unquestionably prove the fact, yet it is probable that each of the above examples may be accepted as examples of reflex vaso-dilatation by direct action on a vaso-dilator center or centers in the cord.

The Relation of Vaso-constrictor and Vaso-dilator Activity. The distribution of two sets of regulative fibers for the muscular walls of the blood-vessels, when considered in connection with the other factors of the vascular apparatus, gives a wonderfully complete mechanism for the coordination of the vascular supply with the activity of the different organs. General and broadly distributed activity of the constrictors produces increase of general blood pressure, of the dilators decrease of pressure, but local activity of either set will produce a great reduction or increase of blood in the local organ with little or no effect on the general pressure. When a vaso-dilatation is produced locally in one organ and there is an accompanying vaso-constriction in other regions, as usually happens, it is evident that the result may be a flooding of the local region. This is exactly the thing that is accomplished in the muscles in violent exercise, in the glands during secretion, in the stomach during digestion. It is this mechanism that is utilized to throw a large volume of blood to the skin when the temperature of the body is above the average, or to blanch the skin when the temperature is low.

Normally, certain regions of the body are associated in that when vaso-dilatation occurs in one region, vaso-constriction occurs in the other. This is particularly true with the skin or surface of the body and the viscera or deeper organs. The same relation is said to exist between some of the visceral organs.

General Course of the Vaso-constrictor and Vaso-dilator Nerves. The cell bodies forming the medullary vaso-motor center give off axones, axis-cylinder processes, some of which go to the nuclei of origin of certain cranial nerves, while others pass down the cord to end at different levels in contact with certain cells, probably small cells in the anterior horn and lateral part of the gray matter. These cells constitute the spinal centers. The neuraxones of the spinal cells leave the cord in certain spinal nerves in the anterior roots, pass by the white rami to the sympathetic ganglion chain, where they end in physiological connection with the ganglionic cells. Axones from these latter cells pass by an uninterrupted course to their terminations on the blood-vessel walls. The vaso-constrictor fibers leave the central nervous axis by the ventral roots of all the dorsal nerves and the first two lumbar roots, a comparatively restricted region. The vaso-dilators have the same origin with two exceptions, viz., the vaso-dilators of the salivary glands found in the seventh and ninth cranial nerves, and the nervi erigentes, which arise in the roots of the second and third sacrals. The nerves to the viscera pass direct to their blood-vessels, but the vascular nerves for the skin,

muscles, limbs, etc., rejoin the main divisions of the spinal nerves through the gray rami, see figures 417 and 418, and pass to the blood-vessels along with the general nerves of the organ or organs.

VASO-CONSTRICTOR AND VASO-DILATOR NERVES FOR INDIVIDUAL ORGANS.

The particular paths for the vaso-motor nerves has been pretty definitely established by numerous researches, especially by those of Langley and his students.

The course of the vaso-constrictor and the vaso-dilator nerve fibers has been followed satisfactorily in many of the important parts of the body, though the supply for some regions is yet obscure. This is particularly true for the brain, where such supply is apparently absent. The two groups of fibers run the same course, except in the cephalic and sacral regions already mentioned. They may, therefore, be described together.

The Vascular Nerve Supply for the Head. The vascular nerves for the head, face, and mouth have their origin in the cord from the first to the fifth dorsal spinal nerves. They pass through the white rami to sympathetic ganglia, through the stellate ganglion and up the cervical sympathetic nerve to the superior cervical ganglion. From this ganglion they run to their distribution, either along with the arteries, as with the salivary supply, or with the sensory nerves, as in the nerves to the mucous membrane of the mouth, etc. The vascular nerves supplied to the base of the ear follow the above course, but the nerves for the tip leave the stellate ganglion in the ramus vertebralis, run to the third cervical nerve, and pass with its auricular branch to the ear, a circuitous route determined by Fletcher.

The great exception to the above origin is with the vaso-dilator group. Dilator fibers leave the base of the brain in the direct path of the seventh cranial nerve to supply the submaxillary and sublingual glands, in the ninth cranial nerve to the parotid gland, and in both these to the tongue.

The Vascular Regulation in the Brain. The brain requires a large and uniform supply of blood for the due performance of its functions. This object is effected through the number and size of its arteries; the two internal carotids, and the two vertebrals. It is also desirable that the force with which this blood is sent to the brain should be subject to less variation from external circumstances than it is in other parts, an effect that is accomplished by the free anastomoses of the large arteries in the circle of Willis. This arrangement insures that the supply of blood will be uniform even though it may be limited through operation or accident to one or more of the four principal arteries. Uniformity of supply is further insured by the arrangement of the vessels in the pia mater. Previous to their distribution to the substance of the brain the large arteries break up and divide into innumer-

able minute branches. These capillaries after frequent communication with one another enter the brain in a very uniform and equable distribution. The arrangement of the veins within the cranium is also peculiar. The large venous trunks or sinuses are formed so as to be scarcely capable of change of size; and composed, as they are, of the tough tissue of the dura mater, and in some instances bounded by the bony cranium, they are not compressible by any force which the fulness of the arteries might exercise through

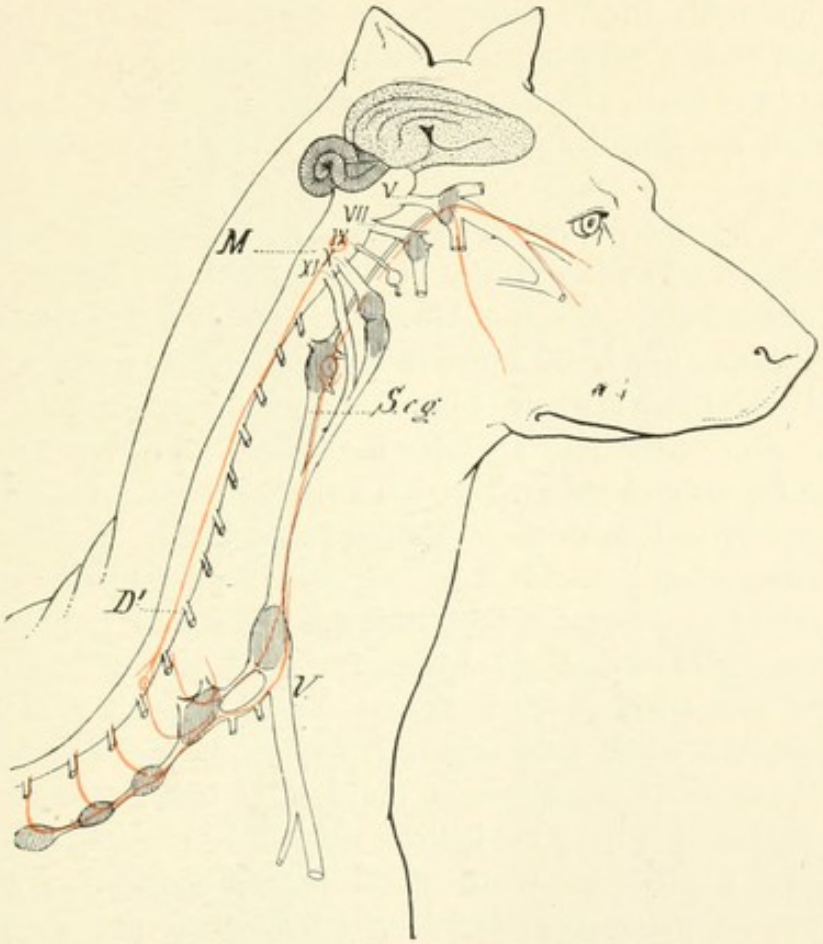


FIG. 208.—Showing the Origin and Course of the Vascular Nerves for the Head. (Modified from Moret.)

the substance of the brain. Nor do they admit of distention when the flow of venous blood from the brain is obstructed.

The mechanical conditions in the brain and skull formerly appeared enough to justify the opinion that the quantity of blood in the brain must be at all times the same. But it was found that in animals bled to death without any aperture being made in the cranium, the brain became pale and anemic like other parts. And in death from strangling or drowning, there was congestion of the cerebral vessels; while in death by prussic acid, the quantity of blood in the cavity of the cranium was determined by the position in which the animal was placed after death, the cerebral vessels being congested when the animal was suspended with its head downward, and com-

paratively empty when the animal was kept suspended by the ears. Thus although the total volume of the contents of the cranium is probably nearly always the same, yet the quantity of blood in it is liable to variation, its increase or diminution being accompanied by a simultaneous diminution or increase in the quantity of the cerebro-spinal fluid. The cerebro-spinal fluid being readily removed from one part of the brain and spinal cord to another, and capable of being rapidly absorbed and as readily effused, would serve as a kind of supplemental fluid to the other contents of the cranium to keep it uniformly filled. Although the arrangement of the blood-vessels insures to the brain an amount of blood which is tolerably uniform, yet with every beat of the heart, and every act of respiration, and under many other circumstances, the quantity of blood in the cavity of the cranium is constantly varying.

The brain, however, is entirely dependent upon the general blood pressure for variations in the quantity of blood which it receives. During a high blood pressure the amount of blood that flows in a given unit of time is greater and during low blood pressure less. Howell has shown that in the decapitated dog's brain the flow of blood is directly proportional to the difference in pressure. Numerous attempts have been made to show vaso-motor mechanisms for the cerebral arteries, but without success. Huber has shown nerve endings in such arteries by histological methods. Bayless, Hill, and Gulland make the statement that "no evidence has been found of the existence of cerebral vaso-motor nerves, either by means of stimulation of the vaso-motor center or central end of the spinal cord, after division of the cord in the upper dorsal region, or by stimulation of the stellate ganglion, and that is to say the whole sympathetic supply to the carotid and vertebral arteries." Vaso-motor regulation of the flow of blood through the brain can be accomplished only by the indirect mechanism of regulation of general blood pressure through variations in the heart's activity, or through the effects of vaso-constrictions or dilatations in large areas other than the brain.

The Vascular Nerves for the Thoracic Viscera. Numerous efforts have been made to determine the vaso-motor nerve supply for the thoracic organs, the heart and lungs. In the heart the observation is rendered complex by the fact of the rhythmic contractions which produce mechanical pressure on the coronary arteries. Martin, by direct observation through a lens, and Porter, by measuring the outflow of the coronaries upon vagus stimulation, came to exactly opposite views; the former that the vagus contained vaso-dilators, the latter that it contained vaso-constrictors. Still other experiments have been made to prove either constrictor or dilator nerves for the coronary arteries.

The lesser circulation through the lungs has also proven a difficult situation to interpret as regards any nervous regulation of the pulmonary arterioles. The evidence, while not conclusive, is that the vaso-constrictor supply to the

lungs is from the third to the fifth thoracic nerves, but that the vaso-constriction produced is slight in comparison with regions of the systemic circulation.

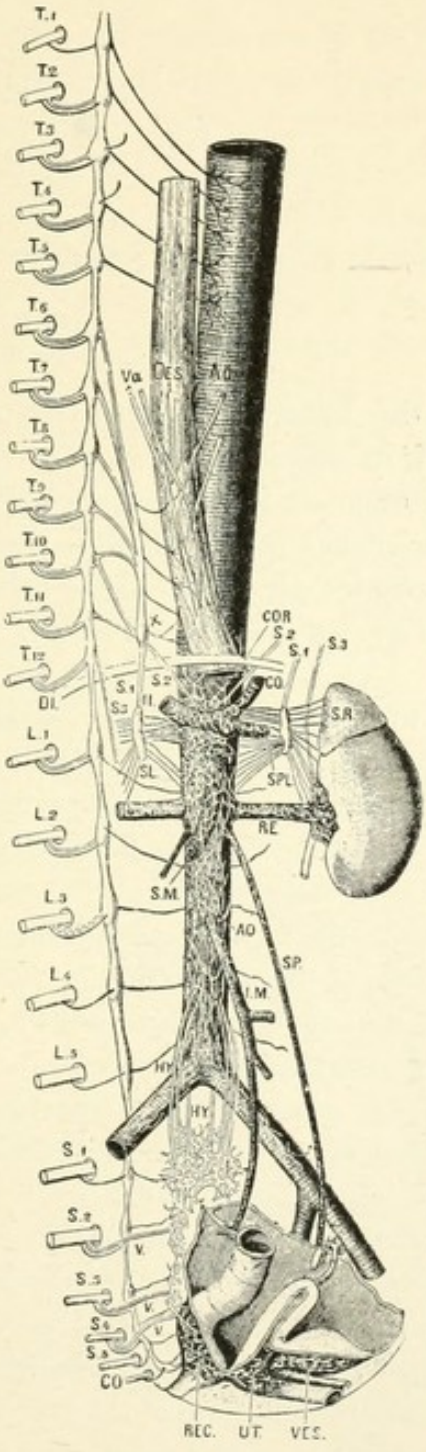


FIG. 209.—Arrangement of the Sympathetic System for the Lower Thorax, Abdomen, and Pelvis of Man. T 1-12; L 1-5; S 1-5: *Co*, Anterior primary divisions of the spinal nerves, connected to the gangliated cord of the sympathetic by rami communicantes, white (double lines) and gray (single lines); *Oes*, esophagus and esophageal plexus; *Ao*, aorta and aortic plexus; *Va*, vagus nerve joining esophageal plexus; *S* 1st, Great splanchnic nerve; *X*, great splanchnic ganglion; *S* 2, small splanchnic nerve; *S* 3, least splanchnic nerve; *Co*, coronary artery and plexus; *Spl*, splenic artery and plexus; *H*, hepatic artery and plexus; *S L*, semilunar ganglion; *Di*, diaphragm; *S R*, suprarenal capsule; *Re*, renal artery and plexus; *S M*, superior mesenteric artery and plexus; *Sp*, spermatic artery and plexus; *I M*, inferior mesenteric artery and plexus; *Hy*, hypogastric nerves and plexus; *Rec*, rectal plexus; *Ut*, uterine plexus; *Ves*, vesical plexus; *V V V*, visceral branches from sacral nerves.

The Vascular Nerves for the Abdominal Viscera. The vaso-constrictors and the vaso-dilators for the organs of the abdominal cavity have a broad origin in the cord; from the first dorsal to the fourth lumbar in the dog and cat. The nerves pass to the organs by the splanchnic nerves,

and by the solar, celiac, and mesenteric ganglia. The vascular nerves for the different organs may be given in tabulated form:

Vascular Nerves for the Abdominal Viscera.

Organ.	Spinal Origin of the Vascular Nerves.	Course to the Organ.
Stomach and intestine.	5, 6, 7, 8, **9, 10, 11, 12,** 13 D, 1 L	Splanchnic nerves and solar and celiac ganglia.
Spleen	3, 4, 5, **6, 7, 8,** 9, 10, 11, 12, 13 D, 1 L	Splanchnic nerves and solar and celiac ganglia.
Liver	3, 4, **5, 6, 7, 8, 9,** 10, 11 D	Splanchnic nerves and solar and celiac ganglia.
Kidney	4, 5, 6, 7, 8, 9, 10, **11, 12, 13** D, 1, 2, 3, 4 L	Splanchnic and celiac ganglia.
Pelvic viscera	**1, 2, 3, 4** L	Inferior splanchnic and inferior mesenteric ganglia.

The Vascular Nerves for the External Genital Organs. The vasodilators for these organs arise from the second and third sacral nerves and pass to the organs by the nervi erigentes and the pelvic plexus. They form the second great exception to the region of general outflow of vascular nerves. The constrictors, on the other hand, arise in the spinal nerves from the last dorsal and first four lumbar. They run the same course as given in the table for the pelvic viscera.

The greatest variations in the quantity of blood contained at different times in the external genital organs are found in certain structures which contain what is known as *erectile tissue*. These organs, under ordinary circumstances, are soft and flaccid, but at certain times they receive an unusually large quantity of blood, become distended and swollen by it, and pass into the state termed *erection*. Such structures are the *corpora cavernosa* and *corpus spongiosum* of the penis of the male, and the *clitoris* in the female. The nipple of the mammary gland in both sexes, and, according to some authors, certain nasal membranes contain erectile tissue.

The corpus cavernosum of the penis, which is the best example of an erectile structure, has an external fibrous membrane or sheath. From the inner surface of the sheath numerous fine lamellæ project into the cavity, dividing it into small compartments, like cells when they are inflated. Within these cells there is a plexus of veins upon which the erectile property of the organ mainly depends. The plexus consists of short veins with very close interlacings and anastomoses with very elastic walls admitting of great variations in size. They collapse in the passive state of the organ, but are capable of an amount of dilatation which exceeds beyond comparison that of the arteries and veins which convey the blood to and from them. The strong fibrous tissue lying in the intervals of the venous plexuses, and the external fibrous membrane or sheath with which it is connected, limit the distention of the vessels and give to the organ its condition of tension and firmness. The same general condition of vessels exists in the corpus spongiosum urethræ,

but the fibrous tissue around the urethra is much weaker than around the body of the penis, while around the glans there is none. The venous blood is returned from the plexuses by comparatively small veins; all of which are liable to the pressure of muscles when they leave the penis. The muscles chiefly concerned in this action are the erector penis and accelerator urinæ. Erection results from the distention of the venous plexuses by a sudden influx of blood resulting from the action of the nervous vascular reflexes. It is facilitated by the special muscular mechanism which prevents the outflow of blood.

The Vascular Nerves for the Trunk and Limbs. The skin and muscles of the trunk receive their cutaneous and motor nerves by a segmental arrangement in which the innervation is by bands corresponding

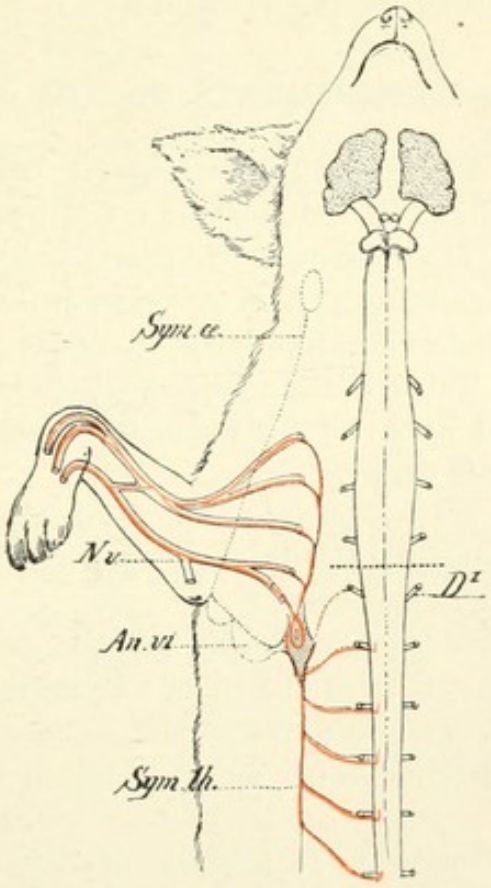


FIG. 210.—Plan of Distribution of Vaso-constrictor Nerves for the Fore Limbs. *An. vi.* Annulus of Vieussens. (Modified from Moret.)

with the segments of the cord and the spinal nerves. It is much the same with the vascular nerves; they are distributed to the skin and walls of the trunk in the same segment in which they arise. Langley says that the successive bands overlap somewhat.

In the fore legs or arms the vascular nerves arise from the first to the fifth dorsal spinal nerves, run to the stellate ganglia, then by the gray rami

back through the ramus vertebralis to join those cervical nerves that enter into the brachial plexus, figure 210.

The nerves for the blood-vessels of the lower limbs arise from the tenth dorsal to the second lumbar nerves. These pass to the ganglionic chain, and gray rami are given off which join the lumbar plexus and run with the divisions of that nerve complex to their distribution in the skin and muscles. Vaso-constrictors and vaso-dilators have a common course to the lower limbs.

The Vaso-constrictor Nerves for the Veins. Mall has proven that vaso-constrictors are present for the portal vein. These fibers are present in the splanchnic nerves. Other evidences have been observed which render the view probable that vaso-motors for the veins in general exist. Hough, for example, in an extended study of the capillary pressure found many variations which were readily explained only on the assumption of veno-motor activity, see figure 201.

LABORATORY EXPERIMENTS ON THE CIRCULATION.

1. **The Rate of the Human Heart-beat.** Determine the rate of the heart-beat per minute by counting the radial pulse, using a watch for the time. Make the determination after sitting quietly in a chair for five minutes. Take the average of at least ten determinations for your own case. Determine the heart-rate under the same conditions for as many different persons as you can. Tabulate these determinations in a table which shows age, sex, weight, and height of the different individuals, and compute a general average for your entire set.

Note the effect on the averages obtained above after the person lies down for five minutes, after standing quietly for the same time, and after five minutes' brisk walk. Tabulate as directed.

Count the heart-rate *immediately* after two minutes' fast running, allowing the person immediately to sit in a chair. Count the rate by two minutes until there is a complete return to the normal, as determined above. Tabulate these results and compare the figures obtained from several different individuals.

Count your own heart-rate at intervals during one entire day, giving special attention to the rate just before and just after meals, but in every case make the count after sitting quietly for five minutes. A marked diurnal variation will usually appear. Determine these rates on several individuals, and tabulate as before.

2. **Human Cardiogram.** Apply a Burdon-Sanderson cardiograph to the thorax over the point between the fifth and sixth ribs of the left side, at which point the cardiac impulse is felt most distinctly. Connect the cardiograph with a recording tambour, Marey's form, adjust the tension of the cardiograph and the pressure of the air within the system, and take a

tracing of the movements of the lever of the recording tambour on the smoked paper of the kymograph. The kymograph cylinder should travel at the rate of about two to three centimeters per second. Take the time of the movements of the kymograph by means of an electric magnet connected with an electric clock beating seconds. After the record is secured the proper description should be written with a pencil on the smoked paper, and the paper removed from the kymograph carefully and the whole record fixed in shellac.

When the record is dry, count the rate of the heart-beat from the record and measure the time of the cardiac systole and diastole, and the time of pause at the end of the diastole. If these facts are taken from records secured under different conditions of exercise, etc., as outlined in the preceding experiment, then they may be brought together in a table for convenience of inspection. A comparison of such results will usually show that with the higher heart-rates the decrease of the time of the cardiac cycle is at the expense of the time of the diastole; in other words, the time of the systole remains fairly constant while the time of the diastole increases or decreases with the rate, a fact to which Hürthle has drawn attention, figure 157.

3. **The Rate and Sequence of the Contractions of the Frog's Heart.** Destroy the brain of the frog and open the thorax, but do not destroy the pericardium. Count the rate of the heart per minute, then

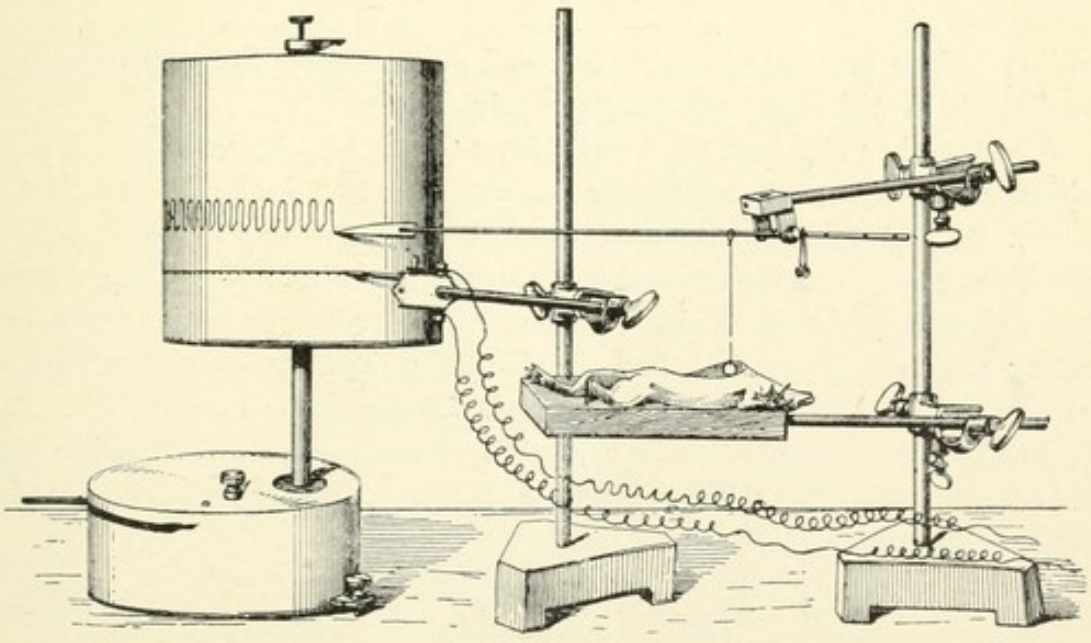


FIG. 211.—Heart Lever for Frog or Turtle Hearts.

remove the pericardium and make a second determination after the heart is exposed to the air. The different parts of the heart when exposed are easily identified and the contractions which take place in definite sequence can be determined without difficulty. Make this determination for the ventricle, auricle, and sinus venosus by direct observation.

Prepare a cardiac lever as shown in figure 211, taking special care to arrange the foot so that it will not bind on the lever when in motion. Adjust the foot of the lever on the exposed ventricle and bring its point to write on the smoked paper of a recording cylinder. This cylinder should travel at the rate of about 1 cm. per second and its speed be determined by the writing point of an electric magnet which is connected with the electric-clock circuit marking seconds. Take care to adjust the time magnet in a vertical line with the writing point of the heart lever, placing the heart lever about 1 cm. above the magnet lever. The tracing of the ventricle's movement, or *cardiogram*, will show alternate contraction, relaxation, and pause of the ventricle. It will also enable one to measure the exact proportion of the total time of the

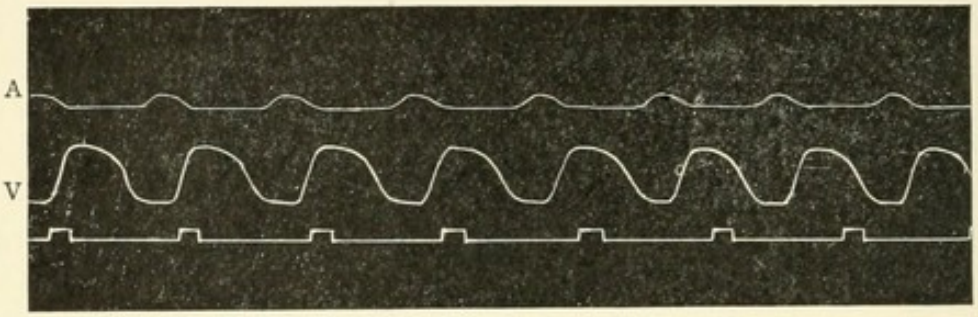


FIG. 212.—Cardiogram Showing Contractions of the Auricle, *a*, and Ventricle, *v*, of a Frog. Time in seconds. The record shows the sequence of the auricle and ventricle. (New figure by Dooley.)

cardiac cycle consumed by the systole and diastole, and also that portion of the diastole in which the ventricle is wholly at rest.

After one has obtained the ventricular tracings and has learned the difficulties of adjusting the apparatus, a second heart lever should be adjusted so that its foot rests upon the auricle, and the auricular movements may therefore be traced on the smoked paper of the recording cylinder at the same time as those of the ventricle. If some care is taken to adjust these two writing points in a vertical line a splendid tracing showing synchronism between auricle and ventricle is obtained. Measure the rate and the time of the different phases of the contraction of the auricle and ventricle and tabulate them in the following form, always expressing fractions in the decimal system:

	Rate per Minute.	Time of Systole in Seconds.	Time of Diastole in Seconds.	Time of Pause in Seconds.
Auricle.....				
Ventricle.....				

4. **The Contractions of the Excised Heart of the Frog.** Pith a frog and expose the heart, as described in the preceding experiment. Re-

move it completely from the body by first cutting the arteries at their branching in front of the bulbus arteriosus, then carefully lifting up the parts of the heart and cutting away the great veins where they enter the sinus. This will remove the entire heart, including all its contractile parts. The frog's heart when thus removed and still wet with its own blood will continue contracting rhythmically and in its natural sequence for some hours. Place such an isolated heart in a watch-glass and take a record of its contractions, by the apparatus described in the preceding experiment.

Set this watch-glass on the metal warming-box supplied, and arrange for the circulation of water of different temperatures through the box. Vary the temperature of the box, and therefore of the heart placed upon it, by allowing water of 0° C., 10° C., 20° C., 30° C., 40° C. to flow through it. Record the contractions of the heart at each of these temperatures on the recording drum as described in experiment 3 above. The heart being exposed will not take the same absolute temperature as the box, but the relative temperature will be decreased or increased. Tabulate the rates at these different temperatures by the plan previously described.

5. **The Influence of Different Nutrient Fluids on the Excised Heart.** Expose a frog's heart, as previously described, and insert a cannula into the ascending vena cava just where it enters the sinus. Ligate the descending vena cava, introduce a cannula into one of the branches of the aorta, and carefully separate the heart from the body without injuring its cavities within the points of ligature. Or the ligatures may be laid and the cannulæ inserted without separating the heart from the body. Connect the venous cannula with a Mariotte's bottle filled with physiological saline, 0.7 per cent sodium chloride. Adjust the constant level tube for a pressure of 6 cm. of fluid and allow the saline to flow through the heart. The arterial cannula should be connected with a short rubber tube the mouth of which allows the fluid to flow into a beaker or glass tumbler. The outlet of the arterial tube should be about 2 cm. above the level of the heart so that the heart must work against a slight pressure. The heart will continue its contractions in good sequence and with a fairly rapid rate. Record the contractions on the smoked paper of the recording drum, together with a time tracing in seconds, the drum traveling at the rate of about 2 to 5 mm. per second.

Use the tracing obtained under the influence of *physiological saline* solution as a normal and compare with it the rate and amplitude of the contractions when the heart is perfused with *Ringer's* solution; with *Locke's* solution; with *saline* and *potassium* in the proportion found in Ringer's solution; with *saline* and *calcium* in the proportion found in Ringer's solution; with *milk* diluted 6 vols. with saline; with normal *serum* or blood; with *blood* or serum diluted four times with saline. Tabulate the rates and amplitude of the heart under these different influences by the method previously followed.

6. **The Heart Volume.** Isolate a frog's heart by the method de-

scribed for irrigating it with fluid in the preceding experiment. Connect it up in a Roy's tonometer, see figure 213, adjust the lever of the tonometer for a tracing on the smoked paper of the recording cylinder. Use a time-marker. This instrument records the change in volume with each heart

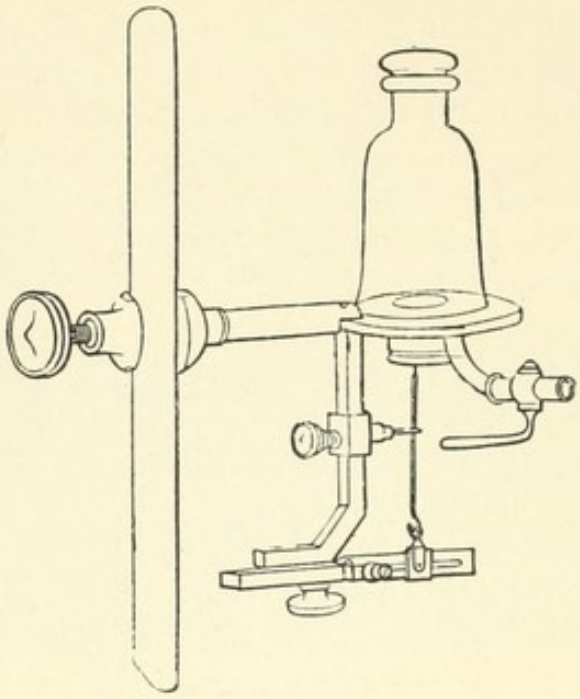


FIG. 213.—Roy's Tonometer.

contraction. The influence of pressure, varied between 2 and 10 cm., and of nutrient fluids on the heart volume may be determined.

7. **The Isolated Heart of the Terrapin.** The heart of the terrapin, being somewhat larger and somewhat more responsive than the heart of the frog, may be substituted in the two immediately preceding experiments. The facts obtained from it will be essentially the same as those obtained from the frog's heart.

8. **The Isolated Mammalian Heart.** The mammalian heart may be isolated from the body and kept alive and contracting for many hours, as has been demonstrated by numerous recent observations. It is only necessary to keep the temperature approximately that of the normal body and to irrigate the heart through the coronary circulation with blood, or diluted blood, containing sufficient hemoglobin to supply the heart with the requisite amount of oxygen. Or, the heart may be kept alive on the inorganic salt solutions, provided these are supplied with oxygen under considerable tension (Porter, Howell). Even the human heart has been isolated and kept contracting for some hours in the above manner (Kuliabko). The method used is to insert a supply cannula into the aorta and irrigate the heart through the coronary circulation, as described by Langendorff. Many interesting experiments and demonstrations can be made on the mammalian

heart, but, as this experiment is usually a demonstration experiment, the detail of procedure is left to be supplied by the demonstrator.

9. **Automatic Contractions of the Cardiac Muscle.** Isolated portions of the dog's ventricle have been kept in rhythmic contraction by Porter, but the best laboratory material is supplied by the heart of the terrapin. Cut a strip from the ventricle of the terrapin extending around its curved apex, as shown by the dotted line in the accompanying figure, 214. Split this strip longitudinally into two parts, each of which will then be about 3 to 5 mm. in diameter. Use care to cut smooth, straight strips. Tie a silk thread around the extreme tips of each end of the strip, tying a loop of about 1 cm. long at one end, and about 10 cm. long at the other. Suspend the strip over a glass hook, figure 215, by the short loop, and connect it with a heart lever by the long loop, as shown in the same figure. Use a tension of one gram. Contractions of this strip as arranged will be recorded with a magnification of about five and with the upstroke of the lever, which is convenient

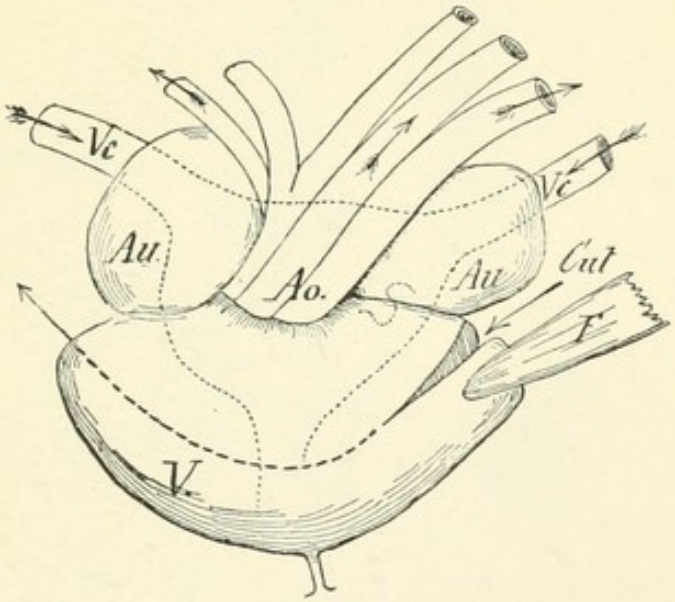


FIG. 214.—Heart of the Terrapin to Show the Method of Cutting the Apex Strip. *V*, Ventricle; *Au*, auricles; *Vc*, venæ cavæ; *Ao*, aorta.

for reading and interpretation. The strip may be kept moist with physiological saline in a specimen tube of about 1 by 3 inches in size, and the arrangement of apparatus figured makes it possible easily and quickly to change this solution for any other that may be desirable.

Contractions of the ventricular strip in saline usually begin in from 10 to 40 minutes after the preparation is made and go through a regular sequence of slight increase in rate and amplitude for from 10 to 20 minutes, followed by a very constant rate, but gradually decreasing amplitude for a period of from 2 to 3 hours, figure 171.

This preparation makes possible many instructive experiments tending to show fundamental properties of cardiac muscle. The preparation con-

tains no nervous mechanism and its behavior may be safely attributed to the muscle substance itself.

Try the following experiments: Submit the strip to saline solutions of different temperatures, varying through steps of 5 degrees from 0° C. to 40° C. Try the effect of the different ingredients in Ringer's solution; combine potassium with saline, figure 172; calcium with saline, figure 173; and potassium, calcium, and saline. Also try Locke's solution; solution of blood diluted with saline; solution of milk with saline in the proportion of one part milk to four of saline.

Cut and mount strips from the auricle and from the sinus, letting the latter extend out on to the vena cava. In these last preparations care must be taken to balance the lever, as a slight overtension paralyzes the muscle. Immerse these strips in pure serum, compare their behavior

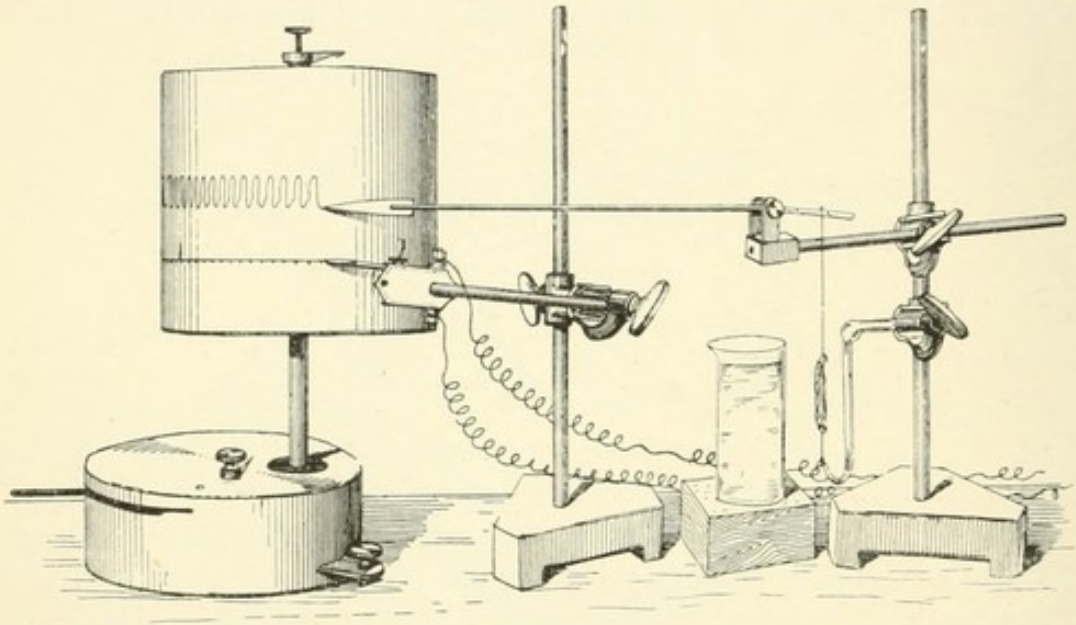


FIG. 215.—Arrangement of Apparatus for Studying the Contractions of the Strip of the Apex of the Ventricle.

with that of the ventricle in pure serum. The sinus and usually the auricle will be found rhythmic in serum, while the ventricle, if it contracts at all, will contract with a very slow rhythm. Often there is a distinct progressive decrease in the rhythm, the sinus having the same rhythm as the whole heart, the auricle a considerably slower rhythm, and the ventricle with a very slow rhythm or even quiet. The sinus preparation will show beside the fundamental rhythm a characteristic slow contraction and relaxation, which has been described as tone, figure 170.

10. **Influence of the Cardiac Nerves on the Frog's Heart.** Carefully pith a frog so as not to break the blood-vessels at the base of the brain, and thus permit the loss of the blood of the animal. Expose the heart as previously described, make a cut through the manubrium, continue it through

the skin and muscles, at the angle of the jaw, thus exposing the vagus nerve. The vagus runs diagonally downward and backward along the edge of the delicate muscle toward the heart. The glossopharyngeal is just in front of the vagus and the hypoglossal just behind it. The latter runs parallel with the vagus near its origin, but lower down turns across the vagus and runs to its distribution in the tongue muscles. These two nerves serve to aid the student in the identification of the vagus, see figure 216. It is usually better to cut the hypoglossal away, and also to cut the brachial and the laryngeal nerves.

Prepare an induction coil, see Laboratory experiments on muscle. Use platinum electrodes of the Harvard pattern, set the coil for a mild stimulus when tested by the lips or the tongue, lift up the vagus gently and lay it on the platinum tips of the electrodes, taking care that the electrodes do not come in contact

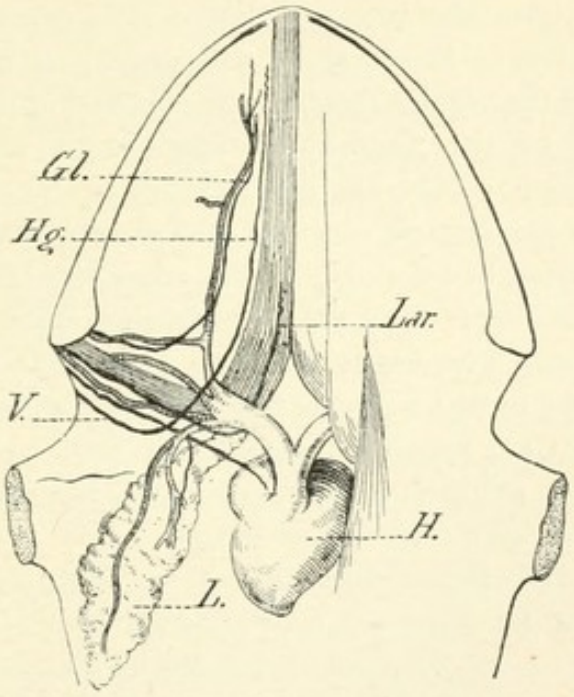


FIG. 216.—Diagram Showing the Relations of the Vago-sympathetic Nerve to the Heart, in the Frog. *Hy*, Hypoglossal; *Gl*, glosso-pharyngeal; *Lar*, laryngeal; *V*, vago-sympathetic; *H*, heart; *L*, lung.

with the adjacent tissue. Arrange a signal magnet as shown in the diagram, so that the signal magnet and the stimulating key of the induction coil may be closed and opened at the same instant. When all is ready stimulate the vagus for five to ten seconds, recording the time with the signal magnet and allowing the record to continue until the heart has returned to its normal rate and amplitude. Most students fail in this experiment by not allowing sufficient time in the record for a normal before stimulation, and by not allowing sufficient time after stimulation for a return to the normal. It will be better to take one good tracing, showing the facts of the experiment, than several partial tracings, none of which are complete. With these sugges-

tions in mind, repeat the above experiment, using stimulating currents of increasing intensity until complete cardiac inhibition is produced. Perform experiments showing the influence of the time of the stimulus on the inhibition, *i.e.*, stimuli of 1 second, 2 seconds, 10 seconds, and 30 seconds.

In the frog the vagus or inhibitory, and sympathetic or accelerator fibers, are found in one trunk, the vago-sympathetic, but the stimuli will usually produce inhibitions and not acceleration. Occasionally with very weak preparations direct acceleration may be produced. To get the pure inhibitory or pure accelerator effects one must dissect back to the origin of the vagus before it is joined by the sympathetic fibers; or to the sympathetic trunk between the third spinal nerve and the point where it joins the vagus trunk. In the study of the conditions in the above experiments one should note the rate per minute and the amplitude in the normal, the period just before stimulation, the rate and amplitude during the period of stimulation, and the same at different times after the stimulation until constant results are obtained. A tabulation of these results will usually enable one to judge the influence of each of the various factors recommended in the experiment.

11. **Influence of the Cardiac Nerves on the Terrapin's Heart.** Instead of the frog one may use the terrapin in the above experiment. In this animal the sympathetic can very readily be isolated, and accelerator fibers have been described for it. In the experience of the laboratory of the author no experiments have yet demonstrated unquestionable cases of cardiac acceleration. The vagus produces inhibitions which differ from the effects in the frog in that complete inhibitions of the ventricle are followed by contractions that are apparently at once maximal. In the frog the contractions when they reappear are at first slight, but gradually increase in amplitude until they have their former value.

12. **The Arterial Blood Pressure in a Mammal.** The arterial blood pressure may be measured on the anesthetized cat, dog, or rabbit. Simple blood pressure was originally measured by Hale's method of connecting the artery with a vertical tube and allowing the blood to flow freely into the tube until a column was raised to the height which balanced the pressure in the vessel. This simple method is decidedly the best for the beginner, since it does not necessitate the use of very complicated apparatus. At the same time it gives practice in anesthesia and in operations of vivisection, and therefore serves as a good preparation for the more complicated experiments which follow.

The necessary apparatus should be prepared first, as follows: A vertical tube supported on a stand with a scale graduated in the metric system, assorted cannulæ of approximately the size of the carotid artery of the animal to be operated on, linen thread ligatures, dissecting set in good condition, an animal-holder with strings or straps firmly to fasten the anesthetized animal, a chloroform-ether mixture for dogs (or other anesthesia according

to the animal to be used). Four men should be assigned to perform this experiment. While two are anesthetizing and preparing the animal, two should arrange the apparatus as nearly ready for connecting with the artery as possible. When all the apparatus is arranged and the animal anesthetized, it should be tied firmly to the animal-holder. *Let one experimenter attend strictly and at all times to anesthetizing the animal; recovery from the anesthesia must not occur.* Let the *operator* quickly expose about 3 cm. of the carotid artery by making an incision through the skin of the neck 5 cm. long, and dissecting down between the muscles. Separate the carotid from the adherent vagus nerve by tearing the connective tissue with the scalpel handle, freeing the vessel from about 2 to 3 cm. of its length. Lay two loose ligatures of linen thread around the vessel, place a small bulldog forceps on the exposed artery nearest the heart, and ligate the end nearest the head with one of the ligatures. Take up the intervening artery with strong forceps and make a V-shaped cut near the ligature, pointing the cut toward the heart, and letting it extend about half way across the artery. Introduce a cannula through the opening toward the heart, and tie it firmly with the second ligature. Connect the cannula with the rubber tubing to the vertical glass tube.

When all is ready remove the bulldog forceps on the artery, following which the blood will flow freely from the artery into the tube until the pressure from the column of liquid is just equal to that inside the artery itself. If an anti-coagulating fluid, 10 per cent magnesium sulphate, is first introduced into the vertical tube of fortunate height little blood will be lost and probably clotting at the cannula will be delayed for some minutes. The mounting of the blood into the empty tube makes indeed a more striking demonstration, but it has the disadvantage of quickly forming a clot which stops the experiment itself.

An accurate measure of the height of the top of the column above the level of the cannula at the artery represents the arterial blood pressure in terms of blood, or of 10 per cent magnesium sulphate. The specific gravity of magnesium sulphate is 1.030; of blood 1.056; of mercury 13.6. Record the pressure you obtain in terms of blood and of mercury. Note also the variations in pressure and account for the rhythm of each. There will be a general variation of pressure, depending upon the degree of anesthesia. If anesthesia is light and muscular movements happen, there will be an increase in the blood pressure. If the anesthesia is heavy, then the blood pressure falls. These points of variation should be marked, or recorded at once in note-books. Make full notes of all accessory facts which would aid you to explain the variation in blood pressure, such as size of the animal, rate of respiration, rate of heartbeat, the variations in anesthesia, the presence of the reflexes, etc., etc.

Chloroform the animal to kill it, and note the change in blood pressure during the process

13. **The Circulation Time.** The circulation time is most satisfactorily determined in the laboratory by introducing a saline solution of methylene blue into the jugular vein on one side. Note directly the time with a stop-watch until the color appears in the jugular artery and the jugular vein of the opposite side.

Anesthetize a cat or dog with a chloroform-ether mixture, tie it on the animal-holder and, when the eye reflexes are lost, expose the jugular vein on the right side, the carotid artery and the jugular vein on the left. Fill a 2-cm. hypodermic syringe with 1 per cent methylene blue in physiological saline, insert the needle into the right jugular vein, pointing it toward the heart. Lift the left carotid artery and place under it a strip of moist white paper 2 cm. wide; prepare the left jugular vein in the same way. Place the animal so that these vessels are lighted to the best advantage. At a given moment inject the contents of the hypodermic syringe, noting the time with a stop-watch. Observe the color of the left carotid and the left jugular, respectively, very carefully, and take the time when the first appearance of the methylene blue is noted. The color will appear first in the artery, second in the vein. The difference in time between the moment of injection and the moment of color in the artery represents, with a slight correction, the circulation time of the pulmonary or lesser circulation. The time from the injection until the color in the jugular vein represents the total time of circulation.

Stewart has made these determinations even more correctly by the electrical-resistance method. He injected 10 per cent salt solution and determined the variation in resistance by a galvanometer. If the galvanometer is available, then check the above determinations by the electrical method, arranging the apparatus under the direction of an instructor.

14. **The Blood-Pressure Model.** An artificial model of the circulatory apparatus, which illustrates all mechanical parts involved, has been arranged by Porter, figure 217. Other forms, which show these as well, are usually available or can be easily constructed. The model should have the following possibilities: A pump, which permits of rhythmic action at a varying rate and varying force; a resistance to the outflow liquid, which can be increased or decreased; and an elastic set of vessels into which the pump discharges.

If Porter's schema is used, determine the following points: The pressure in terms of mercury in the arterial and venous limbs of the apparatus when the pump makes a rate of 72 per minute; the influence on these two pressures when the rate is increased, when it is decreased; the effect on these pressures when the peripheral resistance is great, when it is low. If a sphygmograph is available, take a tracing of the pulse in the elastic tube representing the arterial side of the schema.

If an ordinary bulb syringe and simple apparatus is used, then deter-

mine the following: The character and rate of the outflow when water is pumped into the rigid glass tube with no resistance to the outflow; when a glass tube of smaller caliber is connected with the end of the larger glass tube so as to produce a high resistance to the outflow. Pump the water into a rubber tube of smaller size and compare with the proceeding in which there is no resistance to the outflow; also when a glass tube of small caliber is introduced into the end in order to produce high resistance to the outflow. Determine the amount of resistance necessary to produce a constant outflow when the pump has a rate of 72 beats per minute. In this experiment what effect is produced on the outflow if you vary the rate of the pump? if you vary the force of the stroke? if you vary the elasticity of the rubber tube representing the artery? if you vary the resistance represented by the size of the glass tube at the outflow?

15. **The Arterial Pulse.** The form of the arterial pulse may be taken by one of the various sphygmographs applied to the radial artery at the wrist or the common carotid in the neck. If the tambour method is used, apply a sphygmograph tambour on the wrist with the central pressure over the radial artery. Fasten it in place by the proper bands, adjusting the tension by flexing the wrist. Connect the receiving tambour with a delicately balanced, small-sized recording tambour, which should write its movements on a cylinder revolving at the rate of 1 to 2 cm. per second.

A more convenient clinical instrument is the Dudgeon or the Jacquet sphygmograph. These are to be applied at the wrist and give tracings showing delicate variations in the form of the pulse wave with great magnification and a considerable degree of accuracy. Make a comparison of the form of the pulse wave from tracings taken from at least six different individuals.

The sphygmogram from the carotid artery may best be taken by applying a tambour sphygmograph to the neck over the carotid and fastening it in position, usually by a spring.

16. **The Rate of Propagation of the Pulse Wave.** Apply tambour sphygmographs to the carotid in the neck and to the radial at the wrist, and make simultaneous record on a recording drum, adjusting the writing levers of the two recording tambours in an *exact vertical line*. Let the recording drum travel at the speed of 2 cm. or more per second, and record the speed by a 50 double-vibration tuning-fork. The carotid pulse will be found to precede the radial pulse by the fraction of a second. This short interval, which can be determined in hundredths of a second by comparison with the time tracing below, represents the time required for the pulse wave to travel the distance from the carotid to the radial. Measure the distance on the individual used in the experiment and calculate the rate of propagation of the pulse wave in centimeters per second.

If the writing points of the recording levers in this experiment are made of very delicate strips of note paper, so as to offer little resistance to the surface of the drum, the detail of the pulse wave at the two points will be accurately transcribed and may be compared.

17. **The Capillary Circulation.** The capillary circulation is best demonstrated in the laboratory by direct observation on the web of the frog's foot by the use of the compound microscope. Give a 40-gram frog a hypodermic injection of 0.3 c.c. of ether under the skin of the back. Wet a piece of cheese cloth the size of a handkerchief with tap water and wrap the etherized frog so as to cover the entire body with the exception of the foot. When the anesthesia has progressed so as to destroy voluntary movements, bind the foot on an ordinary frog board and spread the web over the window in the board. Choose an area of the skin which shows small arteries, capillaries, and veins, and in which the blood is flowing freely and rapidly. Examine with a low-power compound microscope. In a favorable field small arteries, capillaries, and veins with blood flowing rapidly through them will be easily found. Choose one such field, cover with a piece of thin cover glass, moistening with a drop of water if necessary, and examine with a high power. Note in the small artery the pulsating current; the border of clear fluid along the side of the main stream of blood; the slight pulsations; and the white corpuscles that will be found flowing along the borders of the current. In the small veins there are usually no pulsations and the speed of the current is somewhat less. In the capillaries a careful examination will reveal a delicate wall, the individual corpuscles, and the fact that the red corpuscles are actually larger than the diameter of the capillary at some points and must be bent to pass through. Note that the capillaries form an intricate and anastomosing network; that the current may occasionally reverse itself in some of the anastomoses.

The anesthetizing effect of the dose of ether recommended will usually continue about 15 to 20 minutes. If the observation is more prolonged a second dose of ether should be given. The capillaries in the tails of small fish are often very readily observed and these may be substituted for the frog's web.

18. **Capillary Blood Pressure.** Measure the capillary blood pressure in your own finger by von Krie's method. This apparatus consists of a small piece of glass an inch square, or less, which is placed across the knuckle of the finger just back of the nail. A small weight pan is suspended by a loop of thread over this glass plate so that weights put in the pan will bring varying pressure on the plate above. Add weights to the pan until an area of the skin, about 5 mm. in diameter, is blanched by the pressure. Mark the outline of this bloodless area on the glass, take off the apparatus and measure the exact area of glass so marked, weigh the entire apparatus and compute the pressure per square centimeter for the area. This pressure in terms of mercury represents the capillary blood pressure in the vessels

of the skin of the finger at that level. Vary the experiment by measuring the pressure with the finger held at the level of the top of the head; with the finger held as low as possible; held at the level of the heart. Tabulate the measurements. The capillary blood pressure at the level of the heart is usually from 40 to 50 mm. of mercury.

19. **The Arterial Blood Pressure in a Mammal and Its Nervous Regulation.** After the student has measured the arterial blood pressure by Hale's method, described above, he is in a position to study the variations and coordinations in the blood circulatory apparatus. The recording apparatus consists of writing pens, seconds time marker, signal marker, blood-pressure manometer preferably Ludwig's mercury manometer, and a continuous paper kymograph preferably Ludwig's weight-driven form for a continuous record of the arterial blood pressure. Connect the cannula with the mercury manometer which is provided with a pressure bottle. Use a cannula of the form shown in figure 185, connecting the side limb of the cannula with the mercury manometer, and the end limb with the pressure bottle. When the apparatus is ready anesthetize a mammal (dog, cat, or rabbit), and bind it down to the animal-holder. *Let one operator attend strictly and at all times to the anesthetic, for the animal must not under any condition recover consciousness during the experiment.*

Expose the carotid artery in the neck, as described in experiment 12 above, arrange it with ligatures for inserting the cannula, expose the vagus nerve with the same care, and throw ligatures around it for convenience in lifting it out of its bed. Make in the carotid a V-shaped cut directed toward the heart, insert and ligate the cannula as previously described. Before beginning the experiment one should see that all the tubes are filled with the anticoagulating liquid and that the manometer is under pressure from 100 to 150 mm. mercury. When all is ready start the kymograph, ink the recording pens, see that they are recording properly and that the adjustments are secured, remove the bulldog forceps from the artery, and the pressure record begins.

1. Take a tracing of the normal arterial pressure and heart rhythm with the recording paper moving at the rate of 0.5 cm. per second.

2. Stimulate the vagus nerve with a mild-strength induction current. If this stimulus is strong enough to produce change in blood pressure or inhibitions of the heart rate, then allow sufficient time following the stimulus for the blood pressure to return to the previous normal. Observing these rules, vary the intensity of the stimulus from that which produces no apparent effect to that which produces complete inhibition of the heart. Vary the time of the stimulus from 1 to 10 seconds, using different strengths.

3. Allow the vagus to fall back in its warm bed and stimulate the skin of the animal at some sensory surface, say the lips, the ear, or the foot. By varying the intensity of the stimulus, a strength will be found which will

produce no reflexes of the voluntary muscles, but which will produce marked effects on the heart rate and on the blood pressure. Expose the sciatic nerve, or any other general nerve trunk, cut it, and stimulate the central end for 5 seconds. With a proper strength of stimulus a greater effect is produced on the heart and on the blood pressure than by stimulating a small spot of skin.

4. Cut the right vagus nerve and mark the exact time on the tracing by the signal marker. After 10 to 15 seconds cut the left vagus, marking the time of cutting with the same care on the tracing. As soon as the nerves are cut, the heart-rate will be observed to increase sharply and the blood pressure to rise. The respirations also change in rate and depth, a fact which can be noted on the blood-pressure tracing. Do not disturb the animal or record until stable equilibrium is again reached.

5. Now lift up the distal end of the divided vagus, and stimulate it with an electric current of the strength which previously just produced inhibition. Repeat the experiment on the proximal end of the divided vagus. The stimulation of the proximal end of the vagus produces no direct effect on the heart rate when both vagi are cut, but does produce profound changes on the blood pressure owing to vaso-motor effects.

6. If the rabbit is used, stimulate the depressor nerve, which produces marked fall in blood pressure from reflex effects.

7. Repeat the stimulation of the central end of the sciatic as described in 3, now that the vagus nerves are cut. The stimulation of this nerve no longer produces changes in the heart-rate, but the blood pressure is influenced as before, showing that the vaso-motor centers are reflexly stimulated.

8. When you have finished the outline of experiments, give an excess of the anesthetic to kill the animal and continue the record until the animal is dead. The blood pressure will fall rapidly, the heart-rate will become slower but does not cease for a long time.

Should a clot form in the cannula, put a bulldog forceps on the artery, disconnect the manometer tube, and wash the clot out by a stream of liquid from the pressure bottle. Use care not to allow this fluid to enter the exposed wound.

Represent the results of each individual experiment in the above series in tabulated form which shall show 1, the *blood pressure* and *heart rate* just before each experiment; 2, during the experiment; and 3, at different times after the experiment until the normal is reached. After the facts are taken from the tracings and arranged in tabular form, make a study of these facts and draw all the conclusions you can concerning the nervous regulations of the heart and of the blood pressure.

20. **Arterial Blood Pressure in Man.** The arterial blood pressure in man can be measured only indirectly by measuring the pressure which it takes around the arm completely to close the artery. Some form of the Riva-Rocci apparatus, preferably Erlanger's sphygmomanometer, should

be used. Adjust the rubber bag and leather sleeve of the Erlanger apparatus, figure 189, to an arm, and connect it to the sphygmomanometer, set the valve and quickly pump the pressure up to a point which occludes the pulse. Adjust the writing point of the recording tambour to the smoked paper on the cylinder, then lower the pressure by 10-mm. steps until the first pulse appears. Now proceed with care, changing the pressure by 5-mm. steps until a record has been obtained which passes the maximal amplitude. Now release the pressure from the arm. The first point in the decreasing pressure at which the pulse tracing begins to increase is known as the systolic pressure; the point in the pressure which records the highest point in the amplitude of the pulse wave is known as the diastolic pressure. The systolic pressure will vary from 120 to 150 mm. of mercury; the diastolic from 90 to 120 in different individuals of the average physiology class.

21. **The Vaso-motor Changes in the Finger, the Plethysmogram.** Insert the finger in the Porter finger plethysmograph, fill the tube with water, and connect it with a small-sized air tambour. The variations in volume of the finger are slight, so that one must use a rather long, delicately balanced recording lever. Take a tracing on a recording cylinder moving at a slow speed, 1 mm. per second. The finger and its plethysmograph should be supported by a swinging support so that no mechanical movements will destroy the accuracy of the record. Observations through several minutes will usually show variations in volume of the finger, which will be recorded by the tambour. Cold air in the face or cold water on the hand will usually be marked by a decrease in volume indicating vaso-constriction. Application of heat to other fingers of the same hand will lead to increase in volume.

22. **The Vaso-motors of the Frog's Web.** Prepare a frog for observation of the circulation of the web under the microscope, as described above; but give it just enough 1 per cent curari to destroy voluntary movements. Quickly dissect the sciatic nerve in the thigh, using extreme care not to interfere with the circulation. Mount the preparation, pick out an active field of capillaries, small arteries, and veins with the low power of the microscope, then adjust the high power to a field which shows one or more small arteries. Make a drawing of a diameter of these arteries, using pigment cells for land-marks. Now quickly stimulate the exposed sciatic nerve while keeping the selected artery under constant observation. After a short stimulation the diameter of the vessels will be seen to decrease considerably, sometimes to the point of complete occlusion. When the stimulation ceases, the vessel will remain contracted for a few seconds, then will slowly regain its usual caliber, figure 201. This is an exceptionally good method for direct observation of the vaso-motor changes in the smaller vessels.

23. **The Plethysmogram of the Kidney.** Anesthetize a dog or cat, see experiments 12 and 19 above, and take blood-pressure tracings on the con-

tinuous-paper kymograph. Now open the abdominal wall by an incision along the median line, expose the left kidney and carefully dissect off its capsule, taking care not to injure its artery and vein. Enclose the kidney in the renal onkometer, fill the onkometer with oil, and connect it with a recording apparatus. Brodie's bellows recorder is probably the best recording apparatus for this purpose. Adjust the recording apparatus in the vertical line with the manometer and signal pens.

Stimulation of the nerves which affect the general blood pressure through the medium of the heart will be found to produce changes in the volume of the kidney in the same direction as the blood-pressure change. On the other hand, stimuli which give variations of the blood pressure without direct change in the heart itself affect the volume of the kidney independent of the blood pressure:

1. Dissect out and stimulate the splanchnic nerves just where they pass through the pillars of the diaphragm. Stimulation of these nerves will cause vaso-constriction in the kidney, which takes place without sharply affecting the blood pressure.

2. Stimulate the depressor nerve or the central end of the divided vagus. In this case the volume of the kidney will increase though the general blood pressure decreases, showing that the fall of blood pressure is due to peripheral vascular dilatation.

3. Stimulate the peripheral end of the divided vagus so as to slow or even completely stop the heart. The sharp fall in blood pressure is now accompanied by decrease in the volume of the kidney, showing that the kidney change is merely passively following that of the blood pressure.

CHAPTER VI

RESPIRATION

THE maintenance of animal life necessitates the continual absorption of oxygen and the excretion of carbon dioxide by the living tissues. The blood is the medium, in all animals which possess a well-developed blood-vascular system, by which these gases are carried. Oxygen is absorbed by the blood from without and conveyed to all parts of the organism; and carbon dioxide which comes from the cells within is carried by the blood to the surfaces, from which it may escape from the body. The two processes—absorption of oxygen and excretion of carbon dioxide—are complementary, and their sum is termed the process of *Respiration*.

In all Vertebrata, and in a large number of Invertebrata, certain parts, either *lungs* or *gills*, are specially constructed for bringing the blood into proximity with the aërating medium (atmospheric air, or water containing air in solution). In some of the lower Vertebrata (frogs and other naked Amphibia) the skin is important as a respiratory organ, and is capable of supplementing to some extent the functions of the proper breathing apparatus.

A lung or a gill is constructed essentially of a fine transparent membrane, one surface of which is exposed to the air or water, as the case may be, while on the other surface is a network of blood-vessels. The only separation between the blood and aërating medium is the thin wall of the blood-vessels and the fine membrane on which the vessels are distributed. The difference between the simplest and the most complicated respiratory membrane is one of degree only.

In the mammals and the higher vertebrates the respiratory membrane is included within a respiratory cavity, the chest or thorax, which carries on regular movements, the respiratory movements, to bring changes of air into close contact with the respiratory surface.

The complexity of the respiratory membrane, the kind of aërating medium, and the respiratory movements are not, however, the only conditions which cause a difference in the respiratory capacity of different animals. The quantity and composition of the blood, especially as regards the number and size of the red corpuscles, and the vigor and efficiency of the circulatory apparatus in driving the blood to and fro between the lungs and the active tissues, these are conditions of equal, if not greater, importance.

It may be as well to state here that the lungs are only the medium for the

exchange, on the part of the blood, of carbon dioxide for oxygen. The living tissues are the seat of those combustion processes which consume oxygen and produce carbon dioxide. These processes occur in all parts of the body in the substance of the living active tissues, and are the true respiratory processes, sometimes called *internal* or *tissue respiration*.

THE RESPIRATORY APPARATUS.

The object of the respiratory movements being the interchange of gases in the lungs, it is necessary that the atmospheric air shall pass into them and that the changed air shall be expelled from them. The lungs are contained in the chest or thorax, which is a closed cavity having no communica-

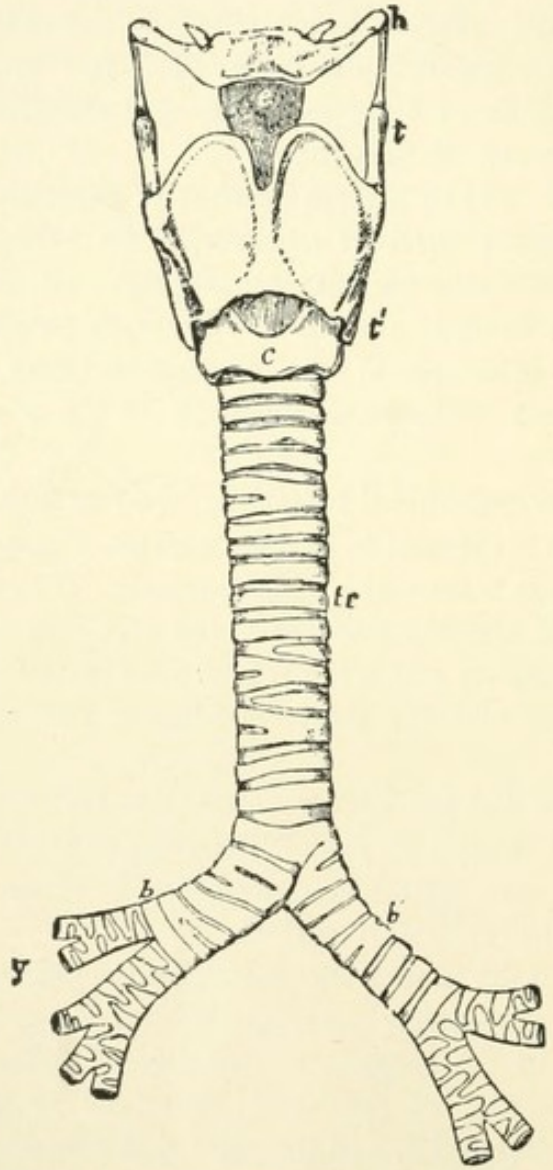


FIG. 218.—Outline Showing the General Form of the Larynx, Trachea, and Bronchi, as seen from Before. *h*, The great cornu of the hyoid bone; *e*, epiglottis; *t*, superior, and *t'*, inferior cornu of the thyroid cartilage; *c*, middle of the cricoid cartilage; *tr*, the trachea, showing sixteen cartilaginous rings; *b*, the right, and *b'*, the left bronchus. × ½. (Allen Thomson.)

tion with the outside except by means of the respiratory passages. The air enters these passages through the nostrils or through the mouth, thence it passes through the larynx into the trachea or windpipe, which about the middle of the chest divides into two tubes, the bronchi, one to each lung.

The Larynx. The upper part of the passage which leads exclusively to the lung is formed by the thyroid, cricoid, and arytenoid cartilages, figure 218, and contains the *vocal cords*, by the vibration of which the voice is chiefly produced. These vocal cords are ligamentous bands covered with mucous membrane and attached to certain cartilages which are capable of movement by muscles. By their approximation the cords can entirely close the entrance into the larynx; but under ordinary conditions the entrance of the larynx is formed by a more or less triangular opening between them, called the *rima glottidis*. Projecting at an acute angle between the base of the tongue and the larynx, to which it is attached, is a leaf-shaped cartilage with its larger extremity free. This is called the *epiglottis*. The whole of the larynx is lined by mucous membrane, which, however, is extremely thin over the vocal cords. At its lower extremity the larynx joins the trachea.

Taste buds have been found in the epithelium of the posterior surface of the epiglottis, and in several other situations in the laryngeal mucous membrane.

The Trachea and Bronchi. The trachea extends from the cricoid cartilage, which is on a level with the fifth cervical vertebra, to a point opposite the third dorsal vertebra, where it divides into the two bronchi, one for each lung, figure 218. The trachea measures, on an average, four or four and a half inches, 12 to 14 cm., in length, and from three-quarters of an inch to an inch, 2 to 2.5 cm., in diameter, and is essentially a tube of fibro-elastic membrane within the layers of which are enclosed a series of cartilaginous rings, from sixteen to twenty in number. These rings extend only around the front and sides of the trachea, about two-thirds of its circumference, and are deficient behind; the interval between their posterior extremities being bridged over by a continuation of the fibrous membrane in which they are enclosed, figure 219, *h*.

Immediately within this tube and at the back is a layer of unstriped muscular fibers. This muscular layer extends transversely between the ends of the cartilaginous rings to which it is attached, and also opposite the intervals between them; its evident function being to diminish the caliber of the trachea by approximating the ends of the cartilages. Outside there are a few longitudinal bundles of muscular tissue, which, like the preceding, are attached both to the fibrous and to the cartilaginous framework.

The mucous membrane, figures 219 and 220, consists largely of adenoid tissue, separated from the stratified columnar epithelium, which lines it, by a homogeneous basement membrane. This is penetrated here and there by channels which connect the adenoid tissue of the mucosa with the inter-

cellular substance of the epithelium. The stratified columnar epithelium is formed of several layers, of which the most superficial layer is ciliated and the cells often branched downward. Many of the superficial cells are of the goblet variety. In the deeper part of the mucosa are many elastic fibers between which lie connective-tissue corpuscles and capillary blood-vessels.

Numerous mucous glands are situated on the exterior and in the substance of the fibrous framework of the trachea; their ducts perforating the various

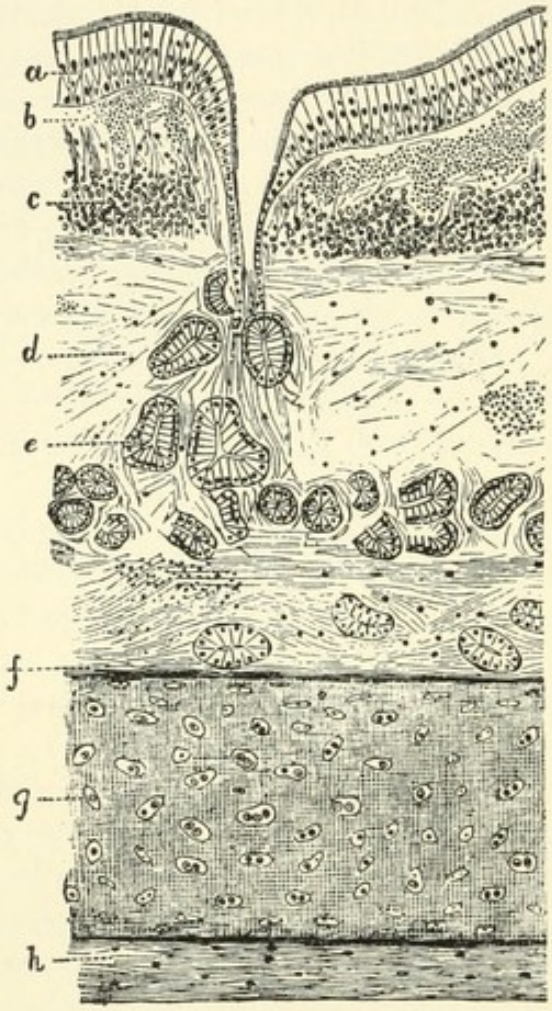


FIG. 219.—Section of the Trachea. *a*, Columnar ciliated epithelium; *b* and *c*, proper structure of the mucous membrane, containing elastic fibers cut across transversely; *d*, submucous tissue containing mucous glands, *e*, separated from the hyaline cartilage, *g*, by a fine fibrous tissue, *f*. *h*, external investment of fine fibrous tissue. (S. K. Alcock.)

structures which form the wall of the trachea, and opening through the mucous membrane into the cavity of the trachea.

The two bronchi into which the trachea divides resemble the trachea in structure, with the difference that in them there is a distinct layer of unstriped muscle arranged circularly beneath the mucous membrane, forming the *muscularis mucosæ*. On entering the substance of the lungs the cartilaginous rings, although they still form only larger or smaller segments of

a circle, are no longer confined to the front and sides of the tubes, but are distributed impartially to all parts of their circumference.

The bronchi divide and subdivide in the substance of the lungs into smaller and smaller branches, which penetrate into every part of the organ

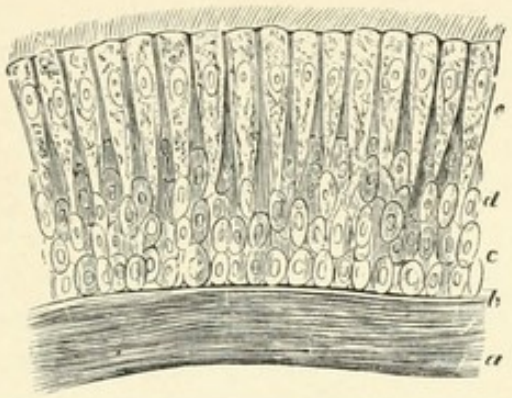


FIG. 220.—Ciliary Epithelium of the Human Trachea. *a*, Layer of longitudinally arranged elastic fibers; *b*, basement membrane; *c*, deepest cells, circular in form; *d*, intermediate elongated cells; *e*, outermost layer of cells fully developed and bearing cilia. × 350. (Kölliker.)

until at length they end in the smaller subdivisions of the lungs called *lobules*.

All the larger branches have walls formed of tough membrane, containing portions of cartilaginous rings, by which they are held open, and unstriped muscular fibers, as well as longitudinal bundles of elastic tissue.

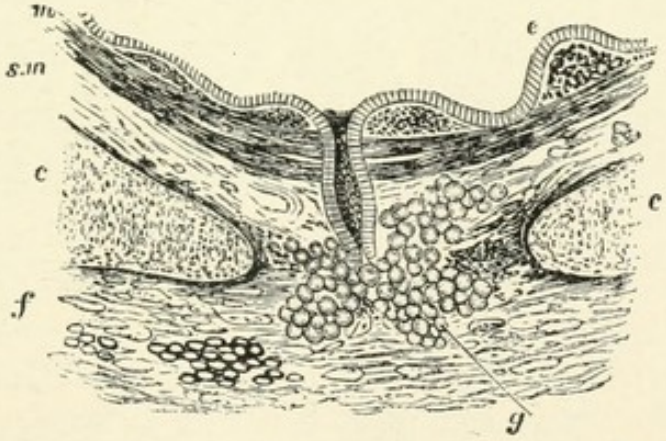


FIG. 221.—Transverse Section of a Bronchus, about ½ inch in Diameter. *e*, Epithelium (ciliated); immediately beneath it is the mucous membrane or internal fibrous layer, of varying thickness; *m*, muscular layer; *s. m*, submucous tissue; *f*, fibrous tissue; *c*, cartilage enclosed within the layers of fibrous tissue; *g*, mucous gland. (F. E. Schulze.)

They are lined by mucous membrane, the surface of which, like that of the larynx and trachea, is covered with ciliated epithelium; but the several layers become less and less distinct until the lining consists of a single layer of more or less cubical cells covered with cilia, figure 221. The mucous membrane is abundantly provided with mucous glands.

As the bronchi become smaller and smaller and their walls thinner, the cartilaginous rings become fewer and more irregular, until in the smaller bronchial tubes they are represented only by minute and scattered cartilaginous flakes. And when the bronchi by successive branches are reduced to about $\frac{1}{40}$ of an inch, 0.6 mm., in diameter, they lose their cartilaginous element altogether and their walls are formed only of a tough, fibrous, elastic membrane with circular muscular fibers. They are still lined, however, by a thin mucous membrane with ciliated epithelium, the length of the cells bearing the cilia having become so far diminished that the cells are almost cubical. In the smaller bronchi the circular muscular fibers are relatively more abundant than in the larger bronchi and form a distinct circular coat.

The Lungs and Pluræ. The lungs occupy the greater portion of the thorax. They are of a spongy elastic texture, and on section appear to the naked eye as if they were in great part solid organs, except where branches of the open bronchi or air-tubes may have been cut across and show on the surface of the section. In fact, however, the lungs are hollow organs

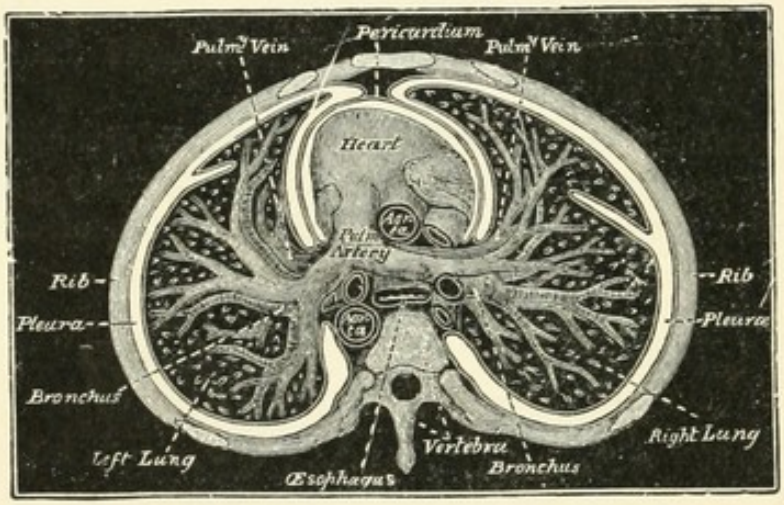


FIG. 222.—Transverse Section of the Chest.

composed of a mass of air cavities all of which communicate finally with the common air-tube, the trachea.

Each lung is enveloped by a serous membrane, the *pleura*, which adheres closely to its surface and provides it with its smooth and slippery covering. This same membrane lines the inner surface of the chest wall. The continuity of this membrane, which forms a closed sac as in the case of other serous membranes, will be best understood by reference to figure 222. The appearance of a space, however, between the pleura which covers the lung, *visceral* layer, and that which lines the inner surface of the chest, *parietal* layer, is inserted in the drawing only for the sake of distinctness. These layers are, in health, everywhere in contact, one with the other; and between them is only just as much fluid as will insure frictionless movement in their expansion and contraction.

When considering the subject of normal respiration, one may discard altogether the notion of the existence of any space or cavity between the lungs and the wall of the chest. If, however, an opening be made so as to permit air or fluid to enter the pleural sac, the lung in virtue of its elasticity recoils, and a considerable space is left between it and the chest wall. In other words, the natural elasticity of the lungs would cause them at all times to contract away from the ribs were it not that the contraction is resisted by atmospheric pressure which bears only on the inner surface of the air-tubes and air-cells.

The pulmonary pleura consists of an outer or denser layer and an inner looser tissue in which there is a lymph-canalicular system. Numerous lymphatics are to be met with, which form a dense plexus of vessels, many of which contain valves. They are simple endothelial tubes, and take origin in the lymph-canalicular system of the pleura proper. Scattered bundles of unstriped muscular fiber occur in the pulmonary pleura. They are especially strongly developed on the anterior and internal surfaces of the lungs, the parts which move most freely in respiration. Their function is doubtless to aid in expiration.

The Finer Structure of the Lung. Each lung is partially subdivided into separate portions called *lobes;* the right lung into three lobes,

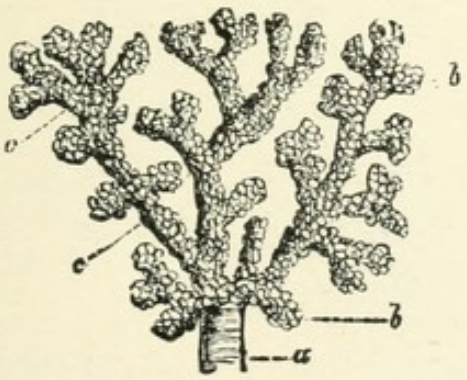


FIG. 223.

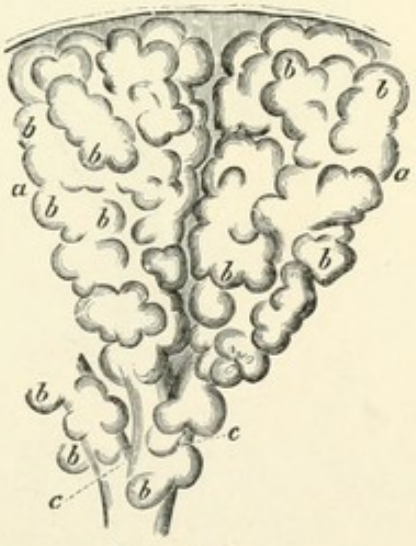


FIG. 224.

FIG. 223.—Terminal Branch of a Bronchial Tube, with its Infundibula and Air-cells, from the Margin of the Lung Injected with Quicksilver; Monkey. *a*, Terminal bronchial twig; *b*, *b*, infundibula and air-cells. × 10. (F. E. Schulze.)

FIG. 224.—Two Small Infundibula, *a*, *a*, with air-cells, *b*, *b*, and the ultimate bronchial tubes, *c*, *c*, with which the air-cells communicate. From a new-born child. (Kölliker.)

and the left into two. Each of these lobes, again, is composed of a large number of minute parts, called *lobules*. Each pulmonary lobule may be considered to be a lung in miniature, consisting, as it does, of a branch of the bronchial tube, of air-cells, blood-vessels, nerves, and lymphatics, with a small amount of areolar tissue.

On entering a lobule, the small bronchial tube, the structure of which has just been described, *a*, figure 210, divides and subdivides; its walls at the same time becoming thinner and thinner, until at length they are formed only of a thin membrane of areolar and elastic tissue, lined by a layer of *squamous epithelium*, no longer provided with cilia. At the same time they are altered in shape; each of the minute terminal branches widening out funnel-wise, and its walls being pouched out irregularly into small saccular dilatations, called *air-cells*, figure 223, *b*. Such a funnel-shaped terminal branch of the bronchial tube, with its group of pouches or air-cells, has been called an *infundibulum*, figures 223 and 224, and the irregular oblong space in its center, with which the air-cells communicate, an *intercellular passage*.

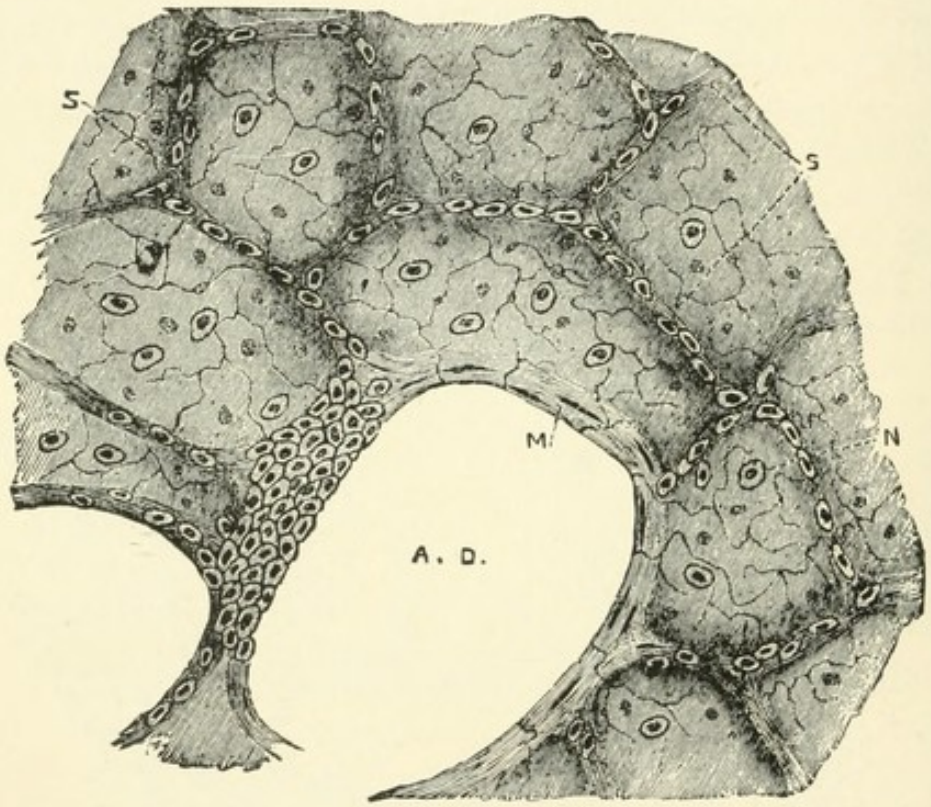


FIG. 225.—From a Section of the Lung of a Cat, Stained with Silver Nitrate. *A. D*, Alveolar duct or intercellular passage; *S*, alveolar septa, *N*, alveoli or air-cells, lined with large flat, nuleated cells, with some smaller polyhedral nucleated cells; *M*, unstriped muscular fibers. Circular muscular fibers are seen surrounding the interior of the alveolar duct, and at one part is seen a group of small polyhedral cells continued from the bronchus. (Klein and Noble Smith.)

An inflated and dried turtle's lung is the homologue of a lobule. Such a preparation can be cut across to illustrate the intercellular passage, the infundibulum, and the air-cells.

The air-cells, or air-vessels, are sometimes placed singly, like recesses from the intercellular passage, but more often they are arranged in groups or even rows, like minute sacculated tubes, so that a short series of vesicles all communicating with one another open by a common orifice into the tube. The vesicles are of various forms according to the mutual pressure to which

they are subject. Their walls are nearly in contact, and they vary from 0.5 to 0.3 mm. in diameter. Their walls are formed of fine membrane similar to that of the intercellular passages and continuous with it. The membrane is folded on itself so as to form a sharp-edged border at each circular orifice of communication between contiguous air-vesicles, or between the vesicles and the bronchial passages. Numerous fibers of elastic tissue are spread out in the walls between contiguous air-cells, and many of these are attached to the outer surface of the wall of which each cell is composed, imparting to it additional strength and the power of recoil after distention.

The air-cells are lined by a layer of epithelium, figure 225, the cells of which are very thin and plate-like. The thin epithelial membrane is free on one side, where it comes in contact with the air of the lungs, but on the other

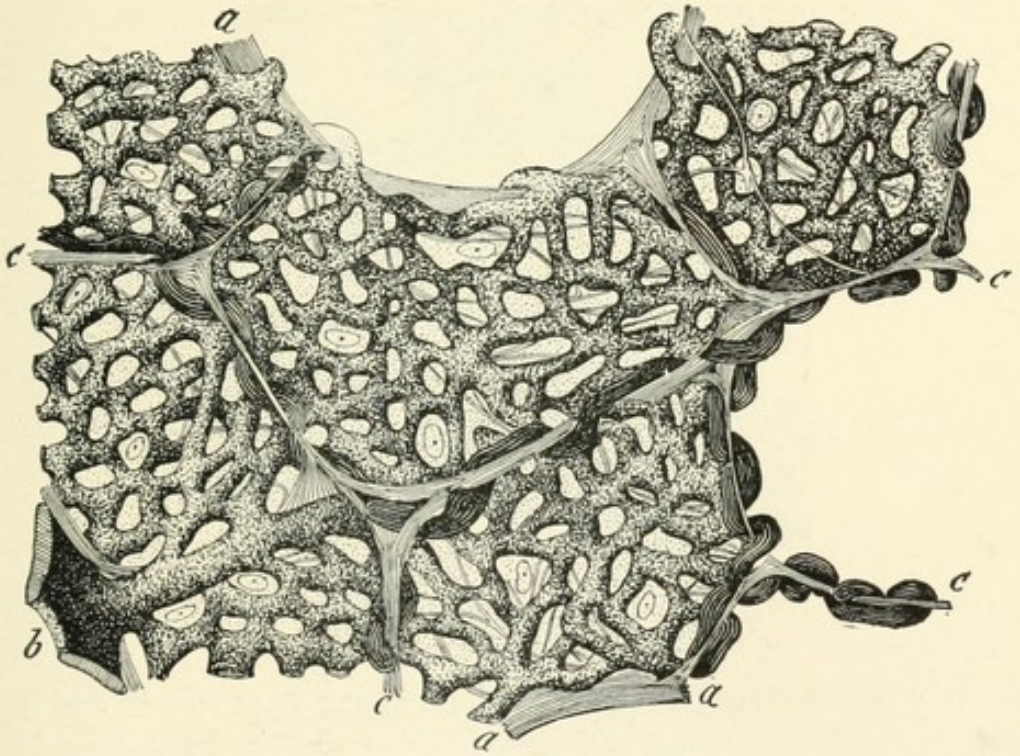


FIG. 226.—Section of Injected Lung, Including Several Contiguous Alveoli. (F. E. Schulze.) Highly magnified. *a*, *a*, Free edges of alveoli; *c*, *c*, partitions between neighboring alveoli, seen in section; *b*, small arterial branch giving off capillaries to the alveoli. The looping of the vessels to either side of the partitions is well exhibited. Between the capillaries is seen the homogeneous alveolar wall with nuclei of connective-tissue corpuscles and elastic fibers.

side a network of pulmonary capillaries is spread out so densely, figure 226, that the interspaces or meshes are even narrower than the vessels. These are on an average $\frac{1}{3000}$ of an inch, or 8 micromillimeters, in diameter. Between the atmospheric air-cells and the blood in these vessels, nothing intervenes but the thin walls of the cells and capillaries. The exposure of the blood to the air is the more complete because the wall between contiguous air-cells, and often the spaces between the walls of the same, contain only a single layer of capillaries both sides of which are at once exposed to the air.

The air-vesicles situated nearest to the center of the lung are smaller and their networks of capillaries are closer than those nearer to the circumference. The vesicles of adjacent lobules do not communicate. Those of the same lobule or proceeding from the same intercellular passage communicate as a general rule only near angles of bifurcation, so that when any bronchial tube is closed or obstructed the supply of air is lost for all the blood-vessels of that lobule and its branches.

Blood-supply. The lungs receive blood from two sources: *a*, the pulmonary artery; *b*, the bronchial arteries. The former conveys *venous* blood to the lungs for its oxidation, and this blood takes no share in the nutrition of the deeper pulmonary tissues through which it passes. The branches of the bronchial arteries are nutrient arteries which ramify in the

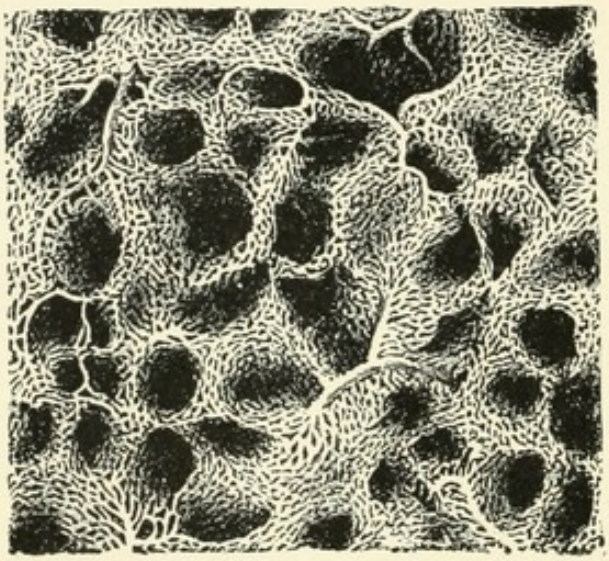


FIG. 227.—Capillary Network of the Pulmonary Blood-vessels in the Human Lung. × 60. (Kölliker.)

walls of the bronchi, in the walls of the larger pulmonary vessels, and in the interlobular connective tissue, etc. The blood of the bronchial vessels is returned chiefly through the bronchial, but partly through the pulmonary, veins.

Lymphatics. The lymphatics are arranged in three sets: 1. Irregular lacunæ in the walls of the alveoli or air-cells. The lymphatic vessels which lead from these accompany the pulmonary vessels toward the root of the lung. 2, Irregular anastomosing spaces in the walls of the bronchi. 3, Lymph-spaces in the pulmonary pleura. The lymphatic vessels from all these irregular sinuses pass in toward the root of the lung to reach the bronchial glands.

Nerves. The nerves of the lung are to be traced from the anterior and posterior pulmonary plexuses, which are formed by branches of the vagus and sympathetic. The nerves follow the course of the blood-vessels and bronchi, and many small ganglia are situated in the walls of the latter.

THE MOVEMENTS OF THE RESPIRATORY MECHANISM.

Respiratory movement consists of the alternate expansion and contraction of the thorax, by means of which air is drawn into or expelled from the lungs.

A movement of the side walls or floor of the chest to increase its diameter or length will enlarge the capacity of the interior. By such an increase of capacity there will be of course a diminution of the pressure of the air in the lungs, and a fresh quantity of air will enter through the larynx and trachea to equalize the pressure on the inside and outside of the chest. This movement is called *inspiration*.

The movement which diminishes the capacity of the chest and increases the pressure in the interior expels air until the pressure within and that without the chest are again equal. This movement is called *expiration*. In both cases the air passes through the trachea and larynx, whether in entering or

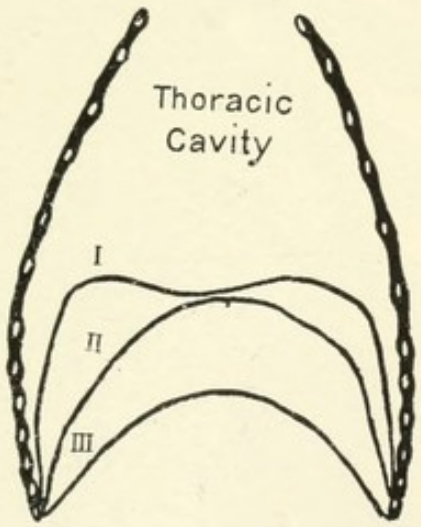


FIG. 228.—Schematic Representation of Diaphragm. In expiration (*I*), quiet inspiration (*II*), and deep inspiration (*III*). (After Schäffer.)

leaving the lungs, there being no other communication with the exterior of the body. And the lung, for the same reason, remains closely in contact with the walls and floor of the chest under all the circumstances described. To speak of expansion of the chest is to speak also of expansion of the lung, and *vice versa*.

Inspiration. The enlargement of the chest during inspiration is due to muscular action, which brings about an increase in the size of the chest cavity through the contraction of the inspiratory muscles, the rôle played by the lungs being a passive one. The chest cavity is increased in its three axes, the vertical, lateral, and antero-posterior diameters. The muscles engaged in ordinary inspiration are: the diaphragm, the external intercostals, and the scaleni and levatores costarum. During forced inspiration

every muscle is brought into play which by its contraction tends to elevate the ribs and sternum or which will fix points against which these muscles can act. This includes almost every muscle of the trunk and neck.

Changes in the *vertical diameter* are due, first, to the contraction of the *diaphragm*. This muscle has the shape of a flattened dome, its highest

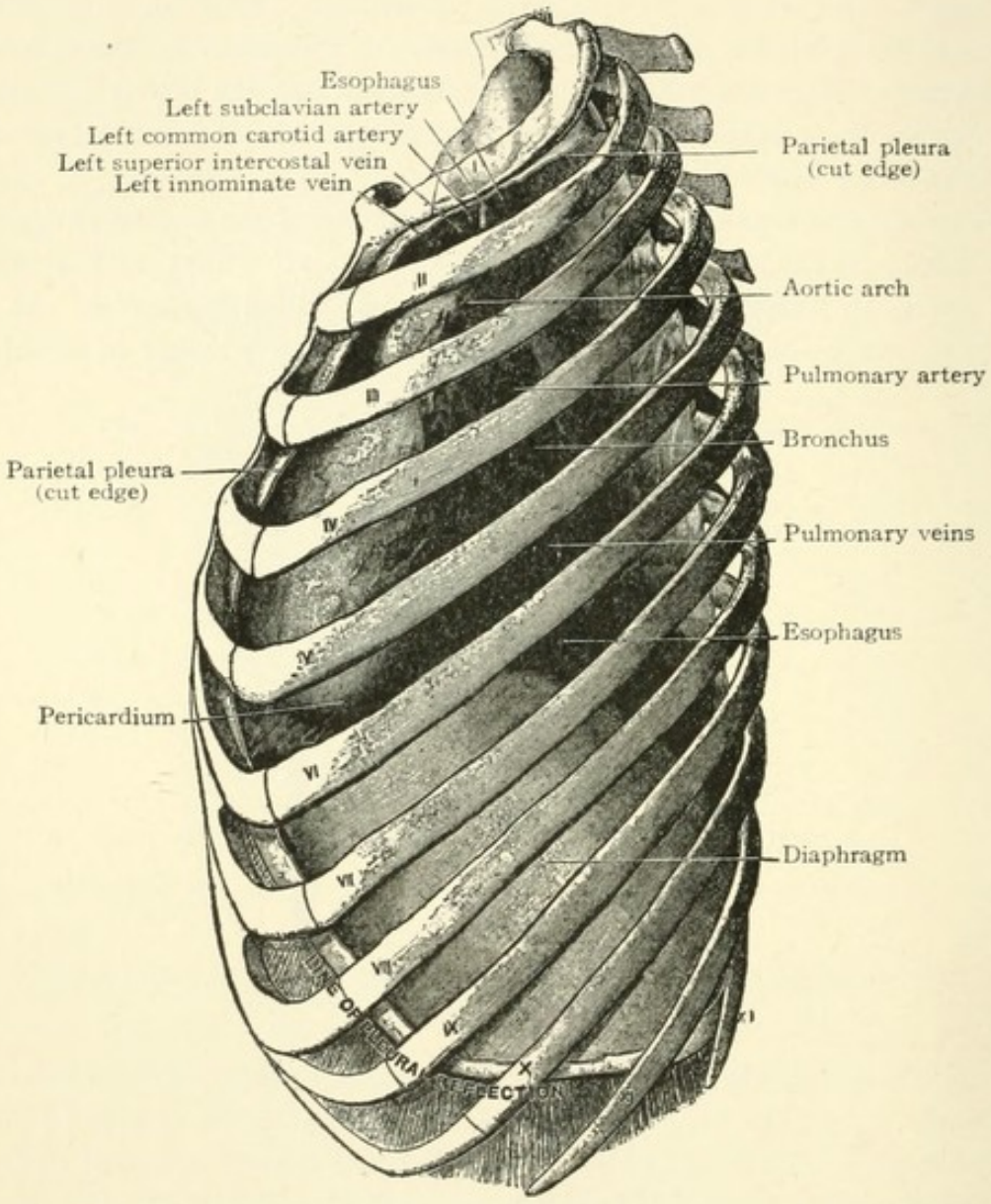


FIG. 229.—Thorax from the Left, Showing Left Pleural Sac, and the Diaphragm. The lung is removed.

point being the central tendon. While passive, its lower portions are in apposition with the chest walls, figure 228, *I*. On contraction, the dome is pulled downward and the lower portion is pulled away from the chest walls, the downward displacement varying from 6 to 12 mm. in normal respiration, and in forced respiration may amount to as much as 45 mm. The tendency of the diaphragm to pull the lower ribs and lower part of the sternum

inward is counteracted by the outward pressure of the abdominal viscera, and by the action of the *quadrati lumborum*, which by their attachment to the last ribs fix these and, in case of deep inspiration, may even pull them downward. The *serrati postici inferiores* also aid, being attached to the four lower ribs.

Changes in the *lateral* and *antero-posterior diameters* are effected by the raising of the ribs, which are attached very obliquely to the spine and sternum. The elevation of the ribs takes place both in front and at the sides—the hinder ends being prevented from performing any upward movement by their pivot attachment to the spine. The movement of the front extremities of the ribs is of necessity limited by an upward and forward movement of the

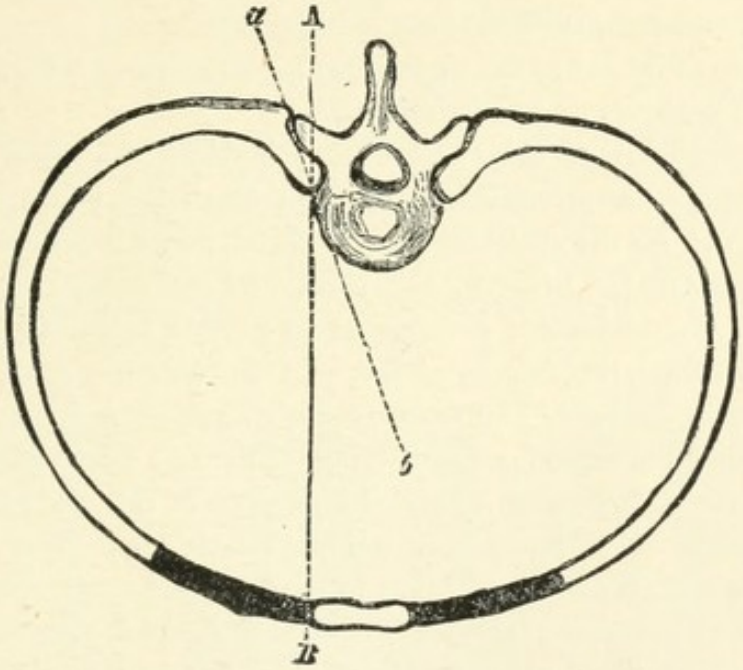


FIG. 230.—Diagram of Axes of Movement of Ribs.

sternum to which they are attached, the movement being greater at the lower end than at the upper end of the sternum.

The axes of rotation in these movements are two: one corresponding with a line drawn through the two articulations which the rib forms with the spine, *a*, *b*, figure 230, and the other with a line drawn from one of these (head of rib) to the sternum, *A B*, figure 230; the motion of the rib around the latter axis being somewhat after the fashion of raising the handle of a bucket. The elevation of the ribs is accompanied by a slight opening out of the angle which the bony part forms with its cartilage, and thus an additional means is provided for increasing the antero-posterior diameter of the chest. The movements of all the ribs except the twelfth consist of a rotation upward, forward, and outward. The twelfth presents only rotation downward and backward.

The muscles involved in these movements of the ribs are the *external intercostals* and the part of the *internal intercostals* situated between the costal cartilages. Their action is to widen the intercostal spaces. The *scaleni* fix the first and second ribs, thereby making a fixed point of action for the other muscles involved. The *serrati postici superiores* assist the above and also raise the third, fourth, and fifth ribs. The *levatores costarum longi* and *brevi* elevate and evert all the ribs from the first to the tenth.

In extraordinary or forced inspiration, which may be due either to violent exercise or to interference with the due entrance of air into the lungs, all the above muscles act more strongly. The diaphragm descends lower, the scaleni raise the first and second ribs instead of merely fixing them, as in ordinary respiration, as do also the sterno-cleido-mastoids. These, together with the *erector spinæ*, which straighten the spine, increase the vertical diameter. The *trapezii* and the *rhomboidii* assist in increasing the antero-posterior and lateral diameters by fixing the shoulders and thus giving a fixed point for the action of the *pectorals* and *latissimi dorsi*.

The enlargement of the chest during inspiration presents peculiarities in different persons. In children of both sexes the principal muscle involved seems to be the diaphragm, and this type of breathing is known as *abdominal breathing*. In men, the chest and sternum, together with the front wall of the abdomen, are subject to a wide movement; this type of breathing is called the *inferior costal*. In women, the movement appears less extensive in the lower and more extensive in the upper part of the chest, which is called the *superior costal* type. This has been shown to be due rather to mode of dress than to a real difference in the sexes (Mosher).

Expiration. Quiet expiration is a passive act due to the return of the thorax and its contained lungs to their normal position when the muscles involved in inspiration relax. This elastic recoil is sufficient in ordinary quiet breathing to expel air from the lungs. In forced expiration, however, which may occur to a slight degree in speaking, singing, etc., as well as in the case of many involuntary and reflex acts, such as coughing, sneezing, etc., other muscles are involved. Of these the principal are the abdominal muscles, *obliquus externus* and *internus*, *rectus abdominis*, *transversalis abdominis* and *pyramidalis*. These act, first, by pressing the abdominal viscera against the diaphragm and thereby forcing it up, their descent into the pelvic cavity being prevented; second, by their attachments to the lower ribs and cartilages, they draw these downward and inward, thereby lessening the size of the thoracic cavity; lastly, by their contraction, they form a fixed point for the action of that part of the *internal* intercostals, not involved in inspiration, to approximate the ribs.

When by the efforts of the expiratory muscles the chest has been squeezed to less than its average diameters, it again, on relaxation of the muscles, returns to the normal dimensions by virtue of its elasticity. The construc-

tion of the chest walls, therefore, admirably adapts them for recoiling against and resisting as well undue contraction as undue dilatation.

Respiratory Movements of the Nostrils and of the Glottis. During the action of the inspiratory muscles which directly draw air into the chest, those which guard the opening through which the air enters are also active. In hurried breathing the dilatation of the nostrils is well seen, although under ordinary conditions it may not be noticeable. The opening at the upper part of the larynx, however, the rima glottidis, is dilated at each inspiration for the more ready passage of air, and becomes smaller at each expiration; its condition, therefore, corresponds during respiration with that of the walls of the chest. There is a further likeness between the two acts in that, under ordinary circumstances, the dilatation of the rima glottidis is a muscular act and its contraction chiefly an elastic recoil; although, under various special conditions to be hereafter mentioned, there may be considerable muscular contraction exercised.

Methods of Recording Respiratory Movements. The movements of respiration may be recorded graphically in several ways. The ordinary method is to introduce a tube into the trachea of an animal, and to connect this tube by some gutta-percha tubing with a T-piece, the side branch of which is connected with a Marey's tambour, which may be made to write on a recording surface, figure 173. If the tube attached to the free limb of the T-piece be partially closed with a screw compress, the movements of inspiration

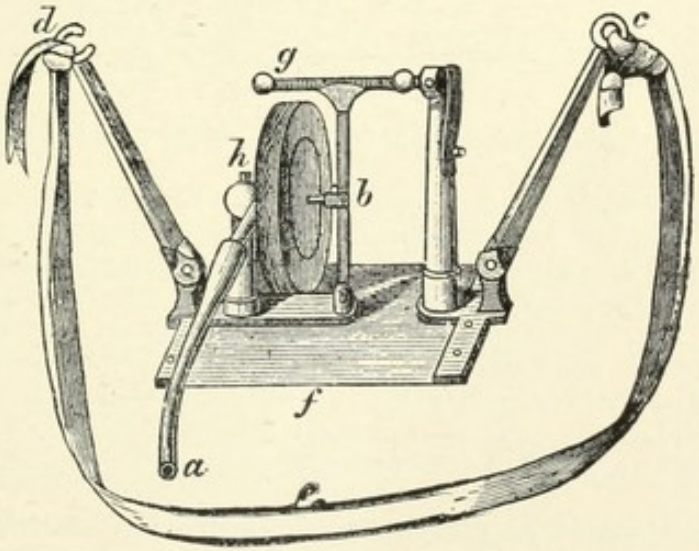


FIG. 231.—Stethograph or Pneumograph. *h*, Tambour fixed at right angles to plate of steel, *f*; *c* and *d*, arms by which instrument is attached to chest by belt, *e*. When the chest expands, the arms are pulled asunder, which bends the steel plate, and the tambour is affected by the pressure of *b*, which is attached to it on the one hand, and to the upright in connection with horizontal screw, *g*. (Modified from Marey's instrument.)

and expiration are larger than if it were open. The alteration of the pressure within the lungs on inspiration and expiration is shown by the movement of the column of air in the trachea and in its extension to the T-piece. By these means a record of the respiratory movements may be obtained.

Various instruments have been devised for recording the movements of the chest by application of apparatus to the exterior. Such is the stethometer of Burdon-Sanderson, figure 233. This consists of a frame formed of two parallel steel bars joined by a third

at one end. At the free end of the bars is attached a leather strap, by means of which the apparatus may be suspended from the neck. Attached to the inner end of one bar is a tambour and ivory button, to the end of the other an ivory button. The apparatus is suspended with the transverse bar posteriorly, the button of the tambour is placed on the part of the chest the movement of which it is desired to record, and the other button is made to press upon the corresponding side of the chest, so that the chest is held as between a pair of calipers. The receiving tambour is connected through a T-piece with a recording tambour of Marey's, and with a bulb by means of which air can be squeezed into the cavity of the tympanum. When adjusted, the tube connected with the air ball is shut off by means of a screw clamp. The movement of the chest is thus communicated to the recording tambour.

A simpler form of this apparatus, called a pneumograph or stethograph, consists of a thick India-rubber bag of elliptical shape about three inches long, to one end of which a rigid gutta-percha tube is attached. This bag may be fixed at any required place on the chest by means of a strap and buckle. By means of the gutta-percha tube the variations of the pressure of air in the bag, produced by the movements of the chest, are communicated

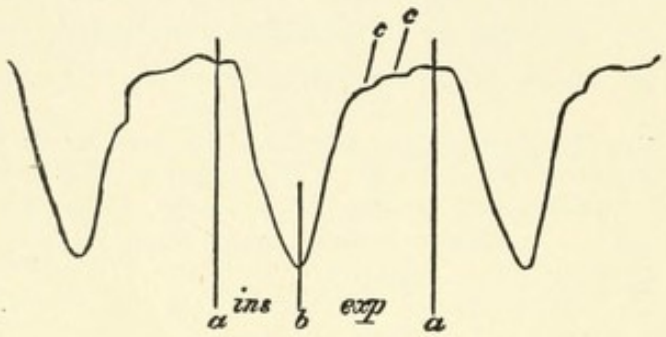


FIG. 232.—Tracing of Thoracic Respiratory Movements obtained by means of Marey's Pneumograph. (Foster.) A whole respiratory phase is comprised between *a* and *a*; inspiration during which the lever *descends*, extending from *a* to *b*, and expiration from *b* to *a*. The undulations at *c* are caused by the heart's beat.

to a recording tambour. This principle is applied in a modified form in Marey's pneumograph, figure 231.

The variations of intrapleural pressure may be recorded by introducing a cannula into the pleural or pericardial cavity. The cannula should be previously connected with a mercury or other form of manometer by tubing filled with physiological saline.

Finally, it has been found possible in various ways to record the diaphragmatic movements. This can be done by inserting a receiving tambour into the abdomen below the diaphragm, by the insertion of needles into different parts of the diaphragm and recording the movement of the free ends of needles about the fulcrum formed where the chest wall is pierced, or by recording the contraction of isolated strips of the diaphragm directly. These records all give an accurate picture of the movements of the diaphragm.

The Relative Time of Inspiration and Expiration and the Respiratory Movement. The acts of inspiration and expiration take up, under ordinary circumstances, a nearly equal time. The time of inspiration, however, especially in women and children, is a little shorter than that of expiration, and there is commonly a very slight pause between the end of expiration and the beginning of the next inspiration, see figure 232. The ratio of the respiratory rhythm may be thus expressed:

Inspiration	6
Expiration	7 to 8
Pause	Very slight

If the ear be placed in contact with the wall of the chest, or be separated from it only by a good conductor of sound or a stethoscope, a faint *respiratory murmur* is heard during inspiration. This sound varies somewhat in different parts, being loudest or coarsest in the neighborhood of the trachea and large bronchi (tracheal and bronchial breathing), and fading off into a faint sighing as the ear is placed at a distance from these (vesicular breathing). It is heard best in children. In them a faint murmur is heard in expiration also. The cause of the vesicular murmur has received various explanations. Most

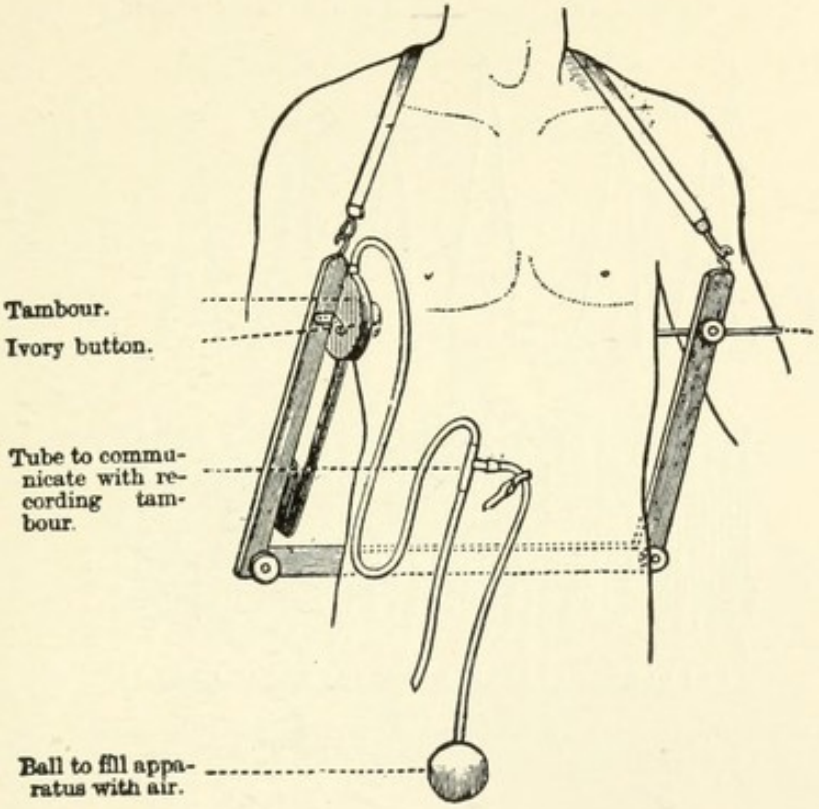


FIG. 233.—Stethometer. (Burdon-Sanderson.)

observers hold that the sound is produced in the glottis and larger bronchial tubes, but that it is modified in its passage to the pulmonary alveoli. In disease of the lungs the vesicular murmur undergoes various modifications, for a description of which one must consult text-books on physical diagnosis.

The Quantity of Air Breathed. *Tidal air* is the quantity of air which is habitually and almost uniformly changed in each act of breathing. In a healthy adult man it is about 30 cubic inches, or about 500 c.c. or half a liter. In college students the tidal air is somewhat less, varying from 300 to 400 c.c.

The Complemental Air is the quantity of air which can be drawn into the lungs by the deepest inspiration over and above that which is in the lungs

at the end of an ordinary inspiration. Its amount varies, but may be reckoned as 100 cubic inches, or about 1,600 c.c.

The Reserve Air is that which may be expelled by a forcible and deeper expiration, after an ordinary expiration, such as that which expels the tidal air. The reserve air amounts to from 1,200 to 1,500 c.c. This is also termed the *supplemental air.*

The Residual Air is the quantity which still remains in the lungs after the most violent expiratory effort. Its amount depends in great measure

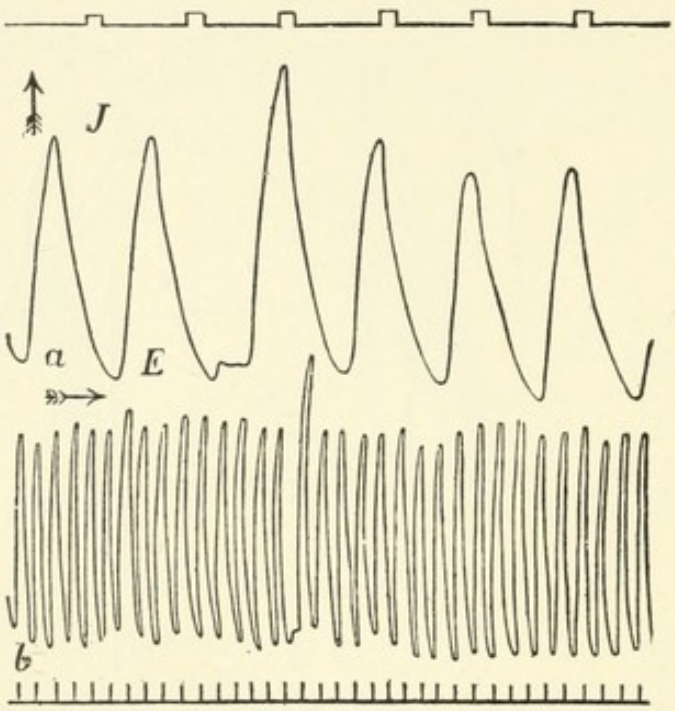


FIG. 234.—Tracing of the Normal Diaphragm Respirations of the Rabbit. *a*, With quick movement of drum; *b*, with slow movement; *J*, inpiration; *E*, expiration. To be read from left to right. (Marckwald.)

on the absolute size of the chest, but may be estimated at about 1,000 c.c. to 1,200 c.c.

The total quantity of air which passes into and out of the lungs of an adult, at rest, in 24 hours, is about 686,000 cubic inches. This quantity, however, is largely increased by exertion; the average amount for a hard-working laborer in the same time being 1,568,390 cubic inches.

The Respiratory Capacity. The greatest respiratory capacity or vital capacity of the chest is indicated by the quantity of air which a person can expel from his lungs by a forcible expiration after the deepest possible inspiration. The vital capacity is the sum of the reserve, tidal, and complemental airs. It expresses the power which a person has of breathing in the emergencies of active exercise, violence, and disease. The average capacity of an adult, at 15.4° C. (60° F.), is about 225 to 250 cubic inches, or 3,500 to 4,000 c.c.

The *respiratory* capacity, or as John Hutchinson called it, *vital* capacity, is usually measured by a modified gasometer or *spirometer*, into which the experimenter breathes, making the most prolonged expiration possible after the deepest possible inspiration. The quantity of air which is thus expelled from the lungs is indicated by the height to which the air chamber of the spirometer rises; and by means of a scale placed in connection with this, the number of cubic inches or centimeters is read off.

In healthy men, the respiratory capacity varies chiefly with the stature, weight, and age.

Circumstances Affecting the Amount of Respiratory Capacity. For every inch of height above the standard the respiratory capacity is increased, on an average, by eight inches; and for every inch below, it is diminished by the same amount.

The influence of *weight* on the capacity of respiration is less manifest, and considerably less than that of height. It is difficult to arrive at any definite conclusions on this

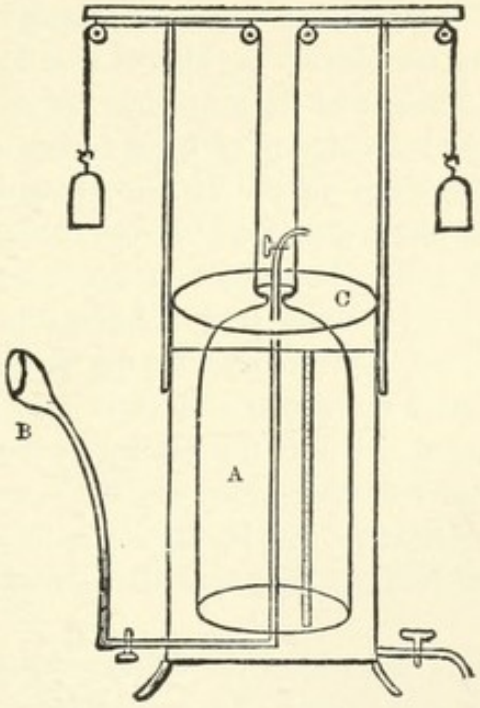


FIG. 235.—Diagram of Hutchinson's Spirometer. (Landois.) *A*, Graduated cylinder serving as a receiver for the breath; it is supplied with a stopcock at the top for the ready expulsion of air, and is balanced by weights passing over pulleys. *B*, Mouthpiece with tube reaching nearly to the top of the graduated receiver (*A*) when the latter is sunk in the reservoir ready for an experiment; there is a stopcock in this tube near the first angle, to prevent regurgitation of air. *C*, Reservoir for the graduated receiver. In using the spirometer the reservoir and graduated receiver are filled with water, or, to prevent the absorption of carbon dioxide, with a saturated aqueous solution of common salt (NaCl). When ready for an experiment, the stopcock at the top of the receiver is closed and that in the tube of the mouthpiece opened, and the breath forced into the receiver. The receiver rises as fast as the breath displaces the water. After the breath is forced into the receiver the stopcock in the tube of the mouthpiece is closed, and the water outside and inside the receiver brought to the same level, so that the air within the receiver shall be at the atmospheric pressure. The amount of breath within the receiver is then read directly from the scale attached to the receiver. For accurate measurement the breath should stand a few minutes to acquire the temperature of the liquid over which it is collected; then the various corrections for aqueous vapor tension, and the variations from the standard temperature and pressure, should be made.

point, because the natural average weight of a healthy man in relation to stature has not yet been determined.

By *age*, the capacity appears to be increased from about the fifteenth to the thirty-fifth year, at the rate of five cubic inches per year; from thirty-five to sixty-five it diminishes at the rate of about one and a half cubic inches per year; so that the capacity of respiration of a man sixty years old would be about thirty cubic inches less than that of a man forty years old, of the same height and weight. (John Hutchinson.)

The *number* of respirations in a healthy adult person usually ranges from 14 to 18 per minute. It is greater in infancy and childhood. It varies also much according to different circumstances, such as exercise or rest, health or disease, etc. Variations in the number of respirations correspond ordinarily with similar variations in the pulsations of the heart. In health the proportion is about 1 to 4, or 1 to 5; and when the rapidity of the heart's action is increased, that of the chest movement is commonly increased also, but not in every case in equal proportion. It happens occasionally in disease, especially of the lungs or air-passages, that the number of *respiratory* acts increases in quicker proportion than the beats of the *pulse;* and, in other affections, much more commonly, that the number of the pulses is greater in proportion than that of the respirations.

The Force of Inspiratory and Expiratory Muscles. The force which the inspiratory muscles are capable of exerting on the chest is greatest in individuals of the height of from five feet seven inches to five feet eight inches, and is equal to a column of three inches of mercury. Above this height the force decreases as the stature increases; so that the average power of men of six feet is measured by about two and a half inches of mercury. The force manifested in the strongest expiratory acts is, on the average, one-third greater than that exercised in inspiration. But this difference is in a great measure due to the power exerted by the elastic reaction of the walls of the chest; and it is also much influenced by the disproportionate strength which the expiratory muscles attain from their being called into use for other purposes than that of simple expiration. The force of the inspiratory act is, therefore, better adapted than that of the expiratory for testing the muscular strength of the body (John Hutchinson).

It has been shown that within the limits of ordinary tranquil respiration the elastic resilience of the walls of the chest favors inspiration; and that it is only in deep inspiration that the ribs and rib-cartilages offer an opposing force to their dilatation. In other words, the elastic resilience of the lungs, at the end of an act of ordinary exhalation has drawn the chest walls within the limits of their normal degree of expansion. Under all circumstances, of course, the elastic tissue of the lungs opposes inspiration and favors expiration.

It is possible that the contractile power which the bronchial tubes and air-vesicles possess, by means of their *muscular fibers* may assist in expiration. But it is more likely that its chief purpose is to regulate and adapt, in some measure, the quantity of air admitted to the lungs, and to each part of them, according to the supply of blood. The muscular tissue contracts upon and gradually expels collections of mucus, which may have accumulated within the tubes, and which cannot be ejected by forced expiratory efforts, owing to collapse or other morbid conditions of the portion of lung connected with the obstructed tubes (Gairdner). Apart from any of the before-mentioned

functions, the presence of muscular fiber in the walls of a hollow viscus, such as a lung, is only what might be expected from analogy with other organs. Subject as the lungs are to such great variation in size, it might be anticipated that the elastic tissue, which enters so largely into their composition, would be supplemented by the presence of much muscular fiber.

RESPIRATORY CHANGES IN THE AIR BREATHED.

Composition of the Atmosphere. The atmosphere we breathe has, in every situation in which it has been examined in its natural state, a nearly uniform composition. It is a mixture of oxygen, nitrogen, carbon dioxide, and watery vapor, with, commonly, traces of other gases, as argon, ammonia, sulphureted hydrogen, etc. Of every 100 *volumes* of pure atmospheric air, 79 volumes, on an average, consist of nitrogen and argon, the remaining 21 of oxygen. The proportion of carbon dioxide is extremely small; 10,000 volumes of atmospheric air contain only about 3 of that gas.

The quantity of watery vapor varies greatly according to the temperature and other circumstances, but the atmosphere is never without some. In this country the average quantity of watery vapor in the atmosphere varies greatly according to the region. In some of our Western arid plains in the dry season the air is almost free of moisture.

Composition of Air which Has Been Breathed. The changes effected by respiration in the atmospheric air are: 1, an increase of temperature; 2, an increase in the quantity of carbon dioxide; 3, a diminution in the quantity of oxygen; 4, a diminution of volume; 5, an increase in the amount of watery vapor; 6, the addition of a minute amount of organic matter and of free ammonia.

Temperature of the Expired Air. Expired air, after its contact with the interior of the lungs, is hotter (at least in most climates) than the inspired air. Its temperature varies between 36° and 37.5° C. (97° and 99.5° F.), the lower temperature being observed when the air has remained but a short time in the lungs. Whatever may be the temperature of the air when inhaled, it acquires nearly that of the blood before it is expelled from the chest.

The Carbon Dioxide of Expired Air. The percentage of carbon dioxide is increased, but the quantity exhaled in a given time is subject to change from various circumstances. From every volume of air inspired 4 to 5 per cent of oxygen is abstracted; while a rather smaller quantity, 4.38 per cent, of carbon dioxide is added in its place; the expired air will contain, therefore, 438 volumes of carbon dioxide in 10,000. The total quantity of carbon dioxide exhaled into the air breathed by a healthy adult, calculating that 15.4 c.c. of the 350 c.c. of the average air breathed out at each expiration consists of carbon dioxide, and that the rate of respiration is on an average 16, would be about 400 liters in the twenty-four hours. From actual experiment this

amount seems to be a trifle too great, since from the average of many investigations the total amount of carbon dioxide excreted per day by the *entire body* has been found to be about 400 liters, weighing 800 grams, and consisting of 218 grams of *carbon*, and 582 grams of *oxygen*. From the 218 grams of carbon must be deducted about 10 grams excreted in other ways

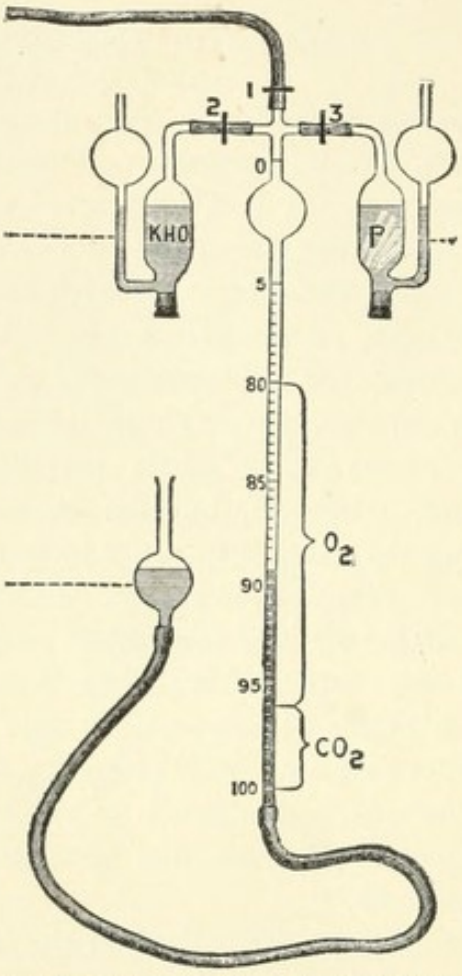


FIG. 236.—Apparatus for Estimating O_2 and CO_2 in Expired Air. (Waller.)

than by the lungs, which leaves about 215 grams as the amount of carbon excreted by the average healthy man by respiration each day and night. These quantities must be considered approximate only, inasmuch as various circumstances, even in health, influence the amount of carbon dioxide excreted, and, correlatively, the amount of oxygen absorbed.

Circumstances Influencing the Amount of Carbon Dioxide Excreted. *Age and Sex.* The quantity of carbon dioxide exhaled into the air breathed by males, regularly increases from 8 to 30 years of age; from 30 to 50 the quantity, after remaining stationary for a while, gradually diminishes, and from 50 to extreme age it goes on diminishing, till it scarcely exceeds the quantity exhaled at 10 years old. In females (in whom the quantity exhaled is always less than in males of the same age) the same regular increase in quantity goes on from the 8th year to the age of puberty, when the quantity abruptly ceases to increase, and remains stationary so long as they continue to menstruate. When menstruation has ceased, the carbon dioxide output soon decreases at the same rate as it does in old men.

Respiratory Movements. The quicker the respirations, the smaller is the percentage of carbon dioxide contained in each volume of the expired air. Although the proportionate quantity of carbon dioxide is thus diminished, the absolute amount exhaled within a given time is increased thereby, owing to the larger quantity of air which is breathed in the time. The last half of a volume of expired air contains more carbonic acid than the half first expired; a circumstance which is explained by the later portion of air coming from the remote part of the lungs, where it has been in more immediate and prolonged contact with the blood than the first portion exhaled has, which comes chiefly from the larger bronchial tubes.

External Temperature. The observation made by Vierordt at various temperatures between 3.4°–23.8° C. (38° F. and 75° F.) show, for warm-blooded animals, that within this range every rise equal to 5.5° C. (10° F.) causes a diminution of about 33 c.c. (2 cubic inches) in the quantity of carbon dioxide exhaled per minute.

Season of the Year. The season of the year, independently of temperature, materially influences the respiratory phenomena since it influences the metabolism of the body; spring being the season of the greatest, and autumn of the least, activity of the respiratory and metabolic functions.

Purity of the Respired Air. The average quantity of carbon dioxide given out by the lungs constitutes about 4.38 per cent of the expired air; but if the air which is breathed be previously impregnated with carbon dioxide (as is the case when the same air is frequently respired), then the quantity of carbon dioxide exhaled becomes relatively much greater.

Hygrometric State of the Atmosphere. The amount of carbon dioxide exhaled is considerably influenced by the degree of moisture of the atmosphere, much more being given off when the air is moist than when it is dry.

Period of the Day. The respiratory quotient, *i.e.*, the ratio between carbon dioxide eliminated and oxygen absorbed, is greater during the day than during the night. In the day, therefore, the CO_2 exhaled in relation to the O_2 absorbed is increased, and it is diminished during the night. This is probably due to the increased production of CO_2 as a result of increased tissue activity during the day, and, consequently, the breaking down or catabolism of more substances.

Food and Drink. By the use of food the quantity of CO_2 is increased, while by fasting it is diminished; it is greater when animals are fed on farinaceous food than when fed on meat. The effects produced by spirituous drinks depend much on the kind of drink taken. Pure alcohol in very small amounts tends rather to increase than to lessen respiratory changes, and the amount, therefore, of carbon dioxide expired. Rum, ale, and porter, also sherry, have very similar effects. On the other hand, brandy, whisky, and gin in greater amounts almost always lessen the respiratory changes, and, consequently, the amount of the gas exhaled. This is primarily due to their influence on the rate of metabolism in each instance.

Exercise. Bodily exercise, in moderation, increases the quantity of CO_2 expired by at least one-third more than it is during rest. For about an hour after exercise the volume of the air expired in the minute is increased nearly 2,000 c.c., or 118 cubic inches; and the quantity of carbon dioxide about 125 c.c., or 7.8 cubic inches per minute. Violent exercise, such as full labor or athletic competition, still further increases the amount of the carbonic acid exhaled.

The Oxygen is Diminished. Pettenkofer and Voit have found that the mean consumption of oxygen during 24 hours, by a man weighing 70 kilos, is about 700 grams or 490 liters. The quantity of oxygen absorbed increases with muscular exercise, and falls during rest. In general terms the quantity absorbed varies with the activity of the metabolic processes, following very closely the variation of carbon dioxide under the conditions outlined above.

The Volume of the Respired Air is Diminished. When allowance has been made for the expansion in heating, the volume of expired air is decreased.

the loss being due to the fact that a portion of the oxygen absorbed is not returned in the form of carbon dioxide. Since the oxygen of a given volume of carbon dioxide would have the same volume as the carbon dioxide itself at a given temperature and pressure, a portion of the oxygen absorbed must be used for other purposes than the formation of carbon dioxide. In fact, some of it is used in the formation of urea, some in the formation of water, etc. The oxygen in the carbon dioxide exhaled, divided by the oxygen absorbed, gives what is known as the *respiratory quotient;* thus

$$\frac{CO_2 \text{ exhaled}}{O_2 \text{ absorbed}}$$

Normally in man on a mixed diet the respiratory quotient is

$$\frac{4.0 \text{ to } 4.5}{5} = 0.8 \text{ to } 0.9.$$

But it is subject to variation through several causes. For example, through variation in diet. On a pure carbohydrate diet the respiratory quotient will rise above 0.9, *i.e.*, to 1.0, since carbohydrates contain enough oxygen to oxidize the hydrogen in their molecule. On a diet containing much fat it is lowest, since relatively more oxygen is needed completely to oxidize fat. The theoretical respiratory quotient for fats is 0.7. The same is true, but to a less degree, in the case of proteids which also require much oxygen for their complete oxidation. Muscular exertion raises the respiratory quotient, because in its performance carbohydrates are used up in relatively greater quantity.

The Watery Vapor in Respired Air is Increased. The quantity emitted is, as a general rule, sufficient to saturate the expired air, or very nearly so. Its absolute amount is, therefore, influenced by the following circumstances: 1, By the quantity of air respired; for the greater this is, the greater also will be the quantity of moisture exhaled; 2, By the quantity of watery vapor contained in the air previous to its being inspired; because the greater this is, the less will be the amount to complete the saturation of the air; 3, By the temperature of the expired air; for the higher this is, the greater will be the quantity of watery vapor required to saturate the air; 4, By the length of time which each volume of inspired air is allowed to remain in the lungs; for although, during ordinary respiration, the expired air is always saturated with watery vapor, yet, when respiration is performed very rapidly, the air has scarcely time to be raised to the highest temperature or be fully charged with moisture ere it is expelled.

The quantity of water exhaled from the lungs in 24 hours ranges (according to the various modifying circumstances already mentioned) from about 200 to 800 c.c., the ordinary quantity being about 400 to 500 c.c. Some of this is probably formed by the chemical combination of oxygen with hydrogen in the system; but the far larger proportion of it is water which has been

absorbed, as such, into the blood from the alimentary canal, and which is exhaled from the surface of the air-passages and cells, as it is from the free surfaces of all moist animal membranes, particularly at the high temperature of warm-blooded animals.

A Small Quantity of Ammonia is added to the ordinary constituents of expired air. It seems probable, however, both from the fact that this substance cannot be always detected and from its minute amount when present, that the whole of it may be derived from decomposing particles of food left in the mouth, or the teeth, and that it is, therefore, only an accidental constituent of expired air.

The Quantity of Organic Matter in Expired Air is Increased. It was formerly supposed that this organic matter was injurious and gave rise to the unpleasant symptoms which are experienced in badly ventilated rooms. But this has been strongly questioned so that the matter cannot be considered settled at the present time.

THE RESPIRATORY CHANGES IN THE BLOOD.

Pressure and Diffusion of the Air. It must be remembered that the tidal air in the lungs amounts only to from 300 to 500 c.c. at each inspiration. This amount at once mixes with the reserve and the residual air already in the lungs. The mixture is facilitated by the air currents set up in the deeper parts of the lungs by the sudden entrance of the tidal air; but, after all is considered, it will be found that *diffusion* is the greatest factor in producing a uniform mixture of the gases in the alveoli and in the air-cells of the lungs. Just as a fresh supply of oxygen introduced within the door of a closed room will quickly diffuse throughout the space of the entire room so will the fresh tidal air diffuse into the space of the lungs. When the tidal air is expired its average composition has been changed so it has only about 16 per cent of oxygen instead of the usual 20.96 per cent of oxygen in air. The oxygen content of the air still left in the lungs is probably somewhat less than the percentage in this expired air for the reason that the air of the respiratory tree, the trachea, bronchi, and bronchioles, is never fully mixed with the alveolar air.

The partial pressure of the oxygen of the air measured under standard conditions is 159 mm. of mercury, that is, 20.96 per cent of 760 mm. of mercury, the standard pressure of one atmosphere. The partial oxygen pressure in expired air with 16 per cent of oxygen is only 122 mm. of mercury. These figures show a diffusion pressure of at least 37 mm. of mercury to carry oxygen into the deeper recesses of the lungs. The constant loss of oxygen to the blood probably keeps the mean difference greater.

The Gases of the Blood. Turning now to the consideration of the gases of the blood in the lungs, a somewhat different picture presents

itself. The blood is a mass of corpuscles floating in the fluid plasma. An analysis of the blood shows that it contains oxygen, carbon dioxide, and nitrogen, the gases of the air. The usual method is completely to extract the blood gases by an air-pump, figure 237, and determine the quantities in cubic centimeters per 100 c.c. of blood.

The Extraction of the Gases from the Blood. As the ordinary air-pumps are not sufficiently powerful for the purpose, the extraction of the gases from the blood is accomplished by means of a mercurial air-pump, of which there are many varieties, those of Ludwig, Alvergnidt, Geissler, and Sprengel being the chief. The principle of action in all is much the same. Ludwig's pump, which may be taken as a type, is represented in figure 237. It consists of two fixed glass globes, *C* and *F*, the upper one communicating by means of the stopcock, *D*, and a stout India-rubber tube with another glass globe, *L*, which can be raised or lowered by means of a pulley; it also communicates by means of a stopcock, *B*, and a bent glass tube, *A*, with a gas receiver (not represented in the figure), *A* dipping into a bowl of mercury, so that the gas may be received over mercury. The lower globe, *F*, communicates with *C* by means of the stopcock, *E*, with *I* in which the blood is contained by the stopcock, *G*, and with a movable glass globe, *M*, similar to *L*, by means of the stopcock, *H*, and the stout India-rubber tube, *K*.

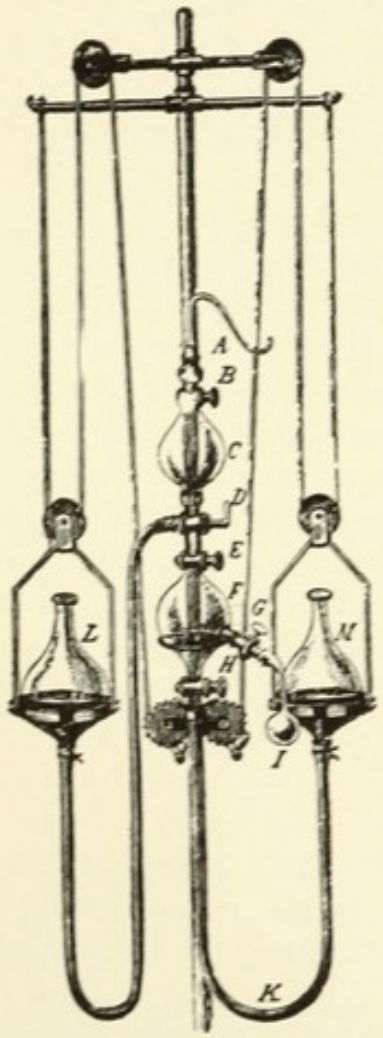


Fig. 237.—Ludwig's Gas-pump.

In order to work the pump, *L* and *M* are filled with mercury, the blood from which the gases are to be extracted is placed in the bulb *I*, the stopcocks *H*, *E*, *D*, and *B* being open, and *G* closed. *M* is raised by means of the pulley until *F* is full of mercury, and the air is driven out. *E* is then closed, and *L* is raised so that *C* becomes full of mercury, and the air driven off. *B* is then closed. On lowering *L* the mercury runs into it from *C*, and a vacuum is established in *C*. On opening *E* and lowering *M*, a vacuum is similarly established in *F*; if *G* be now opened, the blood in *I* will enter ebullition, and the gases will pass off into *F* and *C*, and on raising *M* and then *L*, the stopcock *B* being opened, the gas is driven through *A*, and is received into the receiver over mercury. By repeating the experiment several times the whole of the gases of the specimen of blood is obtained, and may be estimated.

Pflüger's analysis of the arterial blood of the dog gave the following volumes per cent: oxygen 22.6, carbon dioxide 34.3, and nitrogen 1.8. The analysis for the venous blood gives a very much lower oxygen and a higher carbon dioxide per cent. The average oxygen content of venous blood is 10 to 12 per cent and the carbon dioxide 45 per cent. The blood in different veins of the body varies within wide limits as regards its gas content.

	Oxygen.	Carbon Dioxide.	Nitrogen.
100 c.c. Arterial blood.....	22.6 c.c.	34 c.c.	1.7 c.c.
100 c.c. Venous blood.....	12. c.c.	45 c.c.	1.7 c.c.

The large quantity of oxygen found in arterial and in venous blood is the more striking when the facts of absorption of gases by liquids are reviewed. A liquid such as water will, when exposed to a gas, take up the gas by absorption according to definite physical laws. Under constant temperature the amount of gas absorbed, oxygen for example, varies directly as the pressure of the gas, or partial pressure if the gas is a mixture. The oxygen absorbed by water from pure air as compared with expired air is in direct proportion to the partial pressure of oxygen in the two airs, which is as 159 to 122.

The amount of gas absorbed for a unit of fluid under standard temperature and pressure (one atmosphere at 0° C.), called its absorption coefficient, is about the same for blood-plasma as for water. Before one can determine the actual amount of oxygen in the plasma, the tension or absorption pressure must be determined.

The tension of the oxygen in arterial blood is found by an instrument which enables one to measure the pressure at which oxygen is neither absorbed nor given off. The instrument commonly used is called an aërotonometer. The principle of the instrument depends upon the fact that blood exposed to mixtures of the gases in air tends to give up or absorb gases from the air until complete equilibrium is established.

By this means observers have measured the tensions of the blood gases. The results have not been very constant, but the oxygen tension has been found to be from 4 (Strassburg) to 10 (Herter) per cent of an atmosphere. Many determinations have been given of both lower and higher percentages, but, accepting the above limits for a working average, the oxygen tension in arterial blood would be from 30.4 to 76 mm. of mercury.

Blood-plasma exposed to an air with a partial pressure of 30.4 to 76 mm. of mercury would absorb only from 0.1 to 0.3 (0.26 c.c. Pflüger) of a cubic centimeter of oxygen for 100 c.c. of blood. As a matter of fact, 100 c.c. of whole blood contains from 20 to 22 c.c. of oxygen. It is evident that blood cannot hold the oxygen in simple solution, but must retain it in chemical combination. The red blood-corpuscles have been shown to carry the excess of oxygen by virtue of the special respiratory pigment, hemoglobin.

Combining Power of Hemoglobin with Oxygen. One hundred cubic centimeters of blood contain about 14 grams of hemoglobin, page 120. Each gram of hemoglobin, when fully saturated with oxygen, according to Hüfner's earlier determination, combines with 1.56 c.c. of oxygen. By later more careful work he gets the determination of 1.34 c.c. for hemoglobin of ox blood. This last figure indicates that the combining power of the hemoglobin is dependent upon the iron in the molecule, in which one atom of iron combines with one atom of oxygen. The later investigation of the conditions under which hemoglobin combines with oxygen are by Hüfner, on the one hand, and Loewy, on the other. The former worked with purified solutions of hemoglobin, the latter with blood. The average results of the investigations

of these two observers show that when the oxygen tension in the air, which is in contact with the blood, is lowered below a certain point, the amount of oxygen which will be liberated from combination with hemoglobin will be very great, whereas a lowering of the tension of oxygen by an equal amount where the pressures are relatively high leads to practically no liberation of hemoglobin, and the converse is equally true. The critical oxygen pressure in so far as its combination with hemoglobin is concerned varies according to observers. With Loewy the critical dissociation pressure is at or below 76 mm. of mercury, 10 per cent of an atmosphere. Strassburg gives the oxygen tension of arterial blood as 29.64 mm. of mercury, and for venous blood 22.04 mm. of mercury. That is to say, during the brief interval in which the blood is in the pulmonary capillaries the oxygen tension has increased by 7.6 mm. of mercury, an increase of tension which would produce very little increase in simple absorption of oxygen. Yet is it sufficient to cause fixation of from four to five volumes per cent of oxygen by the hemoglobin.

Oxygen Pressure in the Atmosphere.....	159		mm. of mercury
	↓		
" " " Alveolar air.....	122		mm. of mercury
	↓		
" " " Venous blood.....	22.04		mm. of mercury

It is evident that there will be diffusion of oxygen from the high tension toward the lower and in the direction indicated by the arrows in the table above. As fast as the oxygen diffuses into the venous blood, thus tending to raise the pressure of the gas in solution, it is taken up and fixed by the hemoglobin. This process proceeds during the interval the blood is in the pulmonary capillaries far enough to raise the oxygen tension from 22.04 mm. of mercury to 29.64 mm. of mercury, and far enough to permit of the fixation of from four to five volumes per cent of oxygen.

Liberation of Oxygen in the Tissue Capillaries. When the arterial blood reaches the capillaries of the tissues, then the situation which we have just found holding good in the lungs is reversed. As rapidly as the oxygen reaches the living protoplasm of the tissues it enters into fixed combination, thus rendering it inert. The oxygen tension in the tissue cells will, therefore, be zero. Under these conditions the difference in pressure level between the oxygen tension in the blood and that in the tissues is sufficient to cause a rapid diffusion of oxygen through the capillary walls with corresponding liberation of the oxygen from the hemoglobin according to the laws of combination given in the table above. The total effect of this process is to maintain a relatively high diffusion pressure of the oxygen in the blood. During the time the blood remains in the capillaries the total oxygen tension will have been lowered from 29.64 to 22.04 mm. of mercury, yet this slight lowering of tension is sufficient to liberate from four to five volumes per cent of oxygen. This figure, of course, is comparative. In many of the very active

tissues, such as in muscle, a much larger per cent of oxygen will have been disassociated and the oxygen tension correspondingly lowered so that the venous blood returning through such an active organ may not have more than half the average amount of oxygen found in venous blood.

Considering the pressure relations of oxygen from the time of its introduction into the body with the fresh air to its fixation in the tissues we have the following schema:

Oxygen Pressure in the Atmosphere	159 mm.
↓	
" " " Alveolar Air	122 mm.
↓	
" " " Venous Blood	22.04 mm.
Tension of Oxygen in the Arterial Blood	29.64 mm.
↓	
" " " " " Tissues	0.00 mm.

Elimination of Carbon Dioxide by the Blood and the Respiratory Apparatus. The principles of absorption of gas by liquids discussed in the preceding pages apply equally well for carbon dioxide with the exception that carbon dioxide is about three times as soluble in blood as is oxygen. The carbon dioxide results from the oxidative processes going on in the tissues, and this gas is present in large quantities in the tissues and their immediately surrounding lymph. An analysis of the carbon-dioxide content of venous blood reveals the presence of about 45 c.c. of the gas in 100 c.c. of blood. This gas, like oxygen, is held in such large quantity by virtue of the fact that it forms loose chemical combinations in the blood. Of the total quantity not more than 5 per cent is held in simple solution. From 10 to 15 per cent of the total volume is found in firm combination in such forms as carbonates, bicarbonates, etc. The remaining 80 and more volumes per cent is held in loose chemical combination, a combination which is broken up under the same conditions of variation in carbon-dioxide tension as were found to exist for oxygen in combination with hemoglobin. In the case of carbon dioxide an analysis of plasma reveals the fact that the gas is in combination with some compound of the plasma, probably a proteid. In fact, there is some evidence to show that carbon dioxide combines with the globulin group. Carbon dioxide also forms loose chemical compounds with the constituents of the red corpuscles, probably with the proteid portion of the hemoglobin molecule. The pressure relations of this gas as regards its diffusion in the process of elimination are shown in the following table:

Carbon-dioxide Tension in the Tissues	58 mm. of mercury
↓	
" " " " Venous Blood	41 " " "
↓	
" " " " Alveolar Air	23 to 38 mm. of "
↓	
" " " " Expired Air	5.8 mm. " "

Theories of Interchange of Gases in the Lungs and in the Tissues. The above discussion is on the basis of the mechanical interpretation of the transfer of gases in the lungs and in the tissues. By this theory it is assumed that the oxygen passes from the air in the lungs through the moist pulmonary membrane of the alveoli to the capillary walls into the blood-plasma, obeying the physical laws of gas diffusion. Likewise in the tissues this theory presupposes the difference in the mechanical tension in the capillary blood-plasma, the lymph, and the living tissue will lead to diffusion of the oxygen in the direction of lowest pressure.

Some facts have indicated that we cannot account for the transference of oxygen by the purely mechanical theory. The idea has been advanced that the living epithelial wall of the lung, as well as that of the capillary, exerts a distinct influence on the passage of oxygen of such nature as might be regarded as a secretion of this gas. This theory finds some additional support in the fact that in the air bladders of certain fishes a distinct secretion of oxygen has been proven.

THE NERVOUS REGULATION OF THE RESPIRATORY APPARATUS.

Like all other functions of the body the discharge of which is necessary to life, the respiratory movement is essentially an involuntary act. Unless this were the case, life would be in constant danger, and would cease on the loss of consciousness for a few moments, as in sleep. It is, however, of advantage to the body that respiration should be to some extent under the control of the will. For, were it not so, it would be impossible to perform those respiratory acts such as speaking, singing, and the like.

The Respiratory Nerve Center. It has been known for centuries that there exists a region of the central nervous system on the destruction of which both respiration and life cease. Flourens, 1842, after many series of experiments as to the exact position of what he called the "knot of life" (*nœud vital*), placed it in the fourth ventricle, at the point of the V in the gray matter at the lower end of the calamus scriptorius; a district of considerable size, 5 mm., on both sides of the middle line. Observers subsequent to Flourens have attempted to show that the chief respiratory center, on the one hand, is situated higher up in the nervous system, in the floor of the third ventricle (Christiani), or in the corpora quadrigemina (Martin and Booker, Christiani, and Stanier), or lower down in the spinal cord. The balance of experimental evidence, however, is to prove that the sole centers for respiration are in a limited district in the medulla oblongata in close connection with the vagus nucleus on each side, with which they are probably identical. The destruction of this region stops respiration. If the center be left in connection with the muscles of respiration by their nerves, although the

remainder of the central nervous system be separated from it, respiration continues. It may be considered almost certain that the medullary center is the only true respiratory center. Langendorff states that in newly born animals in which the medulla has been immediately cut across at a level a few millimeters below the point of the calamus scriptorius, respiration continues for some time, but this is questionable. Normal respiration does not occur after separation of the bulb from the cord, and the so-called respiratory movements noticed by Langendorff are merely tetanic contractions of the respiratory muscles in which often enough other muscles take part.

The action of the medullary center is to send out impulses during inspiration, which cause contractions of the inspiratory muscles—*a*, of the nostrils and jaws, through the facial and inferior division of the fifth nerves; *b*, of the glottis, chiefly through the inferior laryngeal branches of the vagi; *c*, of the intercostal and other muscles which produce raising of the ribs, chiefly through the intercostal nerves, and *d*, of the diaphragm, through the phrenic nerves. If any one of these sets of nerves be divided, respiratory movements of the corresponding muscles cease. Similarly it may be supposed that the center sends out impulses during expiration to certain other muscles. It has been suggested, however, that the center is double, that it is made up of inspiratory cells which are constantly in action, and of an expiratory group of cells which act less generally, inasmuch as ordinary tranquil expiration is seldom more than an elastic recoil, and not a muscular act to any marked degree.

The respiratory center is also bilateral, as has been proven by the method of antero-posterior section of the medulla. The tracts from each half of the center are separate and distinct. If the cervical cord be split into a right and left half, and one side sectioned at the level of the second cervical vertebra, then the respiratory movements of that side of the diaphragm cease while on the opposite side they continue their rhythm.

Assuming this view of the quadruple nature of the respiratory centers to be correct, there is some difference of opinion of the exact mode of action; it is thought that the center may act automatically, but normally is influenced by afferent impulses from the periphery, as well as by impulses passing down from the cerebrum. The center is, in other words, both *automatic* and *reflex*. It will be simplest to discuss its reflex function first.

Action of Afferent Stimuli on the Respiratory Rhythm. *Action of the vagi.* If both vagi be divided in the neck, the respirations become much slower and deeper. This may be the case, but to a less marked degree, if one of the nerves is divided instead of both. If the central end of the divided nerve be stimulated with a weak but properly adjusted strength of interrupted current, the effect is that the respirations are quickened, and if the stimuli are properly regulated the normal rhythm of respiration may

be resumed. If the stimuli be repeated with stronger currents, the breathing is brought to a standstill, sometimes at the height of inspiration, by tetanus of the diaphragm. Usually, however, stimulation of the central end of the divided vagus produces still greater slowing than that which follows the division so that the respirations cease with the diaphragm in a condition of complete relaxation.

The action of the vagus may be to call forth either inspiration or expiration—the impulses passing up the vagi being necessary to the production of the normal respiratory rhythm. The fibers of the vagus are used under the following circumstances: those fibers which tend to inhibit expiration and to stimulate inspiration are stimulated at their origin in the lung when the

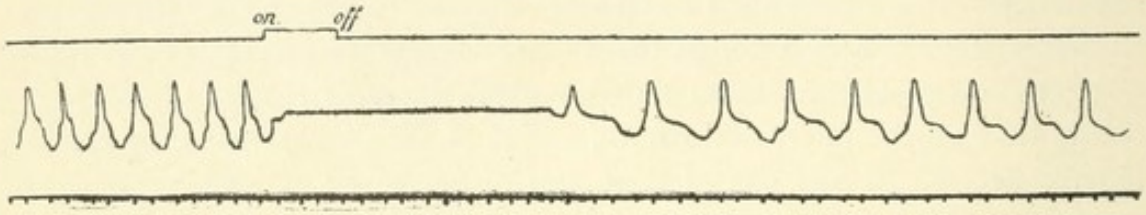


FIG. 239.—The Effect of Stimulating the Vagus Nerve on Respiratory Rate. The stimulus was applied between the points "on" and "off." The inhibition lasts some seconds after the stimulus is removed. Time in seconds. The intratracheal pressure is recorded.

lung is empty and in a condition of expiration, and the fibers which tend to inhibit inspiration and to promote expiration are stimulated when the lung is fully expanded. The afferent impulses by this view are the results of mechanical stimulation, and do not depend altogether upon the chemical nature of the gases within the pulmonary alveoli.

Action of the Superior Laryngeal Nerves. If the superior laryngeal branch of the vagus be divided, which usually produces no apparent effect, and the central end be stimulated, the effect is very constant,—respirations are slowed, but there is a tendency toward expiration, as is shown by the contraction of the abdominal muscles. Thus, the vagus contains fibers which stimulate inspiration and inhibit expiration, as well as other fibers which have the reverse effect; while the superior laryngeal fibers inhibit inspiration and stimulate expiration.

The superior laryngeal nerves are true expiratory nerves, and are normally set in action when the mucous membrane of the larynx is irritated. They are not in constant action like the vagi.

Action of the Glosso-pharyngeal Nerves. It has been ascertained, by the researches of Marckwald, that while division of the glosso-pharyngeal nerves produces no effect upon respiration, stimulation of them causes inhibition of inspiration for a short period. This action accounts for the very necessary cessation of breathing during swallowing. The effect of the stimulation is only temporary, and is followed by normal breathing movements.

Action of Other Sensory Nerves. The respiratory center is in-

fluenced strongly by afferent nerve impulses having their origin in general sensory nerves, particularly the nerves of the skin. Cold water suddenly applied to the surface of the skin is almost invariably followed by a deep inspiration. Stimulation of the splanchnics and of the abdominal branches of the vagi produces expiration. Stimulation of the isolated sciatic nerve of the dog or the rabbit causes a marked acceleration both of the rate and the amplitude of the respiratory movements, see figure 246. This acceleration is due to afferent impulses which reach the respiratory center in the medulla over sensory paths, paths which are not necessarily special respiratory afferent paths, but rather are general afferent paths which affect the respiratory center through their numerous collaterals in the brain stem.

It must be remembered that, although on stimulation many sensory nerves may be made to produce an effect upon the respiratory centers, there is no evidence to show that any one of them, except the vagi, is constantly in action. The vagi indeed are, as far as we know, the normal regulators of respiratory movements, yet one must remember that it is possible reflexly to influence the respiration rate and depth through reflexes that may have their sensory origin in any part of the body.

The respiratory center is also influenced by nerve activity of the cerebral cortex, psychic activity. This is illustrated by the limited voluntary control of the respiration movements.

Automatic Action of the Respiratory Centers. Although it has been very definitely proved that the respiratory centers may be affected by afferent stimuli, and particularly by those reaching them through the vagi, there is reason for believing that the center is capable of sending out efferent impulses to the respiratory muscles without the action of any afferent stimuli. Thus, if the brain be removed above the bulb, respiration continues. If the spinal cord be divided immediately below the bulb, the facial and laryngeal respiratory movements continue, although no afferent impulses can reach the center except through the cranial sensory nerves, and these indeed may be divided without producing any effect, when the bulb and cord are intact. As has been shown, too, respiration continues when the vagi are divided. Isolation of the respiratory center from its sensory relations does not destroy respiratory movements so long as the motor paths through the phrenic nerve are intact. All of these experiments render it highly probable that afferent impulses are not required in order that the respiratory centers should send out efferent impulses to the respiratory muscles. The center, then, is automatic.

Method of Automatic Stimulation of the Respiratory Center. The respiratory center is capable of working automatically apart from afferent impulses, and this fact has been explained by the supposition that it is stimulated to action by the condition of the blood circulating through it. When the blood becomes more and more venous the action of the center becomes

more and more energetic, and if the air is prevented from entering the chest, the respiration in a short time becomes very labored. If the aëration of the blood is much interfered with, not only are the ordinary respiratory muscles employed, but also those muscles of extraordinary inspiration and expiration which have been previously enumerated. Thus, as the blood becomes more and more venous, and by venous we mean that the blood contains a relatively large amount of carbon dioxide and a diminished amount of oxygen, the action of the medullary center becomes more and more profound. The question has been much debated as to what quality of the venous blood it is which causes this increased activity; whether it is its deficiency of oxygen or its excess of carbon dioxide. It has been answered to some extent by experiments which offer no obstruction to the exit of carbon dioxide, as when an animal is placed in an atmosphere of nitrogen. Under these conditions dyspnea occurs, showing that blood which contains a diminished amount of oxygen stimulates the cells of the respiratory center. On the other hand, if the normal amount of oxygen is supplied while the carbon dioxide of the blood is prevented from escaping and thus allowed to accumulate in the blood, there is also a great increase in the respiratory activity of the center; an excess of carbon dioxide in the blood, flowing through the respiratory center, stimulates the cells to greater activity. It is highly probable, therefore, that the respiratory centers may be stimulated to action both by the absence of sufficient oxygen in the blood circulating in it, and by the presence of an excess of carbon dioxide.

These facts are particularly well supported by the experiments of Zuntz who varied the oxygen and the carbon-dioxide content of the air breathed, and measured the volume breathed per minute. When the oxygen of the air breathed was reduced by 10 to 50 per cent, the air breathed was increased only slightly, 5 to 10 per cent. When the oxygen of the air was reduced by 60 per cent, the volume of air breathed was increased 30 to 40 per cent, and even more. Other observations show us that the oxygen in the blood in these experiments will fall in much less per cent than the reduction in the oxygen of the air would lead us to suspect.

When Zuntz kept the oxygen content of the air about constant, but increased the carbon-dioxide content, then the amount of air breathed was greatly increased. Air containing 18.4 per cent of oxygen and 11.5 per cent of carbon dioxide increased the amount breathed per minute from 7.5 liters to 32.5 liters. These experiments indicate that within the limits of the normal variations in blood the carbon dioxide has a much greater influence than oxygen on the irritability of the cells of the respiratory center.

But this is not all, since it has been observed by Marckwald that the medullary center is capable of acting for some time in the absence of any circulation, and after excessive bleeding. The view taken by this author with regard to the action of the center is as follows: The respiratory center

is set to act by the condition of its metabolism, much in the same way as the heart is set to beat rhythmically. When anabolism is completed, catabolism or discharge occurs, and this alternate but crude and spasmodic action will occur without a definite blood supply so long as the centers are properly nourished and stimulated by their own intercellular fluid. It is unreasonable to think, however, that the respiratory center is independent of the character of the blood supply, either as regards quantity or quality of the blood. It has also been shown that the presence of the products of great muscular metabolism in the blood will greatly increase the irritability of the respiratory center, even if the blood itself be not particularly venous in character.

The Establishment of Respiratory Movements at Birth. From the preceding paragraph it appears that the regulation of the respiratory movements is normally due to the automaticity of the respiratory center as influenced, first, by the blood flowing through it and, second, by the afferent nerve impulses which reach the center. The fetus in the womb is supplied by arterial blood from the blood-vessels of the mother. The fetus does not ordinarily give respiratory movements before birth, but it may be made to do so by experimental procedure. At birth the placental circulation is suddenly interrupted, and the blood rapidly increases in venosity until the skin, lips, and mucous membranes are very cyanotic in appearance. It is at this time that the respiratory center begins its rhythmic discharges, being aroused by the direct stimulating effects of the strongly venous blood. It is more than possible that the irritability of the center is also increased by the stimulation of the skin by the air, the contact with clothing, and the hands of the nurse. We have already seen that cutaneous stimulation leads to increase in both respiratory rate and amplitude even in the adult. The primary stimulus for the establishment of the respiratory rhythm at birth, then, is the venosity of the blood, but this cause is supported by the general reflexes which reach the respiratory center.

Certain Special Types of Respiration. Whatever the exact quality of the venous blood which excites the respiratory center to produce normal respirations, there can be no doubt that, as the blood becomes more and more venous from obstruction to the entrance of air into the lung, or from the blood not taking up from the air its usual supply of oxygen, the respiratory center becomes either less or more active and excitable. Conditions ensue which have received the names *Apnea* (diminished breathing), *Hyperpnea* (excessive breathing), *Dyspnea* (difficult breathing), and *Asphyxia* (suffocation).

Apnea. This is a condition of diminished respiratory movement. When we take several deep inspirations in rapid succession by voluntary effort, we find that we can do without breathing for a much longer time than usual; in other words, several rapid respirations seem to inhibit for a time normal

respiratory movements. The reason for this partial cessation of respiration, or *apnea*, is not that we overcharge our blood with oxygen, as was once thought, for Hering has shown that animals in a condition of apnea may have less oxygen in their blood than in a normal state, although the carbon dioxide is less. It is probable that the cause of apnea is that by rapid inflations of the lungs impulses pass up by the vagi, by means of which inspiration is after a while inhibited; or that by the repeated stimulation of the center by vagus impulses which result in rapid respiratory movements, anabolism is at last arrested. Apnea is with difficulty produced, if at all, when the vagi are divided.

Asphyxia. The condition of stress in the respiratory apparatus brought about by insufficient respiratory activity leads to a condition of asphyxia. Progressive asphyxiation may be brought on by anything which interferes with the normal interchange of the respiratory gases of the blood.

Asphyxia may be produced by the prevention of the due entry of oxygen into the blood, either by direct obstruction of the trachea or other part of the respiratory passages, or by introducing instead of ordinary air a gas devoid of oxygen, or, by interference with the due interchange of gases between the air and the blood.

The symptoms of asphyxia may be divided into three groups, which correspond with the stages of the condition which are usually recognized; these are: 1, the stage of exaggerated breathing, hyperpnea; 2, the stage of convulsions, dyspnea; 3, the stage of exhaustion, asphyxiation.

In the *first stage* the breathing becomes more rapid and at the same time deeper than usual, the inspirations at first being especially exaggerated and prolonged. This is soon followed by a similar increase in the expiratory efforts being aided by the muscles of extraordinary expiration. This stage is usually called *hyperpnea*. Hyperpnea soon passes into a condition of labored breathing in which there is marked increase of the force of the expiratory as well as the inspiratory act, a condition described as *dyspnea*. All the muscles capable of aiding either directly or indirectly in respiration are ultimately brought into action. These respiratory convulsions are followed by rather sudden onset of paralysis of the respiratory center and death.

The *conditions of the vascular system* in asphyxia are: 1, more or less interference with the passage of the blood through the systemic and the pulmonary blood-vessels; 2, accumulation of blood in the right side of the heart and in the systemic veins; 3, circulation of impure (non-aërated) blood in all parts of the body, especially through the respiratory center.

Cheyne-Stokes' breathing is a rhythmical irregularity in respirations which has been observed in various diseases. Respirations occur in groups; at the beginning of each group the inspirations are very shallow, but each successive breath is deeper than the preceding, until a climax is reached, after which the inspirations become less and less deep, until they cease altogether for

a time, after which the cycle is repeated. This phenomenon appears to be due to the want of action of some of the usual cerebral influences which pass to and regulate the discharges of the respiratory center.

Effects of Vitiated Air. *Ventilation.* As the air expired from the lungs contains a large proportion of carbon dioxide and a minute amount of organic matter, it is obvious that if the same air be breathed again and again, the proportion of carbon dioxide and organic matter in it will constantly increase till it becomes unfit to breathe; long before this point is reached, however, uneasy sensations occur, such as headache, languor, and a sense of oppression. It is a remarkable fact, however, that the organism after a time adapts itself to a very vitiated atmosphere, and that a person soon comes to breathe, without sensible inconvenience, an atmosphere which, when he first enters it, feels intolerable. Such an adaptation, however, can take place only at the expense of a depression of all the vital functions, which must be injurious if long continued or often repeated. This power of adaptation is well illustrated by an experiment of Claude Bernard. If a sparrow is placed under a bell-glass of such size that it will live for three hours, be taken out at the end of the second hour (when it could have survived another hour), and a fresh healthy sparrow introduced, the latter will die at once.

It must be evident that provision for a constant and plentiful supply of fresh air, and the removal of that which is vitiated, are of greater importance than the actual cubic space per person of occupants. Not less than 2,000 cubic feet per individual should be allowed in sleeping apartments (barracks, hospitals, etc.), and with this allowance the air can be maintained at the proper standard of purity only by such a system of ventilation as provides for the supply of 1,500 to 2,000 cubic feet of fresh air per person per hour.

Effects of Breathing Gases Other than the Atmosphere. Asphyxiation is produced by the direct poisonous action of such gases as *carbon monoxide*, which is contained to a considerable amount in common coal gas. The fatal effects often produced by this gas (as accidents from burning charcoal stoves in small, close rooms) are due to its entering into combinations with the hemoglobin of the blood-corpuscles and thus preventing the formation of oxyhemoglobin because of the more stable carbon-monoxide hemoglobin. The partial pressure of oxygen in the atmosphere may be considerably increased without much effect in displacing the carbon monoxide, hence this is rapidly fatal when breathed. *Hydrogen* may take the place of nitrogen with no marked ill effect, if the oxygen is in the usual proportions. *Sulphureted hydrogen* destroys the hemoglobin of blood and thus produces oxygen starvation. *Nitrous oxide* acts directly on the nervous system as a narcotic, and may also form a compound with hemoglobin. Certain gases, such as *carbon dioxide* in more than a certain proportion, *sulphurous acid gases*, *ammonia*, and *chlorine*, produce spasmodic closure of the glottis and prevent respiration.

Alteration in the Atmospheric Pressure. The normal condition of breathing is that the oxygen of the air breathed should be at the pressure of 20.96 per cent of the atmosphere, that per cent of 760 mm. of mercury, or 159 mm. But it is found that life may be carried on by gradual diminution of the oxygen pressure to considerably less than one-half of this, to a partial pressure of 76 mm. of oxygen, *i.e.*, the oxygen of one-half an atmosphere. This pressure is reached at an altitude above 15,000 feet.* Any pressure less than this may begin to produce alterations in the relations of the gases in the blood, and if an animal is subjected suddenly to a marked decrease of barometric pressure, and so of oxygen pressure (below 7 per cent of oxygen), it is thrown into convulsions. It is found that the gases are set free in the blood-vessels, no doubt carbon dioxide and oxygen as well as nitrogen, although the latter is the only one of the three gases the presence of which has been proven in the vessels in death from this condition of affairs. The other gases are said to be reabsorbed. Other derangements may precede this, bleeding from the nose, dyspnea, and vascular incoordination, etc. On the other hand, the oxygen may be gradually increased to a considerable extent without marked effect, even to the extent of 8 or 10 atmospheres, but when the oxygen pressure is increased up to 20 atmospheres the animals experimented upon by Paul Bert died with severe tetanic convulsions.

THE EFFECT OF RESPIRATION ON THE CIRCULATION.

As the heart, the aorta, and pulmonary vessels are situated in the air-tight thorax, they are exposed to a certain alteration of pressure when the capacity of the latter is varied in respiration. The disturbance of pressure which occurs during inspiration causes, first, a decrease in the intrathoracic cavity, a decrease in pressure which affects all the organs of the thorax—the lungs, the great blood-vessels, the heart. The expansion of the elastic lungs counterbalances this change in pressure in part, but it never does so entirely, since part of the pressure within the lungs is expended in overcoming their elasticity. The amount thus used up increases as the lungs become more and more stretched, so that the intrathoracic pressure during inspiration, as far as the heart and great vessels are concerned, never quite equals the intra-pulmonary pressure, and at the conclusion of inspiration is considerably less than the atmospheric pressure. It has been ascertained that the amount of the pressure used up in the way above described varies from 5 to 7 mm. of mercury in ordinary inspiration, to 30 mm. of mercury at the end of a deep inspiration. So it will be understood that the pressure to which the heart and great vessels are subjected diminishes as inspiration progresses, and at

* For an interesting account of the symptoms produced by diminished atmospheric pressure by very high altitudes, consult Whymper's "Travels amongst the Andes of the Equator."

its minimum is less by from 7 to 30 mm. than the normal atmospheric pressure, 760 mm. of mercury. It will be understood from the accompanying diagram how an increase in the volume of the thorax will have the effect of pumping blood into the heart from the veins. During inspiration the pressure outside the heart and great vessels is diminished, and they, by virtue of their elasticity, have therefore a tendency to expand and to diminish the intravascular pressure. The diminution of pressure within the veins passing to the right auricle and within the right auricle itself, will draw the blood into the thorax, and so assist the circulation. This suction action of the thorax is the cause of the slight negative pressure of the ventricle previously described. The effect of more blood in the right auricle will, *cæteris paribus*, increase the amount passing through the right ventricle, and through the lungs into the left auricle and ventricle, and thus into the aorta. This all tends to increase the blood pressure. The effect of the

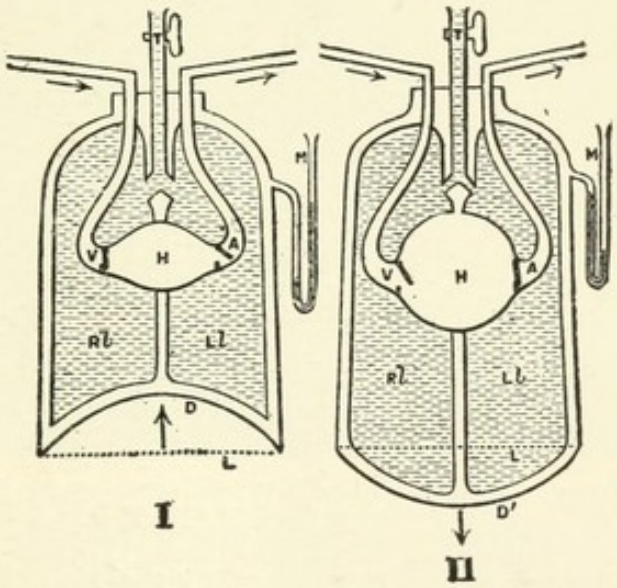


FIG. 240.—Diagram of an Apparatus Illustrating the Effect of Inspiration upon the Heart and Great Vessels within the Thorax. I, The thorax at rest; II, during inspiration; *D* represents the diaphragm when relaxed; *D'*, when contracted (it must be remembered that this position is a mere diagram), *i.e.*, when the capacity of the thorax is enlarged; *H*, the heart; *V*, the veins entering it, and *A*, the aorta; *Rl*, *Ll*, the right and left lung; *T*, the trachea; *M*, mercurial manometer in connection with pleura. The increase in the capacity of the box representing the thorax is seen to dilate the heart as well as the lungs, and so to pump in blood through *V*, whereas the valve prevents reflux through *A*. The position of the mercury in *M* shows also the suction which is taking place. (Landois.)

diminished pressure upon the pulmonary vessels will also help toward the same end, an increased flow through the lungs, so that, as far as the mechanical effects on the heart and its veins are concerned, inspiration increases the blood pressure in the arteries. The effect of inspiration upon the aorta and its branches within the thorax would be, however, contrary; for as the external pressure is diminished, the vessels would tend to expand, and thus to diminish the tension of the blood within them, but, inasmuch as the relative variation in pressure on the large arteries is slight, the diminution of arterial tension caused by this means will be insufficient to counteract the

increase of blood pressure produced by the effect of inspiration upon the volume of discharge of the veins of the chest, and the balance of the whole action would be in favor of an increase of blood pressure during the inspiratory period. When a blood-pressure tracing is taken at the same time that the respiratory movements are being recorded, it will be found that, although, speaking generally, the arterial tension is increased during inspiration, the maximum of arterial tension does not correspond with the acme of inspiration, figure 241. In fact, at the beginning of inspiration the pressure continues to fall for a brief moment, then gradually rises until the end of inspiration, and continues to do so for a moment after expiration has commenced. For explanation of the influence of heart rate in this variation of blood pressure, associated with the respiratory movement, see page 181.

In ordinary expiration all this would be reversed, but if the abdominal muscles are violently contracted, as in extraordinary expiration, the same

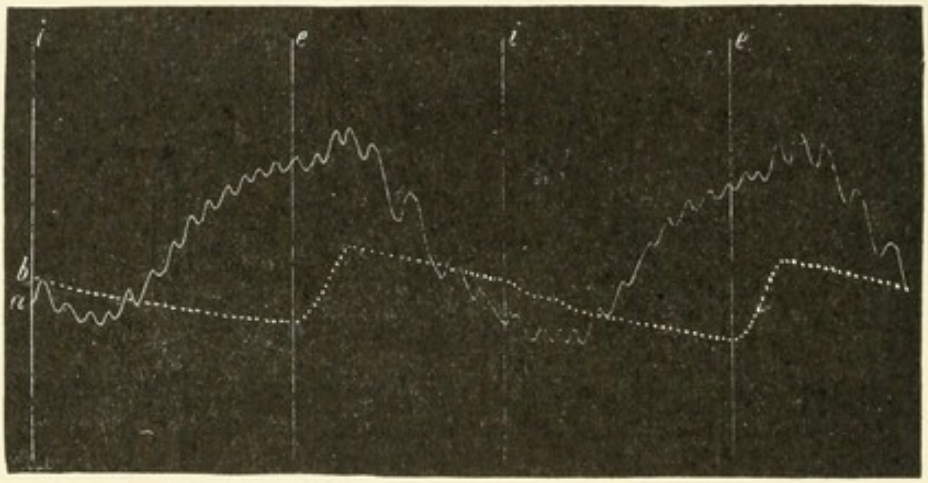


FIG. 241.—Comparison of Blood-Pressure Curve with Curve of Intrathoracic Pressure. (To be read from left to right.) *a* is the curve of blood pressure with its respiratory undulations, the slower beats on the descent being very marked; *b* is the curve of intrathoracic pressure obtained by connecting one limb of a manometer with the pleural cavity. Inspiration begins at *i* and expiration at *e*. The intrathoracic pressure rises very rapidly after the cessation of the inspiratory effort, and then slowly falls as the air issues from the chest; at the beginning of the inspiratory effort the fall becomes more rapid. (M. Foster.)

relative effect would be produced as by inspiration. The immediate effect during inspiration of the diminished intrathoracic pressure upon the pulmonary vessels is to produce an initial dilatation of both artery and veins, and this delays for a moment the passage of blood toward the left side of the heart, resulting in an initial fall in the arterial pressure, but the fall of blood pressure is immediately followed by a steady rise, since the flow is increased by the initial dilatation of the vessels. The converse is the case with expiration. As, however, the pulmonary veins are more easily dilatable than the pulmonary artery, their greater distensibility increases the flow of blood as inspiration proceeds, while during expiration, except at its beginning, this property of theirs acts in the opposite direction, and diminishes the flow. Thus, at the beginning of inspiration the diminution of blood pressure, which

commenced during expiration, is continued, but after a time the diminution is succeeded by a steady rise. The reverse is the case with expiration—at first a rise and then a fall.

As regards the effect of *expiration*, the capacity of the chest is diminished and the intrathoracic pressure returns to the normal, which is still slightly below the atmospheric pressure. The effect of this on the veins is to increase their extravascular and so their intravascular pressure, and to diminish the flow of blood into the left side of the heart, and with it the general blood pressure. Ordinary expiration does not produce a distinct obstruction to the circulation, as even when the expiration is at an end the intrathoracic pressure is less than the extrathoracic. The effect of violent expiratory efforts, however, does have a distinct action in obstructing the current of blood through the lungs, as seen in the congestion in the exaggerated condition of straining, this condition being produced by pressure on the entire group of pulmonary vessels.

There are other mechanical factors, such, for example, as the effect of the abdominal movements, both in inspiration and in expiration, upon the arteries and veins within the abdomen and of the lower extremities, and the influence of the varying intrathoracic pressure upon the pulmonary vessels, both of which ought to be taken into consideration. As regards the first of these, the effect during inspiration—as the cavity of the abdomen is diminished by the descent of the diaphragm—should be twofold: on the one hand, blood would be sent upward into the chest by compression of the vena cava inferior; on the other hand, the passage of blood downward from the chest in the abdominal aorta, and upward in the veins of the lower extremity, would be to a certain extent obstructed.

LABORATORY EXPERIMENTS IN RESPIRATION.

1. **Respiratory Rate in Man.** Count your respirations for from 2 to 4 minutes while sitting quietly, and determine the average number per minute. Repeat the counting after standing for 5 minutes, and after brisk exercise. These determinations involve the element of consciousness, under which condition it is difficult for a person to breathe with his normal rate and depth.

Make a series of determinations of respiratory rates of persons who are sitting quietly but unconscious of your determinations. Count the rates in a number of persons of different ages; where possible, take into consideration height, weight, etc. Tabulate the results for a comparison and for future reference.

2. **The Character of Respiratory Movements in Man.** A number of instruments have been devised for measuring human respiratory movement, many of which measure the change in diameter of the chest in respira-

tory movemen.. Adjust one of these, for example Burdon-Sanderson's stethograph, to the thorax, and record the movement of the receiving tambour on a smoked-paper kymograph which travels at the rate of 1 cm. per second. This record, called a *stethogram*, will exhibit the respiratory rate, the relative time of the inspiratory and expiratory phases, and the character of each.

3. **The Actual Change of Diameter in the Chest in Respiration.** Use a caliper provided for the purpose and measure the dorso-ventral diameter of the chest at a series of points along the sternum, taking the reading

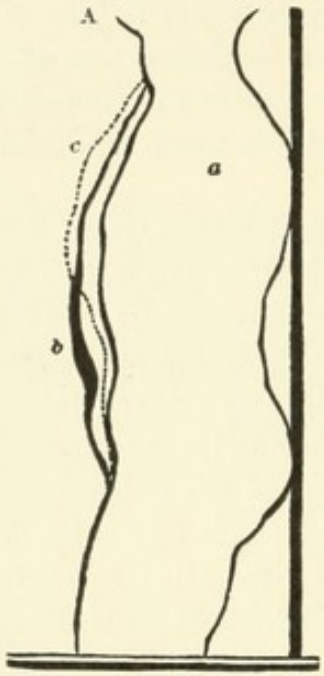


FIG. 242.—Change in Diameter of the Body in Respiration, Costal Type. *a*, Outline of the body in forced expiration. In the heavy continuous line, *b*, the outer margin indicates the contour of the body in ordinary inspiration and the inner margin that of ordinary expiration. *c*, Contour of forced inspiration. (After Hutchinson.)

at the height of the inspiratory phase and of the expiratory phase in ordinary respiration. Repeat the measurement in forced respiration. Map the results on millimeter paper, as indicated in figure 242.

Repeat these measurements in the transverse diameter at the first, fifth, and tenth ribs.

Using the chest pantograph, figure 243, record the outline of the chest at the level of the middle of the sternum during expiration and at the end of inspiration.

4. **The Volume of Air Breathed by Man.** Determine the average volume of air breathed per respiration, using Hutchinson's spirometer, figure 235, set the instrument at the zero point, exhale into the instrument through the tube, using all possible care to breathe with your normal rate and depth. Better results will be obtained by taking the average from sets of ten consecutive inspirations into the instrument. From the average of the volume per

respiration, and the average number of respirations per minute, determined in experiment 1, calculate the amount of air breathed per hour and per day.

5. **Vital Capacities.** Using the spirometer as in the preceding experiment, set the instrument at zero and exhale into it: *a*, Begin with the fullest possible inspiration and exhale the greatest possible amount of air from the lungs. This is known as the *vital capacity*.

b, Beginning at the end of an ordinary expiration exhale into the instrument the greatest possible amount. This is called the *reserve air*.

c, Following ordinary inspiration exhale into the instrument until you reach the ordinary state of expiration. This involves the conscious fixing of two points in the respiratory act, namely, the summit of inspiration and expiration, which are ordinarily automatically adjusted by the body. The error of the determination is therefore great. It is better to make this measurement in sets of ten, as in the preceding experiment, and take the average.

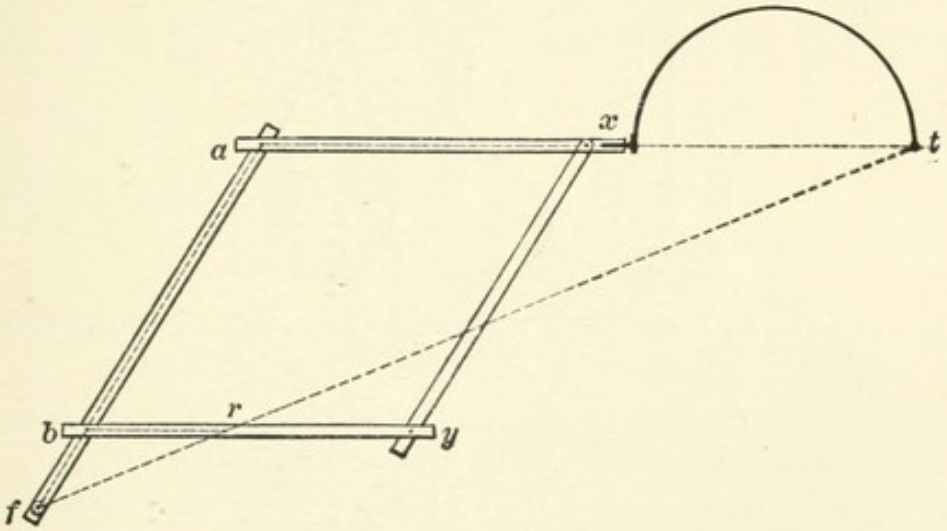


FIG. 243.—The Chest Pantograph for Recording the Outlines of the Chest. The fixed point in the instrument is *f*; the points *a*, *b*, *x*, *y*, are movable joints; when point *t* is made to trace the outline of the chest, point *r* will give a corresponding movement and can be made to trace this movement on recording paper. (Hall.)

This reduces the error. This quantity of air is known as the *tidal air*. One can measure the tidal air and the reserve air together, check them against the sum of the two, as in *a* and *b* separately.

The sum of the tidal and reserve air taken from the vital air will leave the amount which one may inspire over and above that in the chest at the end of ordinary inspiration. This is called *complemental*. The complemental can be measured by inspiring the air from the spirometer, but this is not good hygiene where large numbers are using the same instrument, unless the instrument be thoroughly cleaned before the inspiration is taken.

6. **The Respiratory Pressure in Man.** Measure the respiratory pressure, the pressure of the air in the air-passages, by means of the mercury manometer, or by a graduated Marey's tambour. Connect the piece of

gas tubing with the proximal limb of the mercury manometer and provide it with a glass mouthpiece. Insert this mouthpiece well back into the cavity of the mouth, closing the lips firmly about it, leaving the pharyngeal muscles relaxed. Note the variations in pressure at the height of ordinary inspiration and expiration, with the nasal passages open. Repeat with forced inspiration and expiration, close the nasal passages, and make the maximal expiratory and inspiratory effort. The manometer may be adjusted to write on the smoked paper, or one may read the variations directly from the manometer schedule, in which case it facilitates the reading if one clamps the rubber tube at the moment the reading is desired.

7. **Demonstration of Carbon Dioxide in Expired Air.** Arrange two flasks, as in figure 244, filling each one-third full of baryta water, or

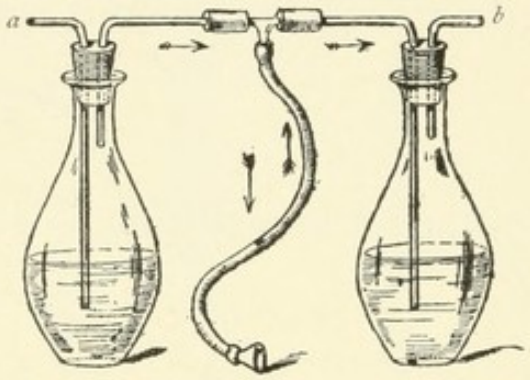


FIG. 244.—Apparatus for Demonstrating Excess of CO_2 in Expired Air. Flasks filled with lime-water.

lime-water. Close the lips around the mouthpiece of the apparatus and inhale and exhale the air through it; close the nostrils if necessary. The inspired air will come through *a*, the expired air out through *b*. The baryta water in *b* will quietly become clouded with a white precipitate, while that in *a* will remain clear or only very slightly clouded, showing the excess of carbon dioxide in expired air.

8. **Quantitative Determination of Carbon Dioxide and Oxygen in Inspired Air and in Expired Air, by Hempel's Method.** *Inspired Air.* Fill a gas buret, see figure 236, with water and close the pinch-cock. Fill it with air taken outside the laboratory. Measure the volume of gas contained at the ordinary temperature and barometric pressure of the laboratory. Connect with a potash pipet, drive the air over into the bulb of the pipet, shake it up until all the carbon dioxide is absorbed. Draw the air back into the buret and measure. The amount of carbon dioxide in the external air is usually so small that it is difficult to measure by this method. Now connect the buret with a pipet containing pyrogallic acid, run the air over into the pyrogallic-acid bulb and shake up thoroughly until no further excess is absorbed, then remeasure the excess in the buret. The loss in volume is due to the absorption of oxygen; the air remaining in the

buret is nitrogen. Compute the amount of carbon dioxide, oxygen, and nitrogen from the results of your test.

Expired Air. Take a large sample of expired air by breathing through a large tube into a gallon aspirator bottle. This is large enough to hold six or eight expirations. Now fill the gas buret with a sample of this expired air and analyze as before, first for carbon dioxide, then for oxygen; compute the percentage of each gas, including nitrogen. The expired air will usually be found to have lost from 4 to 5 per cent of oxygen and have gained a little more than that quantity of carbon dioxide.

From the percentages obtained in these experiments, and the volume of air breathed per unit of time, computed in experiment 4 above, determine the amount of carbon dioxide exhaled per hour per kilogram of weight for your own body. Compute also the amount of oxygen consumed.

9. **The Rate and Character of the Respiratory Movements in the Mammal.** *a*, The rate of respiration can be best determined by direct count per minute, an effort being made to keep the animal under as

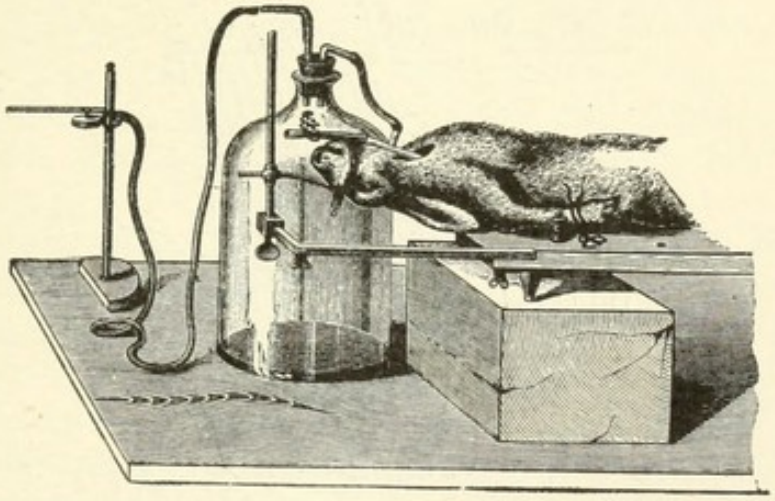


FIG. 245.—Arrangement of Tracheal Cannula and Marey's Tambour for Recording the Changes in Intratracheal Pressure during Respiration. (Langendorff.)

nearly normal conditions as possible; make the same determinations on a cat, a dog, and guinea-pig. *b*, The character of the respiratory movements can be recorded by one of the various forms of stethograph adapted to the size of the animal, or by the arrangement shown in figure 245. It is usually better to make the determination with the animal under the influence of an anesthetic.

10. **The Determination of Carbon Dioxide Given Off in the Mammal.** This determination can be made only by placing the animal in a respiratory calorimeter, and making the following measurements:

a. The amount of air which passes through the animal chamber, the calorimeter.

b. The percentage of carbon dioxide in the air which is in the chamber.

c. The percentage of carbon dioxide in the air which leaves the chamber.

If the animal is small enough, for example, the guinea-pig or a mouse, the absorption tubes may be constructed of proper size to absorb all the carbon dioxide passing through the chamber, and the total quantity of any unit of time determined directly in grams. If now the animal is weighed at the moment it is introduced into the cage, then the amount of carbon dioxide per kilo weight can be quickly computed.

Calorimeters for larger animals require a larger volume of ventilation, and the usual procedure is to measure the percentage in a sample as directed above.

11. **The Nervous Mechanism of Respiratory Movement.**

a. The Effect of Stimulating Cutaneous Nerves. Use a small dog or a cat for this experiment; anesthetize and introduce a tracheal tube with a side branch adapted for measuring the variations of pressure during respiration. Connect the free limb of the tracheal tube with an ether apparatus and adjust to secure constant anesthesia. Connect the side branch of the

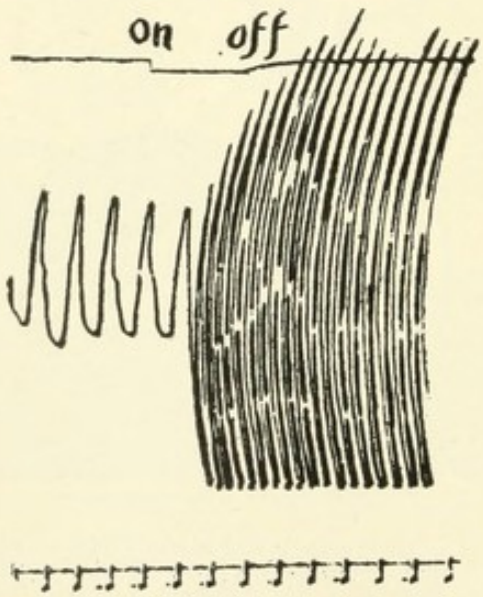


FIG. 246.—Change in Respiration on Stimulating the Central End of the Sciatic Nerve. The rate is sharply increased and the amplitude more than doubled. The stimulation is between the points marked *on* and *off*, time in seconds. The inspiratory movement following the stimulation was greater than the limit of the recording tambour.

tracheal tube with a Marey's recording tambour of medium size and supply with a comparatively delicate membrane. The amplitude of the movements of the tambour may be regulated by a screw compress on a connecting tube. Arrange an induction coil with platinum electrodes in the usual manner, figure 318, for stimulating, by means of the interrupted current. Record the results of the experiment along with the variations of blood pressure on a continuous-paper kymograph; the instrument should be supplied with a time signal, a stimulating signal, etc.

Now stimulate the skin of the abdominal region, the groin, with a comparatively strong induction current, figure 246. Dissect out the sciatic nerve, cut it, stimulate the central end with a mild to medium strength of current. The stimulus should be graduated carefully, for there is often such a great increase in respiratory rate and volume that the animal may become overanesthetized.

b. The Effect of Stimulating the Vagus Nerve. Isolate and stimulate the vagus nerve with a medium strength of stimulus. The effect is usually complete inhibition of respiratory movements. By means of graduated stimuli one may demonstrate the accelerator effects from the stimulation of the vagus. Stimulate also the superior laryngeal, and compare with the effects of stimulating the whole vagus.

c. The Effect of Cutting the Vagus Nerves. Isolate both vagus nerves and section them as nearly at the same moment as possible. Be sure to mark on the tracing the exact moment at which the nerves are cut. This experiment should be performed with every accessory condition as constant as possible, and the animal should not be disturbed for one or two minutes so that the effects of the section will be recorded uncomplicated. The result is always a marked deepening and slowing of the respiratory movements.

d. The Effect of Stimulating the Central End of the Vagus. Upon stimulating the central end of the vagus after section, the respiration rate will be inhibited as in *b*, showing that the vagus nerves carry afferent respiratory fibers, figure 239.

e. The Effect of Stimulation of the Phrenic Nerves. Isolate the right phrenic nerve at its origin from the brachial plexus and stimulate it with a medium strength of stimulus. Upon stimulating a nerve the diaphragm will remain in contraction and the record will show that the thorax is in the inspiratory phase.

Section this nerve and note the change in the character of respiratory movements; make direct observations on the diaphragm, examining from the abdominal side.

12. **Demonstration of Apnea, Dyspnea, and Asphyxia.** Produce deep anesthesia, then disconnect the ether bottle and connect the tracheal tube with a hand bellows. Produce deep and forced artificial respiration for twenty to thirty seconds. Stop the artificial respiration; the animal will remain quiet without any effort at breathing. This is the condition of *apnea*. Allow the animal to recover its normal respiration rate and again produce deep anesthesia. Now clamp off the tracheal tube so that the animal can no longer receive air and leave it so until death. As the blood becomes more and more venous there will first be a marked increase in the respiration rate and depth. This is known as *hyperpnea*. This stage is followed by one of increasing respiratory amplitude in which the accessory respiratory muscles not previously active are brought into forcible contractions, both inspira-

tory and expiratory phases are now forced, *dyspnea*. The movements continue to increase, and the muscles of the neck, larynx, mouth, and nostrils now take part. There is rather a sudden decrease in the respiratory movements, an extension of the limbs, and gasping movements of the mouth, after which the animal remains quiet, death being produced by *asphyxia*.

13. **Respiratory Interchange, Calorimetry.** The experiments are conducted in such a manner that comparative analyses may be made between the air inspired and that expired. Generally an animal is placed in a chamber, called the respiratory chamber, which is then closed except for two openings, one for the entrance of the inspired air, the other for the escape of expired air. Some form of pump is used for renewing the air in the chamber. Both the inspired and expired air is made to pass through agents which will absorb the contained carbon dioxide, such as baryta water or soda lime, and in turn through agents which will absorb the watery vapor. When the experiment is completed the differences between the two are determined. The difference in oxygen has to be calculated, and is open to error. The famous respiratory chamber of Pettenkofer is large enough to perform such experiments on man, and is of very elaborate construction. But the most perfect apparatus assembled for this purpose is the respiration calorimeter of Atwater constructed for man, and the respiration apparatus of Armsby for cattle.

CHAPTER VII

SECRETION IN GENERAL

ALL tissues of the body produce certain chemical changes as a result of their protoplasmic activity. But in certain cells chemical elaborations have come to be the chief function, the cells have been differentiated in that direction, and the name secreting tissue or *gland tissue* is applied. The end result of metabolism in gland tissue is the extrusion on the free borders of the cells of the products of their metabolism. The products are known as *secretions* and the process itself is the act of secretion. Certain secretions which are in the nature of waste products to the body as a whole, such as urine in the kidney, are often called *excretions*, but the use of the term should not be allowed to confuse the general similarity of this to other secretions as regards the physiological changes involved in its production.

Most secretions accomplish some definite office in the economy of the body. Those that are discharged on some free mucous surface, as the saliva, gastric juice, tears, etc., are called *external*, or *true secretions*, or merely *secretions*. Substances that are discharged back into the blood stream later to influence the metabolism of tissues other than the ones which produced them, are called *internal secretions*.

Gland cells, like other tissues, draw their nourishment from the blood and lymph. The product or secretion of gland cells may, in fact usually does, contain some of the substances found in the blood, but there are also present new materials elaborated by the cells, and even where the same substance exists both in the secretion and in the blood and lymph it can make its appearance in the secretion only under the control of the protoplasm of the gland cells. The saliva secreted by the salivary cells, for example, consists of about 98 to 99 per cent water containing in solution small quantities of certain salts, also found in the lymph, and a small percentage of the enzyme, ptyalin. This enzyme is peculiar to the salivary secretion and is manufactured by the salivary-cell protoplasm. As is well known, it acts vigorously in extreme dilution, hence the high per cent of water in the secretion. The passage of water from a solution as concentrated as blood plasma to a solution as dilute as saliva requires a high amount of osmotic energy, an amount that can be supplied only from the chemical energy liberated by the cell in its protoplasmic activity. After the removal of the special organ by which each secretion is manufactured, the secretion is no longer formed. Cases

sometimes occur in which the secretion continues to be formed by the natural organ, but, not being able to escape toward the exterior, on account of some obstruction, is reabsorbed and accumulates in the blood. It may be discharged from the body in other ways; but these are not instances of true vicarious secretions, and must not be so regarded.

Organs and Tissues of Secretion. The principal secreting organs are the following: 1, The serous and synovial membranes; 2, The mucous membranes with their special glands, *e.g.*, the buccal, gastric, and intestinal glands; 3, The salivary glands and pancreas; 4, The liver; 5, The mammary glands; 6, The lachrymal glands; 7, The kidney and skin; and 8, the testes and ovaries.

The special structure and functions of the secreting organs will be given in greater detail in the chapters which immediately follow. The general types of structure and general conditions that influence the functions are introduced at this point.

Structural Types of Secreting Organs. *Serous and Synovial Type.* The serous membranes form closed sacs lining visceral cavities like the abdominal, pericardial, or pleural cavities. The organs are, as it were, pushed into this sac and carry before them an investment of membrane. The serous membranes consist of a single layer of flattened polygonal cells resting on a supporting membrane of connective tissue, supporting a ramification of blood-vessels, lymphatics, and nerves.

In some instances, *i.e.*, synovial membranes, the secreting layer is increased by finger-like elevations. This type of secreting organ produces ordinarily only enough secretion to keep the surface moist.

The Mucous Type. The mucous tracts, and different portions of each of them, present certain structural peculiarities, adapted to the functions which each part has to discharge; yet in some essential characters the mucous membrane is the same, from whatever part it is obtained. In all the principal and larger parts of the several tracts it presents an external layer of *epithelium*, situated upon a *basement membrane*, and beneath this a stratum of *vascular tissue* of variable thickness, containing lymphatic vessels and *nerves*. The vascular stratum, together with the basement membrane and epithelium, in certain cases is elevated into minute papillæ and villi, in others depressed into involutions in the form of glands. But in the invaginations of the secreting membrane of gland cells, the supporting basement membrane and the network of capillaries are still retained in their relative position. With increasing complexity of involution the simple mucous membrane becomes packed away in an apparently solid mass. The equivalent of a large amount of secreting surface is thus condensed into a small space. In the process of invagination some differentiation occurs in that certain of the gland tubes become conducting and have their secretory activity somewhat reduced. But there is no distinction that can be drawn between simple mucous membranes and gland cells.

Secreting Glands. The secreting glands present, amid manifold diversities of form and composition, a general plan of structure; but all are constructed with particular regard to the arrangement of the cells which has just been described.

Secreting glands are classified according to certain structural types, as: 1. The *simple tubular* gland, A, figure 247, examples of which are furnished by the follicles of Lieberkühn, and the tubular peptic glands of the stomach.

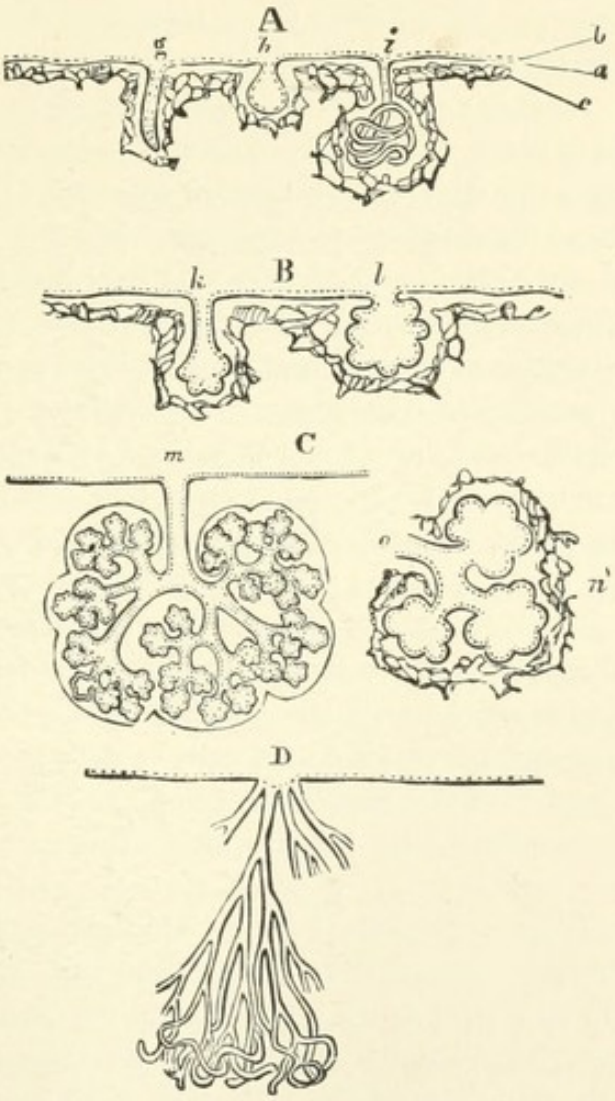


FIG. 247.—Plans of Extension of Secreting Membrane by Inversion or Recession in the Forms of Cavities. A, Simple glands, viz., *g*, straight tube; *h*, sac; *i*, coiled tube. B, Multilocular crypts: *k*, of tubular form; *l*, saccular. C, Racemose or saccular compound gland: *m*, entire gland, showing branched duct and lobular structure; *n*, a lobule, detached with *o*, branch of duct proceeding from it. D, Compound tubular gland. (Sharpey.)

They are simple tubes of mucous membrane, the walls of which are lined with secreting cells arranged as an epithelium. To the same class may be referred the elongated and tortuous sudoriferous glands.

2. The *compound tubular* glands, *D*, figure 247, form another division. These consist of main gland tubes, which divide and subdivide. Each gland may be made up of the subdivisions of one or more main tubes. The ulti-

mate subdivisions of the tubes are sometimes highly convoluted. They are formed of epithelium of various forms, supported by a basement membrane. The larger tubes may have an outside coating of fibrous areolar or muscular tissue. The salivary glands, pancreas, Brunner's glands, kidney, testes, with the lachrymal and mammary glands, are examples of this type, but present more or less marked variations among themselves.

3. The *racemose* glands, in which a number of vesicles or *acini* are arranged in groups of lobules, *C*, figure 247. The Meibomian follicles are examples of this kind of gland. There seem to be glands of mixed character, combining some of the characters of the tubular with others of the racemose type; these are called *tubulo-racemose* or *tubulo-acinous* glands. The acini are formed by a kind of fusion of the walls of several vesicles, which thus combine to form one large cavity with recesses lined or filled with secreting cells. The smallest branches of the gland-ducts sometimes open into the centers of these cavities; sometimes the acini are clustered round the extremities, or by the sides of the ducts; but, whatever secondary arrangement there may be, all have the same essential character of rounded groups of vesicles containing gland-cells, and opening by a common central cavity into minute ducts, which in the large glands converge and unite to form larger and larger branches, and at length one common trunk which opens on a free surface.

The Process of Secretion. The process of secretion is dependent upon the activity of the secreting cells. In the case of the water and salts the physical processes of filtration and diffusion may play a part.

The chemical processes constitute the process of *secretion* properly so called, as distinguished from mere transudation spoken of above. In the process of secretion, various materials which do not exist as such in the blood are manufactured by the agency of the gland-cells, using as a nutrient fluid the blood, or, to speak more accurately, the lymph which fills the interstices of the gland textures.

Evidences in favor of this view are: 1. That gland cells are constituents of all glands, however diverse their outer forms and other characters, and they are placed in all glands on the surfaces or in the cavity whence the secretion is poured. 2. That certain materials of secretions are visible with the microscope in the gland cells before they are discharged. Thus, granules probably representing the precursors of the ferments of the pancreas may be discerned in the cells of that gland. Granules of uric acid are found in the cells of the kidneys of birds and fish, and fatty particles, like those of milk, in the cells of the mammary gland.

Certain secreting cells, like the cells of the sebaceous glands, appear to develop, grow, and attain their individual perfection by appropriating nutriment from the fluid exuded by adjacent blood-vessels and building it up so that it shall form part of their own substance. In this perfected state the cells subsist for some brief time and then appear to dissolve, wholly or in part, and

yield their contents to the peculiar material of the secretion. The changes which have been noticed from actual experiment in the cells of the salivary glands, pancreas, and peptic glands will be described more fully in the chapter on Digestion.

Discharge of secretions from the glands may either take place as soon as formed, or the secretion may be long retained within the gland or its ducts. The former is the case with the sweat glands. But the secretions of those glands whose activity of function is periodical are usually retained in the cells in an undeveloped form during the period of the gland's inaction.

When discharged into the ducts, the further course of secretions is affected: (1) partly by the pressure from behind; the fresh quantities of secretion propelling those that were formed before. In the larger ducts, its propulsion is (2) assisted by the contraction of their walls. All the larger ducts, such as the ureter and common bile-duct, possess in their coats plain muscular fibers; they contract when irritated, and sometimes manifest peristaltic movements. Rhythmic contractions in the pancreatic and bile ducts have been observed, and also in the ureters and vasa deferentia. It is probable that the contractile power extends along the ducts to a considerable distance within the substance of the glands whose secretions can be rapidly expelled. Saliva and milk, for instance, are sometimes ejected with much force.

Circumstances Influencing Secretion. The principal conditions which influence secretion are variations in the quantity of blood, and variations in nerve impulses passing to the gland cells over secretory nerve fibers.

An increase in the quantity of blood traversing a gland, as in nearly all the instances before quoted, coincides generally with an augmentation of its secretion. Thus the mucous membrane of the stomach becomes florid when, on the introduction of food, its glands begin to secrete. The mammary gland becomes much more vascular during lactation. All circumstances which give rise to an increase in the quantity of material secreted by an organ produce, coincidently, an increased supply of blood. But we shall see that a discharge of saliva may occur under extraordinary circumstances without increase of blood-supply, and so it may be inferred that this condition of increased blood-supply is not absolutely essential to the immediate formation of secretion, but that it favors the prolonged activity of glands.

Influence of the Nervous System on Secretion. The process of secretion is largely regulated through the nervous system. The exact mode in which the influence is exhibited must still be regarded as somewhat obscure. In part, it exerts its influence by increasing or diminishing the quantity of blood supplied to the secreting gland, in virtue of the power which it exercises over the contractility of the smaller blood-vessels. It also has a more direct influence, as is described at length in the case of the submaxillary gland, upon the secreting cells themselves. This may be called *trophic* influence. Its influence over secretion, as well as over other functions of the body, may be

excited by causes acting directly upon the nervous centers, upon the nerves going to the secreting organ, or upon the nerves of other parts. In the latter case a reflex action is produced: thus the impression produced upon the sensory nerves by the contact of food in the mouth leads to afferent nerve impulses to the secretory center in the central nervous system which is reflected by the nerves supplying the salivary glands, and produces, through these, a more abundant secretion of the saliva.

Through the nerves, various conditions of the brain also influence the secretions. Thus, the thought of food may be sufficient to excite an abundant flow of saliva. And, probably, it is the mental state which excites the abundant secretion of urine in hysterical paroxysms, as well as the perspirations, and occasionally diarrhea, which ensue under the influence of terror, and the tears excited by sorrow or excess of joy. The quality of a secretion may also be affected by mental conditions, as in the cases in which, through grief or passion, the secretion of milk is altered, and is sometimes so changed as to produce irritation in the alimentary canal of the child.

CHAPTER VIII

FOOD AND DIGESTION

THE term digestion includes those changes taking place in the body which bring the materials of the food into such condition that they may be taken up by the blood and lymphatic vessels and thus rendered available for the metabolism of the tissues. In the process the foods are rendered more soluble and more diffusible. Certain bodies which are already soluble and diffusible are converted into forms which are more available for the tissues; as an example cane-sugar, although both soluble and diffusible, cannot be readily used by the body until it is converted from a disaccharide to a monosaccharide. In fact few of the food materials are fit for immediate use when taken into the body and are therefore practically useless until digested.

FOOD AND FOOD PRINCIPLES.

We have been accustomed to classify foods into certain main groups, chiefly according to their chemical character, as follows:

Proteids. Such as albumin, myosin, gluten, casein, etc.; glucoproteid, nucleoproteid, etc.; gelatin, elastin, etc. These furnish nitrogen in available form.

Carbohydrates. Such as starch, dextrose, cane-sugar, etc.

Fats. Such as olein.

Minerals. The various salines found in animal and vegetable food.

Water.

The classes of foods just enumerated usually exist in mixtures rather than in simple forms, as, for example, a beef roast contains a representative of each of the five classes enumerated, though it is composed chiefly of proteids and fats. The human body is capable of using materials of a great variety of forms, but most of these have the foods mixed in such a way as to give representatives of each of the classes above in certain general proportions.

Nitrogenous Foods. The *Flesh of Animals*, *e.g.*, beef, veal, mutton, pork, bacon, ham, chicken, eggs, milk, etc., are typical nitrogenous foods.

Of these, beef and eggs are richest in nitrogenous matters, containing about 20 per cent. Mutton contains about 18 per cent, veal 16.5, and pork 10. Beef is firmer, more satisfying, and is supposed to be more strengthening than

mutton, whereas the latter is more digestible. The flesh of young animals, such as lamb and veal, is less digestible and less nutritious. Pork contains a large amount of fat and is, therefore, comparatively indigestible.

PERCENTAGE COMPOSITION AND FUEL VALUE PER POUND OF SOME COMMON FOOD STUFFS. (ATWATER AND BRYANT.)

	Water. Per Cent.	Proteid. Per Cent.	Fat. Per Cent.	Carbohydrate. Per Cent.	Ash. Per Cent.	Fuel Value. Per Cent.
Meat (Beef, round)	73.6	22.6	2.8	....	1.3	540
Meat (Pork loin)	52.0	16.6	30.1	....	1.0	1,580
Fish (King salmon)	63.6	17.8	17.8	....	1.1	1,080
Eggs	73.7	13.4	10.5	....	1.0	720
Milk (Cow's)	87.0	3.3	4.0	5.0	0.7	325
Milk (Human)	89.7	2.0	3.1	6.0	0.2	....
Cheese (American)	31.6	28.8	35.9	0.3	3.4	2,055
Butter	11.0	1.0	85.0	....	3.0	3,605
Bread (White)	33.2	10.9	1.3	53.6	1.0	1,255
Bread (Corn)	38.9	7.9	4.7	46.3	2.2	1,205
Rice	12.3	8.0	0.3	79.0	0.4	1,630
Oatmeal	7.3	16.1	7.2	67.5	1.9	1,860
Beans (Dry)	12.6	22.5	1.8	59.6	3.5	1,605
Potatoes (White)	78.3	2.2	0.1	18.4	1.0	385
Potatoes (Sweet)	69.0	1.8	0.7	27.4	1.2	570
Fruit (Strawberries)	90.4	1.0	0.6	7.4	0.6	180
Watermelon (Edible portion)	92.4	0.4	0.2	6.7	0.3	140

Meat contains: (1) Nitrogenous bodies; chiefly *myosin*, and one or more *globulins*, *serum albumin*, *gelatin* (from the interstitial fibrous connective tissue), *elastin* (from the elastic tissue), as well as *hemoglobin*. (2) Fats, including *lecithin* and *cholesterin*. (3) Extractives, some of which are agreeable to the palate, and others weakly stimulating. Besides, there are *sarcolactic* and *inositic acids*, *taurin*, *xanthin*, and others. (4) Salts, chiefly of potassium, calcium, and magnesium. (5) Water, the amount of which varies from 15 per cent in dried bacon to 39 in pork, 51 to 53 in fat beef and mutton, and 72 per cent in lean beef and mutton. (6) A certain amount of carbohydrate material is found in the meat of some animals, in the form of *inosite*, *dextrin*, *grape sugar*, and *glycogen*.

TABLE OF PERCENTAGE COMPOSITION OF BEEF, MUTTON, PORK, AND VEAL. (LETHEBY.)

	Water.	Proteid.	Fats.	Salts.
Beef—Lean	72	19.3	3.6	5.1
" *Fat*	51	14.8	29.8	4.4
Mutton—Lean	72	18.3	4.9	4.8
" *Fat*	53	12.4	31.1	3.5
Veal	63	16.5	15.8	4.7
Pork—Fat	39	9.8	48.9	2.3

TABLE OF PERCENTAGE COMPOSITION OF POULTRY AND FISH. (LETHEBY.)

	Water.	Proteid.	Fats.	Salts.
Poultry	74	21.	3.8	1.2
White Fish	78	18.1	2.9	1.
Salmon	77	16.1	5.5	1.4
Eels (very rich in fat)	75	9.9	13.8	1.3
Oysters	75.74	11.72	2.42	2.73

The flesh of nearly all animals has been occasionally eaten, and we may presume that except for difference of flavor, etc., the average composition is nearly the same in every case.

Milk. Milk is the entire food of young animals, and contains all the elements of a typical diet. Albuminous substances are represented in the form of *caseinogen,* and *serum* or *lact albumin;* fats in the cream; carbohydrates in the form of *lactose* or milk-sugar; salts, chiefly as *calcium phosphate;* and water. From milk we obtain a number of food preparations such as *cheese* rich in proteid and fat, *butter* and *cream, buttermilk* rich in proteids and peculiarly well adapted for invalid diet, and *whey* which contains all the sugar salts and the albumin.

TABLE OF COMPOSITION OF MILK, BUTTERMILK, CREAM, AND CHEESE. (LETHEBY AND PAYEN.)

	Nitrogenous Matters.	Fats.	Lactose.	Salts.	Water.
Milk (Cow)	4.1	3.9	5.2	.8	86
Buttermilk	4.1	.7	6.4	.8	88
Cream	4.1	26.7	2.8	1.8	66
Cheese—Skim	44.8	6.3	...	4.9	44
Cheese—Cheddar	28.4	31.1	...	4.5	36

Eggs. The yolk and albumin of eggs of oviparous animals bear the same relation as food for the embryos that milk bears to the young of mammalia, and afford another example of the natural admixture of the various alimentary principles. The proteids of eggs are *egg albumin* and *globulin,* of which the *vitellin* of the yolk is most important; *nuclein* in combination with iron is also found. In addition to the three common fats there is a yellow fatty pigment, *lutein* (lipochrome), *lecithin,* and *cholesterin,* a small quantity of *grape-sugar,* and *inorganic salts,* chiefly potassium chloride and phosphates.

TABLE OF THE PERCENTAGE COMPOSITION OF FOWLS' EGGS.

	Nitrogenous Substances.	Fats.	Salts.	Water.
White	20.4	...	1.6	78
Yolk	16.	30.7	1.3	52

Legumes are used by vegetarians as the principal source of the nitrogen of the food. Those chiefly used are *peas, beans, lentils,* etc.; they contain a nitrogenous substance called *legumin,* allied to albumin. Legumes contain

about 25.30 per cent of this nitrogenous body, and twice as much nitrogen as wheat. *Nuts* also form a very nutritious article of diet.

Carbohydrate Foods. *Bread*, made from the ground grain obtained from various so-called cereals, viz., wheat, rye, maize, barley, rice, oats, etc., is the direct form in which the carbo-hydrate is supplied in an ordinary diet. It contains starch, dextrin, and a little sugar. It also contains gluten, composed of vegetable proteids, and a small amount of fat.

TABLE OF PERCENTAGE COMPOSITION OF BREAD AND FLOUR.

	Nitrogenous matters.	Carbo-hydrates.	Fats.	Salts.	Water.
Bread	8.1	51.	1.6	2.3	37
Flour	10.8	70.85	2	1.7	15

Various articles besides bread are made from flour, *e.g.*, spaghetti, macaroni, etc. Dextrin and a small amount of dextrose are present in bread, particularly in the crust.

Vegetables, especially potatoes. They contain starch and sugar. In cabbage, turnips, etc., the salts of potassium are abundant.

Fruits contain sugar, and organic acids, tartaric, malic, citric, and others.

Sugar, chiefly saccharose, used pure or in various sweetmeats.

Oils and Fats. The substances supplying the oils and fats of the food are chiefly *butter*, *bacon and lard*, *suet* (beef and mutton fat), and vegetable oils. These contain the fats olein, stearin, and palmitin. Butter contains others in addition, while vegetable oils, as a rule, contain no stearin.

Mineral or Inorganic Foods. *The salts of the food.* Nearly all the substances in the preceding classes contain a greater or less amount of the salts required in food. Green vegetables and fruit contain certain salts, chiefly potassium. Sodium chloride is an essential food; it is contained in nearly all solids, but so much is required that it has also to be taken as a condiment. Potassium salts are found in muscle, nerve, and in meats generally, and in potatoes. Calcium salts are contained in eggs, blood of meat, wheat, and vegetables. Iron is contained in hemoglobin, in milk, eggs, and vegetables.

Liquid Foods. Water is essential to life, and from two to two and a half pints a day must be consumed in addition to that taken mixed with solid food. Of the non-alcoholic substances which may be added to it for flavoring purposes, such as tea, coffee, cocoa, etc., the last can alone be considered to have a certain food value, as it contains fats, albuminous material, and starch, the other constituents of such substances being a volatile oil, an alkaloid caffeine, and tannic acid. The food value of alcoholic beverages, which has long been a subject of controversy, as now generally agreed is but slight. Beer, wines, and spirits contain ethyl alcohol, the amount varying from 1.5 to 4.5 per cent in beer to 60 to 80 per cent in spirits.

The Effect of Cooking on Foods. In general terms cooking may be said to render food more easily digestible, both directly and indirectly, through increased palatability. Subjecting food to high degrees of heat also serves to kill parasites, such as trichinæ and the various tapeworms, which may be present and alive in raw meats. In the case of meats various methods of cooking are employed. In *roasting*, the meat in bulk is subjected to a high temperature in an oven for a short time, followed by a somewhat lower temperature until the cooking is completed, which causes a coagulation of the outer layers of albumin so that the juices of the meat are retained. In *boiling*, the meat is first immersed in boiling water for a time and then the cooking continues at a lower temperature. If a *broth* is to be made, the extractives may be obtained by heating the meat in water for a long period at a temperature below the coagulation point of albumin. Such a broth contains the flavoring and the stimulating extracts of the meat, but is of only slight nutritive value. For small pieces of meat, *broiling* practically serves the same purpose as does roasting for larger pieces. *Frying*, as usually employed, is the least serviceable method of preparation, since the fat or other oily material used so permeates the food as to render it difficult of penetration by the digestive juices.

Cooking produces upon vegetables the necessary effect of rendering them softer, so that they can be more readily broken up in the mouth. It also causes the starch grains to swell up and burst, and so aids the digestive fluids in penetrating into their substance. The albuminous matters are coagulated, and the gummy, saccharine, and saline matters are removed. The conversion of flour into dough is effected by mixing it with water, and adding a little salt and a certain amount of yeast. Yeast consists of the cells of an organized ferment (*Torula cerevisiæ*); this plant in its growth changes by ferment action the sugar produced from the starch of the flour, and a quantity of carbon dioxide and alcohol is formed; the gas together with the action of heat during baking causes the dough to rise, and the gluten being coagulated, the bread sets as a permanently vesiculated mass.

THE PROCESS OF DIGESTION.

The Enzymes. The digestive process involves both mechanical and chemical changes. The former are secured by the crushing and grinding in the mouth, together with the mixing and kneading that come from the peristalses of the stomach and intestine. The chemical changes are the most important factors of the digestive process. The various secretions that are poured into the mouth, stomach, and intestines all contain substances which react on the foods to render the latter more soluble. The special agency in each secretion is the presence of representatives of the chemical groups known as enzymes. These enzymes, or unorganized ferments, are the essen-

tial factors in the secretions which produce the chemical changes in the foods. Their predominant action is one of hydrolytic cleavage; that is, the substance acted upon takes up water and then splits into two different substances, usually of the same class. The chemical nature of the enzymes is as yet undetermined because of the difficulty of getting absolutely pure specimens. Their mode of action is at present regarded in the nature of catalysis. That is to say, the enzymes by their presence facilitate reactions that would otherwise take place, but very slowly. Practically all are secreted in the glands as *zymogens*, which bear the same relation to enzymes as fibrinogen does to fibrin; they are transformed to enzymes by the proper stimulus, but never exist as such in the glands.

Each enzyme has a special point of temperature at which it acts best, and any change in the temperature retards its action; the action is suspended at a definite point of low temperature, but the enzyme is not destroyed by cold. The action is suspended at a somewhat higher temperature, and at a still higher point the enzyme is destroyed. Some enzymes act only in an alkaline medium, being destroyed in an acid medium, and *vice versa*. Others act in either alkaline, or neutral, or acid media. Enzymes are hindered in their action by the accumulation of the products of their activity. Most of them cease acting altogether when these products reach a certain concentration, but will begin acting again on the removal of these products or if the mixture be simply diluted.

The quantity of the enzyme determines the rapidity of the action, but not the amount; a small quantity will digest as much as a large quantity, but will take longer. The enzymes are not used up in the course of their activity, as far as can be seen, and do not seem to undergo any change in their composition.

Enzymes are more or less specific in their action. That is, each enzyme is supposed to produce its change in only one particular substance, as in starch, maltose, proteid, fat, etc. An enzyme that can cause cleavage of the starch molecule will not act on fat or proteid or even on other members of the starch group. This specific action is doubtless expressive of a definite relation between the structure of the enzyme and the substance acted on.

An interesting fact as to enzyme action is its reversibility—a phenomenon now well known and well established for carbohydrates and fats. Kastle and Löwenhart have shown that lipase, which acts to split neutral fats into fatty acid and glycerin, will also produce a synthesis, at least of butyric acid and alcohol into ethylbutyrate. Taylor and Robertson in independent papers have recently made the far-reaching discovery that the proteid molecule can be synthesized by the agency (apparent reversible action) of enzymes.

Enzymes are classified either according to the chemical nature of their action or according to the class of substances on which they act; the former

classification is more logical, but the latter is more convenient and more generally used.

TABLE OF DIGESTIVE ENZYMES.

Amylolytic.

Ptyalin of saliva, and *amylopsin* of pancreatic juice, change starch to maltose. *Maltase* in the saliva, and pancreatic juice in the small intestine, change maltose to dextrose. *Lactase* splits lactose to galactose and dextrose, and *invertase* splits cane-sugar to levulose and dextrose in the small intestine.

Lipolytic.

Steapsin or *lipase*, found in the pancreatic juice, splits neutral fats into glycerin and fatty acid.

Proteolytic.

Pepsin of the gastric secretion, and *trypsin* of the pancreatic secretion, change proteids to proteoses and peptones, trypsin breaking the proteid down to simpler nitrogenous products. *Erepsin* of the intestine splits peptones to simpler products.

Coagulating.

Rennin of the gastric juice coagulates milk.

Activating.

Enterokinase of the intestinal juice converts trypsinogen to trypsin. (Thrombokin of the blood is of this class.)

DIGESTION IN THE MOUTH.

The food is received into the *mouth*, and is subjected to the action of the *teeth* and *tongue*, being at the same time mixed with the first of the digestive juices, the *saliva*. It is then swallowed, and, passing through the *pharynx* and *esophagus* into the *stomach*, is subjected to the action of the *gastric juice*, the second digestive juice. Thence it passes into the small *intestines*, where it meets with the *bile*, the *pancreatic juice*, and the *intestinal juices*, all of which exercise a digestive influence upon the portion of the food not already digested and absorbed. In the *large intestine* some further digestion and absorption take place, and the residue of undigested matter leaves the body in the form of feces.

Mastication. The act of mastication is performed by the biting and grinding movement of the lower range of teeth against the upper. The simultaneous movements of the tongue and cheeks assist by crushing the softer portions of the food against the hard palate and gums, thus supplementing the action of the teeth, and by returning the morsels of food to the action of the teeth as they are squeezed out from between them until they have been sufficiently chewed.

The simple up-and-down or *biting* movements of the lower jaw are performed by the *temporal*, *masseter*, and *internal pterygoid* muscles, the action of which in closing the jaws alternates with that of the *digastric* and other muscles passing from the os hyoides to the lower jaw, which open the jaws. The *grinding* or side movements of the lower jaw are performed mainly by the *external pterygoid* muscles, the muscle of one side acting alternately with

the other. When both external pterygoids act together, the lower jaw is pulled directly forward, so that the lower incisor teeth are brought in front of the level of the upper.

The act of mastication is voluntary. It will suffice here to state that the afferent nerves chiefly concerned are the sensory branches of the fifth and tenth or glosso-pharyngeal, and the efferent are the motor branches of the fifth and the twelfth, or hypoglossal, cerebral nerves.

The act of mastication is much assisted by the saliva, which is secreted by the salivary glands in largely increased amount during the process. The intimate incorporation of the saliva with the food is termed *insalivation*.

The Salivary Glands. The glands which secrete the saliva in the human subject are the salivary glands proper, the *parotid*, the *submaxillary*, and the *sublingual*, and numerous smaller bodies of similar structure, and with separate ducts, which are scattered thickly beneath the mucous membrane of the lips, cheeks, soft palate, and root of the tongue.

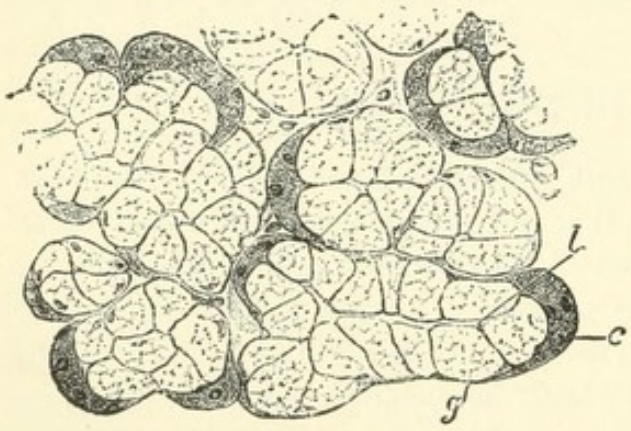


FIG. 248.

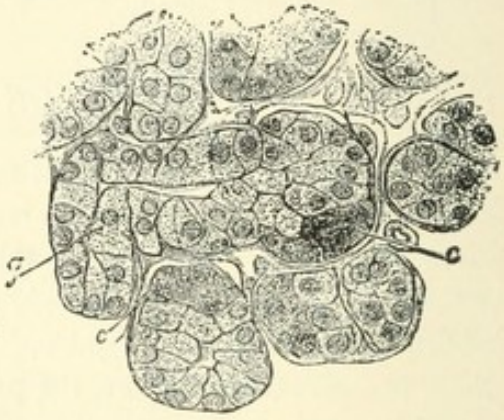


FIG. 249.

FIG. 248.—Section of the Submaxillary Gland of a Dog, Resting Stage. Most of the Alveolar cells are large and clear, being filled with the material for secretion (in this case, mucigen), which obscures their protoplasm; some of the cells, however, are small and protoplasmic, forming the crescents seen in most of the alveoli. (Ranvier.)

FIG. 249.—Section of a Similar Gland after a Period of Activity. The mucigen has been discharged from the mucin-secreting cells, which consequently appear shrunken and less clear. Both the cells and the alveoli are much smaller, and the protoplasm of the cells is more apparent. The crescents of Gianuzzi are enlarged. *c*, Crescent cells; *g*, mucus-secreting cells; *l*, lumen of alveolus. (Ranvier.)

Histological Structure. The salivary glands are compound tubular or tubulo-racemose glands. They are made up of lobules. Each lobule consists of the branchings of a division of the main duct of the gland, which are generally more or less convoluted toward the extremities, that form the *alveoli*, or proper secreting parts of the gland. The salivary secreting cells are of cubical or columnar form and are arranged around a central canal. The granular appearance frequently seen in the salivary cells is due to the numerous *zymogen granules* which they contain.

During the rest period the cells are larger, highly granular, with obscured

nuclei and smaller lumen. During activity the cells become smaller and their contents more opaque.

When the mucous type of gland is secreting, or on stimulation of the nerve, *mucigen* is converted into *mucin*, the cells swell up, appear more transparent, and stain deeply in logwood, figure 249. After stimulation, the cells become smaller, more granular, and more easily stained, from having discharged their contents, and the nuclei appear more distinct.

Nerves of large size are found in the salivary glands. They are principally contained in the connective tissue of the alveoli, and certain glands, especially in the dog, are provided with ganglia. Some nerves have special endings in Pacinian corpuscles, some supply the blood-vessels, and others penetrate the basement membrane of the alveoli and end upon, but not in, the salivary cells.

The blood-vessels form a dense capillary network around the ducts of the alveoli, being carried in by the fibrous trabeculæ between the alveoli, in which also the lymphatics begin by lacunar spaces.

The Nervous Mechanism of the Secretion of Saliva. The secretion of saliva is under the control of the nervous system. Under ordinary conditions it is excited by the stimulation of the peripheral branches of two nerves, the *gustatory* or *lingual* branch of the inferior maxillary division of the fifth nerve, and of the *glosso-pharyngeal*, which are distributed to the mucous membrane of the tongue and pharynx conjointly. The stimulation occurs on the introduction of sapid substances into the mouth, and the secretion is brought about in the following way: From the terminations of the above-mentioned sensory nerves distributed in the mucous membrane an impression is conveyed upward (afferent) to the special nerve center situated in the medulla oblongata which controls the process, and by it is reflected to certain nerves supplied to the salivary glands, which will be presently indicated. In other words, the center, when stimulated to action by the sensory impressions carried to it, sends out impulses along efferent or secretory nerves supplied to the salivary glands. These cause the saliva to be secreted by and discharged from the gland cells. Other stimuli, however, besides that of the food, and other sensory nerves than those mentioned, may reflexly produce the same effects. For example, saliva may be caused to flow by irritation of the mucous membrane of the mouth with mechanical, chemical, electrical, or thermal stimuli, also by the irritation of the mucous membrane of the stomach in some way, as in nausea which precedes vomiting, when some of the peripheral fibers of the *vagi* are irritated. Stimulation of the *olfactory* nerves by smell of food, of the *optic* nerves by the sight of it, and of the *auditory* nerves by the sounds which are known by experience to accompany the preparation of a meal may also stimulate the nerve center to action. In addition to these, as a secretion of saliva follows the movement of the muscles of mastication, it may be assumed that this movement stimulates the secreting nerve fibers of the gland, direct or reflexly. From the fact

that the flow of saliva may be increased or diminished by mental states, it is evident that impressions from the cerebrum also are capable of stimulating the center to action or of inhibiting its action.

Influence of Nerves on the Submaxillary Gland. The submaxillary gland has been the gland chiefly employed for the purpose of experimentally demonstrating the influence of the nervous system upon the secretion of saliva, because of the comparative facility with which the gland, with its blood-vessels and nerves, can be exposed to view in the dog, rabbit, and other animals.

The chief nerves supplied to the gland are: (1) the *chorda tympani*, a branch given off from the *facial* in the canal through which it passes in the temporal bone; and (2) branches of the *sympathetic* nerve from the plexus around the facial artery and its branches to the gland. The chorda, figure 250, *ch. t*, passes downward and forward, under cover of the external pterygoid muscle, and joins the lingual or gustatory nerve, proceeds with it for a short distance, and then passes along the submaxillary-gland duct, *sm. d*, giving branches to the submaxillary ganglion, *sm. gl*, and sending others to terminate in the superficial muscles of the tongue. It consists of fine medullated fibers which lose their medulla in the gland. If this nerve be exposed and divided anywhere in its course from its exit from the skull to the gland no immediate result will follow, nor will stimulation either of the lingual or of the glosso-pharyngeal produce a flow of saliva. But if the peripheral end of the divided nerve be stimulated, an abundant secretion of saliva ensues, and the blood supply is enormously increased by dilatation of the arteries. The veins may even pulsate, and the blood contained within them is more arterial than venous in character.

When, on the other hand, the stimulus is applied to the *sympathetic* filaments (mere division producing no apparent effect), the arteries contract, and the blood stream is in consequence much diminished; and only a sluggish stream of dark blood escapes from the veins. The saliva, instead of being abundant and watery, becomes scanty and tenacious. If both chorda tympani and sympathetic branches be divided, the gland, released from nervous control, may secrete continuously and abundantly (*paralytic* secretion).

The abundant secretion of saliva which follows stimulation of the chorda tympani is not merely the result of a filtration of fluid from the blood-vessels, in consequence of the largely increased circulation through them. This is proved by the fact that, when the main duct is obstructed, the pressure within may considerably exceed the blood pressure in the arteries, and also that when into the veins of the animal experimented upon some *atropine* has been previously injected, stimulation of the peripheral end of the divided chorda produces all the vascular effects as before, without any secretion of saliva accompanying them. Again, if an animal's head be cut off, and the chorda be rapidly exposed and stimulated with an interrupted current, a secretion of

saliva ensues for a short time, although the blood supply is necessarily absent. These experiments serve to prove that the chorda contains two sets of nerve fibers, one set, *vaso-dilator*, which, when stimulated, act upon a local vaso-motor center for regulating the blood supply, inhibiting its action, and causing the vessels to dilate, and so producing an increased supply of blood to the gland; while another set, which are paralyzed by injection of atropine, directly stimulate the cells themselves to activity, whereby the cells secrete and discharge the constituents of the saliva which they produce, *the secretory nerves*. These latter fibers very possibly terminate on the salivary cells themselves. If, on the other hand, the sympathetic fibers be divided, stimulation of the

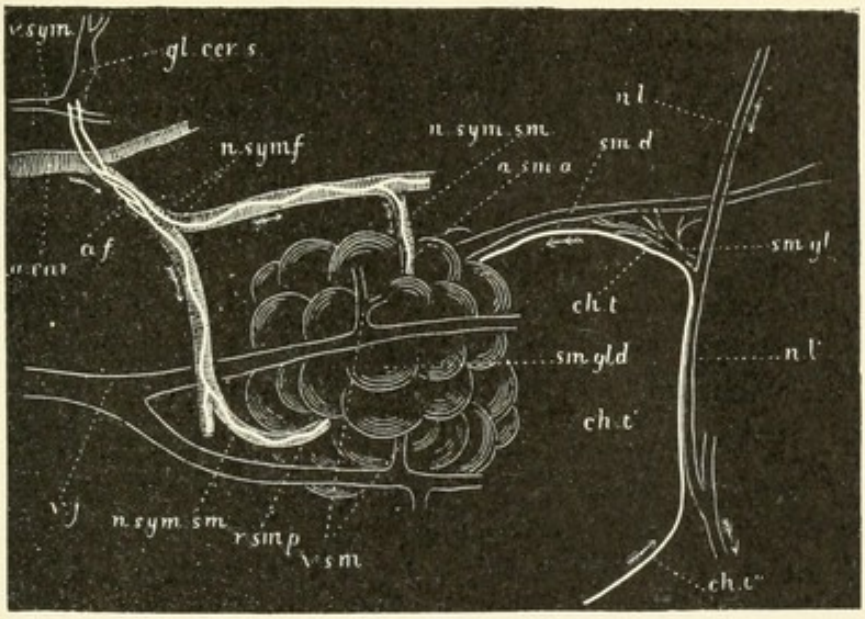


FIG. 250.—Diagrammatic Representation of the Submaxillary Gland of the Dog with its Nerves and Blood-vessels. (This is not intended to illustrate the exact anatomical relations of the several structures.) *sm. gld.*, The submaxillary gland into the duct (*sm. d.*) of which a cannula has been tied. The sublingual gland and duct are not shown. *n. l.*, *n. l'.*, The lingual or gustatory nerve; *ch. t.*, *ch. t'.*, the chorda tympani proceeding from the facial nerve, becoming conjoined with the lingual at *n. l'.*, and afterward diverging and passing to the gland along the duct; *sm. gl.*, submaxillary ganglion with its roots; *n. l.*, the lingual nerve proceeding to the tongue; *a. car.*, the carotid artery, two branches of which, *a. sm. a.* and *r. sm. p.*, pass to the anterior and posterior parts of the gland; *v. sm.*, the anterior and posterior veins from the gland ending in *v. j.*, the jugular vein; *v. sym.*, the conjoined vagus and sympathetic trunks; *gl. cer. s.*, the superior-cervical ganglion, two branches of which forming a plexus, *a. f.*, over the facial artery, are distributed, *n. sym. sm.*, along the two glandular arteries to the anterior and posterior portion of the gland. The arrows indicate the direction taken by the nervous impulses; during reflex stimulations of the gland they ascend to the brain by the lingual and descend by the chorda tympani. (M. Foster.)

tongue by sapid substances, or electrical stimulation of the trunk of the lingual or of the glosso-pharyngeal, continues to produce a flow of saliva. From these experiments it is evident that the chorda-tympani nerve is the principal nerve through which efferent impulses proceed from the center to excite the secretion of this gland.

The sympathetic nerve also contains two sets of fibers, *vaso-constrictor* and *secretory*. But the flow of saliva, upon stimulating the sympathetic, is scanty, and the saliva itself viscid. At the same time the vessels of the gland

are constricted. The secretory fibers may be paralyzed by the administration of atropine.

Nerves of the Parotid Gland. The nerves which influence secretion in the parotid gland are branches of the facial (lesser superficial petrosal) and of the sympathetic. The former nerve, after passing through the otic ganglion, joins the auriculo-temporal branch of the fifth cerebral nerve, and, with it, is distributed to the gland. The nerves by which the stimulus ordinarily exciting secretion is conveyed to the medulla oblongata, are, as in the case of the submaxillary gland, the fifth and the glosso-pharyngeal. The pneumogastric nerves convey a further stimulus to the secretion of saliva when food has entered the stomach; the nerve center is the same as in the case of the submaxillary gland.

Changes in the Gland Cells. The method by which the salivary cells produce the secretion of saliva appears to be divided into two stages, which differ somewhat according to the class to which the gland belongs, viz., whether to (1) the true salivary, or to (2) the mucous type. In the former case, it has been noticed, as already described, that during the rest which follows an active secretion the lumen of the alveolus becomes smaller, the gland cells larger and very granular. During secretion the alveoli and their cells become smaller, and the granular appearance in the latter to a considerable extent disappears, and at the end of secretion the granules are confined to the inner part of the cell nearest to the lumen, which is now quite distinct, figure 251.

It is supposed from these appearances that the first stage in the act of secretion consists in the protoplasm of the salivary cell taking up from the lymph certain materials from which it manufactures the elements of its own

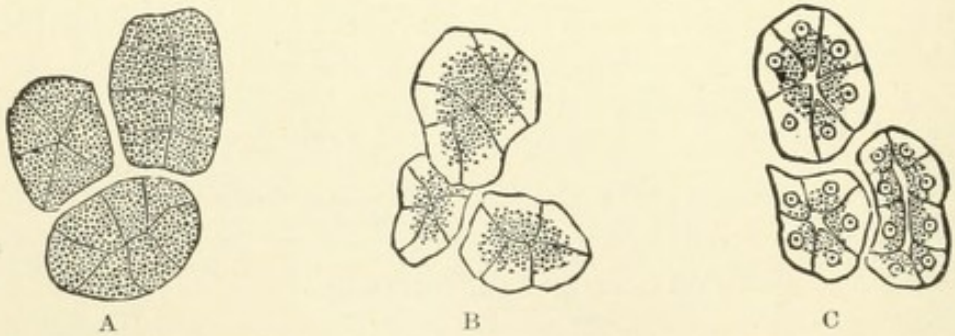


FIG. 251.—Alveoli of True Salivary Gland. A, At rest; B, in the first stage of secretion; C, after prolonged secretion. (Langley.)

secretion, and which are stored up in the form of granules in the cell during rest; the second stage consists of the actual discharge of these granules, with or without previous change. The granules are zymogen granules, and represent the chief substance of the salivary secretion, ptyalin. In the case of the submaxillary gland of the dog, at any rate, the sympathetic nerve fibers appear to have to do with the first stage of the process, and when stimulated the proto-

plasm is extremely active in manufacturing the granules, whereas the chorda tympani is concerned in the production of the second act, the actual discharge from the cells of the materials of secretion, together with a considerable amount of fluid, the latter being an actual secretion by the protoplasm, as it ceases to occur when atropine has been subcutaneously injected.

In the mucus-secreting gland, the changes in the cells during secretion have been already spoken of. They consist in the gradual production by the protoplasm of the cell of a substance called *mucigen*, which is converted into *mucin*, and discharged on secretion into the canal of the alveoli. The mucigen is, for the most part, collected into the inner part of the cells during rest, pressing the nucleus and the small portion of the protoplasm which remains, against the limiting membrane of the alveoli.

The process of secretion in the salivary glands is identical with that of glands in general. The cells which line the ultimate branches of the ducts are the agents by which the special constituents of the saliva are formed. The material which they have incorporated within themselves, which is doubtless a product of the metabolism of the protoplasm of the cells, is given up again almost at once in the form of a fluid, *secretion*, which escapes from the ducts of the gland. The cells themselves undergo diminution in the mass of their protoplasm, which is again renewed in the intervals of the active exercise of the functions. The source whence the cells obtain the materials for the construction of secretion is the blood-plasma, which is filtered off from the circulating blood into the interstices of the glands, as in all living tissues.

Saliva. Saliva, as it commonly flows from the mouth, is the mixed secretion of the salivary glands proper and of the glands of the buccal mucous membrane and tongue. When obtained from parotid ducts, and free from mucus, saliva is a transparent watery fluid, the specific gravity of which varies from 1004 to 1008, and in which, when examined with the microscope, are found floating a number of minute particles, derived from the secreting ducts and vesicles of the glands. In the impure or mixed saliva are found, besides these particles, numerous epithelial scales separated from the surface of the mucous membrane of the mouth and tongue, and the so-called salivary corpuscles, discharged probably from the mucous glands of the mouth and the tonsils, which subside when the saliva is collected in a deep vessel and left at rest. They form a white opaque sediment leaving the supernatant fluid transparent and colorless, or with a pale bluish-gray tint. Saliva also contains various kinds of micro-organisms (bacteria). The saliva, when first secreted, appears to be always alkaline in *reaction;* the alkalinity is about equal to .08 per cent of sodium carbonate, and is due to the presence of disodium phosphate, Na_2HPO_4.

The mucin is the largest representative of the organic nitrogenous class of bodies in the saliva. It may be thrown down by addition of acetic acid. It gives the three chief proteid reactions, and may easily be split up by the

action of a dilute mineral acid into globulin and a carbohydrate whose exact character has not yet been established, though it resembles a sugar in reducing copper-sulphate solutions. The presence of *potassium sulphocyanide*, KCNS, in saliva may be shown by the blood-red coloration which the fluid gives with a solution of ferric chloride, Fe_2Cl_6, and which is bleached on the addition of a solution of mercuric chloride, $HgCl_2$, but not by hydrochloric acid.

CHEMICAL COMPOSITION OF HUMAN SALIVA. (HAMMERBACHER.)

	In 1,000 Parts.
Water	994.2
Solids	5.8
Mucus and epithelium	2.2
Soluble organic matter (ptyalin)	1.4
Potassium sulphocyanide	0.04
Salts	2.20

Saliva from the parotid is less viscid; less alkaline, the first few drops discharged in secretion being even acid in reaction; clearer, although it may become cloudy on standing from the precipitation of calcium carbonate by the escape of carbon dioxide; and more watery than that from the submaxillary. It has moreover a less powerful action on starch. Sublingual saliva is the most viscid, and contains more solids than either of the other two, but has little diastasic action.

Rate of Secretion and Quantity of Saliva. The rate at which saliva is secreted is subject to considerable variation. When the tongue and muscles concerned in mastication are at rest, and the nerves of the mouth are subject to no unusual stimulus, the quantity secreted is not more than sufficient with the mucus to keep the mouth moist. During actual secretion the flow is much accelerated.

The *quantity* secreted in twenty-four hours varies greatly, but is at least 1 liter.

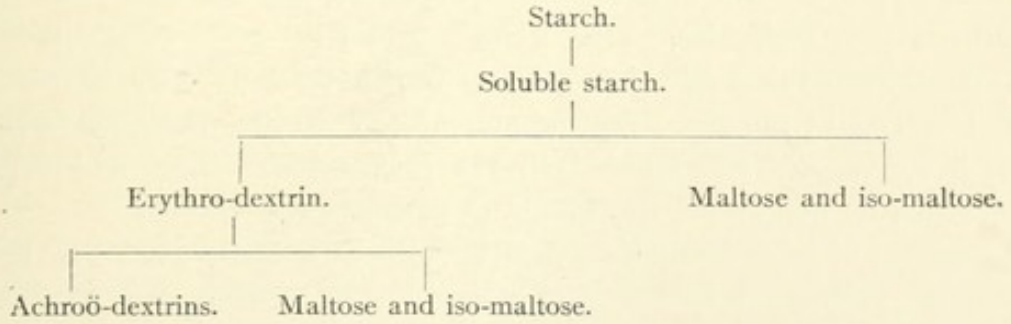
Function of Saliva. The purposes served by saliva are mechanical and chemical.

Mechanical. (1) It keeps the mouth in a due condition of moisture, facilitating the movements of the tongue in speaking, and the mastication of food. (2) It serves also in dissolving sapid substances, and renders them capable of exciting the nerves of taste. (3) But the principal mechanical purpose of the saliva is that, by mixing with the food during mastication, it makes a soft pulpy mass such as may be easily swallowed. To this purpose the saliva is adapted both by quantity and quality. For, speaking generally, the quantity secreted during feeding is in direct proportion to the dryness and hardness of the food.

Chemical. The chemical action which the saliva exerts upon the food in the mouth is to convert the starchy materials which it contains into soluble starch and then into sugar. This power the saliva owes to the enzyme *ptyalin*.

Certain investigators have of late asserted that saliva contains another enzyme, known as *maltase*, which has the power of splitting the disaccharides into monosaccharides, or maltose into dextrose. The action of this ferment is certainly very limited. The conversion of the starch under the influence of the ferment into sugar takes place in several stages, and in order to understand it a knowledge of the structure and composition of starch granules is necessary. A starch granule consists of two parts: an envelope of *cellulose*, which does not give a blue color with iodine except on addition of sulphuric acid, and of *granulose*, which is contained within, and which gives a blue color with iodine alone. Brücke states that a third body is contained in the granule, which gives a red color with iodine, viz., *erythro-granulose*. On boiling, the granulose swells up, bursts the envelope, and the whole granule is more or less completely converted into a paste or gruel, which is called gelatinous starch.

When ptyalin acts upon boiled starch, it first changes the latter, by hydrolysis, into soluble starch, or *amidulin;* this is more limpid and more like a true solution, though it still gives the blue coloration on the addition of iodine. This stage is very brief, only thirty seconds being sometimes required in laboratory experiments to render a stiff starch paste completely fluid when a few drops of saliva are added at body temperature. This rapidity of action is of great importance, as under proper conditions of mastication practically all the boiled starch of the food ought to enter the stomach as soluble starch. When the starch has not been previously boiled, the envelope of cellulose retards the action of the ptyalin to a very marked degree.



The further stages of hydrolytic cleavage result in the formation of a variable mixture of maltose and iso-maltose with a series of dextrins, but apparently never result (in laboratory experiments) in the complete conversion of the dextrins into sugars. Gradually, as the starch is converted, the blue coloration with iodine is replaced by a purplish-red and finally by a red color: the latter color is produced by *erythro-dextrin* (so-called from the color). In the later stages no coloration is obtained with iodine, and for this reason the dextrins formed are known as *achroö-dextrins;* there are probably several of these, but they have not yet been sufficiently isolated. As sugar appears very early in the process, even at the stage of erythro-dextrin, and

gradually increases in amount, it is generally concluded that maltose is formed early in the decomposition of the starch molecule. The process is usually represented schematically as above.

The sugars formed are maltose ($C_{12}H_{22}O_{11}$) and a closely allied sugar known as iso-maltose. A small percentage of dextrose has been found by some observers, and this is due to the action of maltose. Maltose is allied to saccharose or cane-sugar more nearly than to glucose; it is crystalline; its solution has the property of polarizing light to the right to a greater degree than solutions of glucose (3 to 1); it is not so sweet, and reduces copper sulphate less easily. It can be converted into glucose by boiling with dilute acids and by the action of the enzyme maltase present in saliva.

According to Brown and Heron the reactions may be represented thus:

One molecule of gelatinous starch is converted by the action of an amylolytic ferment into *n* molecules of soluble starch.

One molecule of soluble starch = 10 ($C_{12}H_{20}O_{10}$) + 8 (H_2O), which is further converted by the ferment into

1. Erythro-dextrin, 9 ($C_{12}H_{20}O_{10}$) (giving red with iodine) + Maltose ($C_{12}H_{22}O_{11}$).

then into 2. Erythro-dextrin 8 ($C_{12}H_{20}O_{10}$) (giving yellow with iodine) + Maltose 2 ($C_{12}H_{22}O_{11}$).

next into 3. Achroö-dextrin 7 ($C_{12}H_{20}O_{10}$) + Maltose 3 ($C_{12}H_{22}O_{11}$).

And so on; the resultant being:

Soluble starch 10 ($C_{12}H_{20}O_{10}$) + Water 8 (H_2O) = Maltose 8 ($C_{12}H_{22}O_{11}$) + Achroö-dextrin 2 ($C_{12}H_{20}O_{10}$).

Many observers, however, believe that the maltose simultaneously present with erythro-dextrin is not actually split off from the starch molecule in the formation of erythro-dextrin, but that it is the product of more advanced hydrolysis in other starch molecules. They point out that in such a chemical reaction of considerable time duration, it is improbable that all the starch molecules are attacked at the same rate or are, at any given moment, equally advanced in cleavage. Their theory is that there is a series of more and more simple dextrins formed giving rise finally to the disaccharides.

The presence of sugar in such an experiment is at once discovered by the application of Trommer's test, which consists in the addition of a drop or two of a solution of copper sulphate, followed by a larger quantity of caustic potash. When the liquid is boiled, an orange-red precipitate of copper suboxide indicates the presence of sugar.

Influences which Affect the Action of Saliva on Starch. Moderate heat, about 37.8° to 40° C., is most favorable to the rapid cleavage of starch by the ptyalin. Cold retards and 0° C. suspends the action but does not destroy the ferment. A temperature of 60° C. destroys the ptyalin.

Removal of the products of salivary digestion as they are formed facilitates the action of the enzyme, as an excess of these products is detrimental to further action.

The reaction between starch and saliva takes place best in a neutral or

very faintly alkaline medium and is inhibited by strong alkalies and especially by acids even as weak as the acidity of the gastric juice. This last is of particular importance since it raises the question as to how long the ptyalin may act.

The action of saliva on starch is not limited to the brief interval during which food remains in the mouth, as is now well known, but may continue for a time in the stomach.

Ptyalin is strictly an *amylolytic* ferment.

Starch appears to be the only principle of food upon which the saliva acts chemically. The secretion has no apparent influence on gum, cellulose, or on fat, and is equally destitute of power over albuminous and gelatinous substances.

The salivary glands of children do not become functionally active till the age of 4 to 6 months, and hence the bad effects of feeding them before this age on starchy food, corn-flour, etc., which they are unable to render soluble and capable of absorption.

Salivary Digestion in the Stomach. Laboratory experiments have demonstrated that while the addition of even 0.05 per cent of hydrochloric acid will inhibit the action of ptyalin on a solution of starch, if any proteids be present in the solution much more acid must be added before the action of the ptyalin is stopped. The explanation of the latter fact is that the acid unites with the proteids in some chemical combination forming "combined acid," which has little effect, comparatively, on ptyalin. This "combined acid" gives a red color with litmus, but is distinguished from free acid by giving a brownish instead of a bluish color with Congo red. When food enters an empty stomach, as happens at the beginning of a meal the acid first combines with the proteid food stuffs and so does not at once affect the ptyalin.

A still more important fact in its bearing on this subject was recently discovered by Cannon, who showed experimentally that starchy foods mixed with weak alkali remain alkaline in the stomach for as much as an hour and a half. Such foods when swallowed into the stomach are packed away in that organ in a mass. The secretion of the acid gastric juice comes in contact only with the outer surface of the mass, which is not materially disturbed by the stomach peristalses. The center of the mass may, therefore, remain alkaline until the outer layers are completely eroded away, and the ptyalin may continue to act on starch during the whole time.

DEGLUTITION.

When properly masticated, the food is transmitted in successive portions to the stomach by the act of deglutition or swallowing. The following account of deglutition is based upon the researches of Kronecker and Meltzer, whose experiments seem to modify in some details the earlier theory of Magendie:

The mouth is closed, and the food after thorough mixing with the saliva is rolled into a bolus on the dorsum of the tongue. The tip of the tongue is pressed upward and forward against the hard palate, thus shutting off the anterior part of the mouth cavity. The mylo-hyoid muscles then suddenly contract, the bolus of food is put under great pressure and shot backward and downward through the pharynx and into the esophagus and, if the food be fluid enough, even to the cardiac orifice of the stomach. Coincidently with

FIG. 252.—Transverse Section of the Human Esophagus. *a*, Fibrous covering; *b*, longitudinal muscular fibers; *c*, transverse muscular fibers; *d*, areolar or submucous coat; *e*, muscularis mucosæ; *f*, mucous membrane, with part of a lymphoid nodule; *g*, stratified epithelial lining; *h*, mucous gland; *i*, gland duct; *m'*, striated muscle fibers. (V. Horsley.)

the contraction of the mylo-hyoid muscles, the hyoglossi are thrown into action, drawing the tongue backward and downward, not only increasing the pressure upon the food, but forcing the epiglottis over the glottis, closing the larynx.

It has been shown by the Roentgen-ray method that the character of the food determines somewhat its passage through the esophagus. The dry and semisolid foods are seized by the musculation of the esophagus and passed down that organ by a peristaltic wave. The longitudinal muscles contract, tending to enlarge the diameter of the esophagus in advance of the food, while contractions of the circular muscles produce pressure on the bolus just behind, thus forcing it along to the cardia. This wave reaching the cardiac orifice about six seconds after the commencement of the act of

deglutition, forces the food into the stomach, the sphincter having previously relaxed. The interval of time between the commencement of the act of deglutition and the arrival of the more fluid food at the cardiac orifice of the stomach may not be more than one-tenth second, though it remains at the cardiac orifice without entering the stomach until the first parts of the act of swallowing is reinforced by the subsequent contraction of the constrictors of the pharynx and the passage of a peristaltic wave down the esophagus. In some cases, however, the liquid food is not stopped at the cardiac orifice, but is sent through the relaxed sphincter by the original force of the mylo-hyoid contraction.

In man the esophagus was said to contract in three separate segments, the first segment lying in the neck and being about six centimeters long, the second being the next ten centimeters of the tube, and the third the remaining portion to the stomach. But the later Roentgen-ray observations show no break in the continuous passage of the food, though the movement of the food is slower in the lower segment of the esophagus.

The act of swallowing consists, then, of the contraction in sequence of the mylo-hyoids, the constrictors of the pharynx, and the esophagus. The computed time of contraction is as follows:

	Seconds.
Contraction of mylo-hyoids and constrictors of the pharynx	0.3
Contraction of the first part of the esophagus	0.9
Contraction of the second part of the esophagus	1.8
Contraction of the third part of the esophagus	3.0
	6.0

If a second attempt at swallowing be made before the first has been completed (that is, before six seconds have elapsed), the remaining portion of the first act is inhibited, and the contraction wave reaches the stomach six seconds after the commencement of the second act.

During the act of deglutition the posterior nares are closed through the action of the levator palati and tensor palati muscles, which raise the velum; the palato-pharyngei, drawing the posterior pillars of the fauces together; and the azygos uvulæ, which raises the uvula—thus forming a complete curtain. Otherwise the food would pass into the nose, as happens in the case of cleft palate. At the same time the larynx is closed by the adductor muscles of the vocal cords and the descent of the epiglottis, the larynx being drawn upward as a whole through the action of the mylo-hyoid, genio-hyoid, thyro-hyoid, and digastric muscles. The presence of the epiglottis is not necessary for the completion of the act of deglutition.

Nervous Mechanism of Deglutition. The *sensory* nerves engaged in the reflex act of deglutition are branches of the fifth cerebral supplying the soft palate; glosso-pharyngeal, supplying the tongue and pharynx; the superior laryngeal branch of the vagus, supplying the epiglottis and the glottis. The

motor fibers concerned are branches of the fifth, supplying part of the digastric and mylo-hyoid muscles and the muscles of mastication; the facial, supplying the levator palati; the glosso-pharyngeal, supplying the muscles of the pharynx; the vagus, supplying the muscles of the larynx through the inferior laryngeal branch; and the hypoglossal, the muscles of the tongue. The nerve center by which the muscles are harmonized in their action is situated in the medulla oblongata. It cannot be definitely circumscribed, but is in the general level of the vagus origin. The movements of the esophagus are coordinated by the complex of sensory and motor fibers of the fifth and the ninth to twelfth cranial nerves, which all take some part in this complicated reflex.

DIGESTION IN THE STOMACH.

The stomach in man and those mammalia which are provided with a single stomach consists of a dilatation of the alimentary canal placed between and continuous with the esophagus, which enters its larger or cardiac end on the one hand, and the small intestine, which commences at its narrowed end or pylorus, on the other. It varies in shape and size according to its state of distention. It is supplied with nerves from the vagus and from the sympathetic and receives a special artery, the gastric artery.

Structure of the Stomach. The stomach is composed of four coats, called respectively, the external or *peritoneal*, the *muscular*, the *submucous*, and the *mucous* coat. Blood-vessels, lymphatics, and nerves are distributed in and between them.

The *muscular* coat consists of three separate layers of fibers which, according to their several directions, are named the longitudinal, circular, and oblique. The *longitudinal* set are the most superficial and are continuous with the longitudinal fibers of the esophagus and spread out in a diverging manner over the cardiac end and sides of the stomach to the pylorus. The *circular* or *transverse* coat more or less completely encircles all parts of the stomach; this coat is thickest at the middle and in the pyloric portion of the organ, and forms the chief part of the thick ring of the pylorus. The next and consequently deepest coat, the *oblique*, is continuous with the circular muscular fibers of the esophagus at the cardiac orifice of the stomach. This coat is quite interrupted and more or less incomplete. The muscular fibers of the stomach and intestinal canal are *unstriated*.

The *mucous membrane* of the stomach, which rests upon a layer of loose cellular membrane, or *submucous tissue*, is smooth, soft, and velvety. It is of a pale pink color during life, and in the contracted state is thrown into numerous longitudinal folds or rugæ, which disappear when the organ is distended. It is composed of a mass of short tubular secreting glands.

The Gastric Glands. The glands of the mucous membrane of the stomach are of two varieties, *Cardiac* and *Pyloric*.

Cardiac glands are found throughout the whole of the cardiac end of the stomach. They are arranged in groups of four or five, which are separated by a fine connective tissue. Two or three tubes often open into one duct,

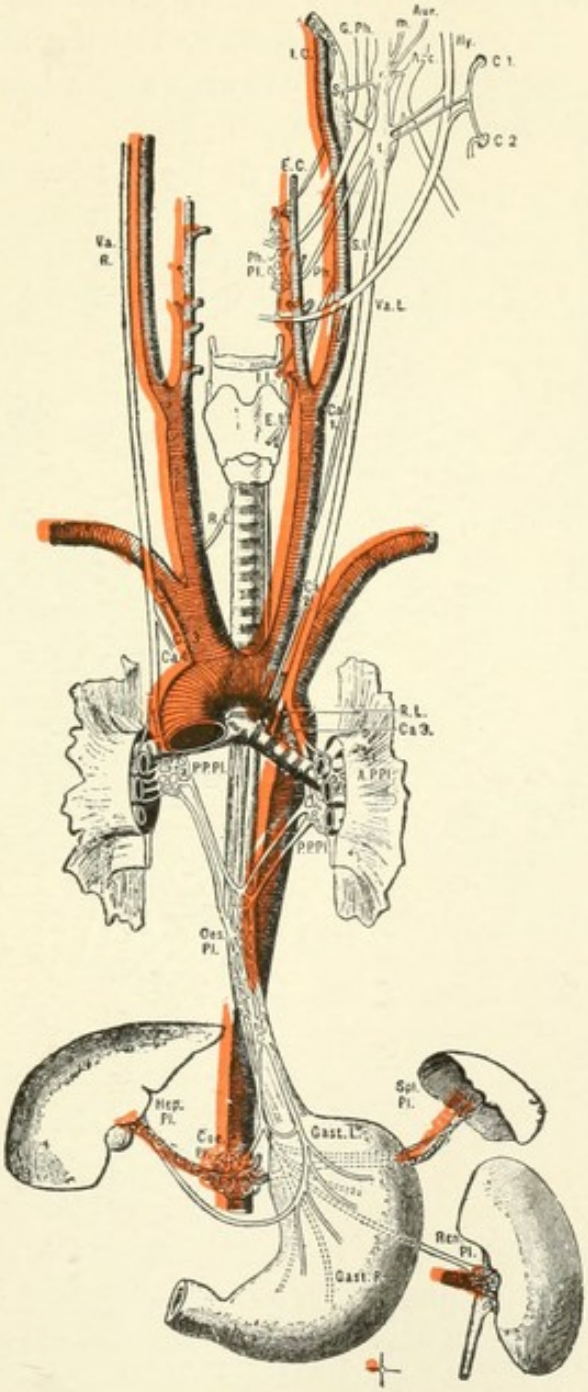


FIG. 253.—The Human Stomach and the Vagus Distribution. *R. L.*, Recurrent laryngeal; *Ca2*, inferior cervical cardiac branch; *Ca3*, *Ca4*, cardiac branches of vagus; *A. P. Pl.*, *P. P. Pl.*, anterior and posterior pulmonary plexuses; *Oes. Pl.*, esophageal plexus; *Gast. R.* and *L.*, gastric branches of vagus, right and left; *Coe. Pl.*, coeliac plexus; *Hep. Pl.*, hepatic plexus.

figure 254, which forms about a third of the whole length of the tube and opens on the surface. The ducts and the free surface are lined with columnar

epithelium. The body of the gland is composed of granular secreting cells called *chief cells* or *peptic cells*. Between these cells and the membrana propria of the tubes are large oval or spherical cells, granular in appearance with clear oval nuclei; these cells are call *oxyntic* or *parietal cells*. They do not form a continuous layer, figure 254. Intercellular tubules extending from the duct of the gland between the chief cells and connecting with intracellular secretory tubules in the parietal cells have been shown by the Golgi method, figure 256.

As the pylorus is approached the gland ducts become longer and the tube proper becomes shorter, and occasionally branched at the fundus.

The Pyloric Glands. These glands have much longer ducts and larger mouths than the peptic glands.

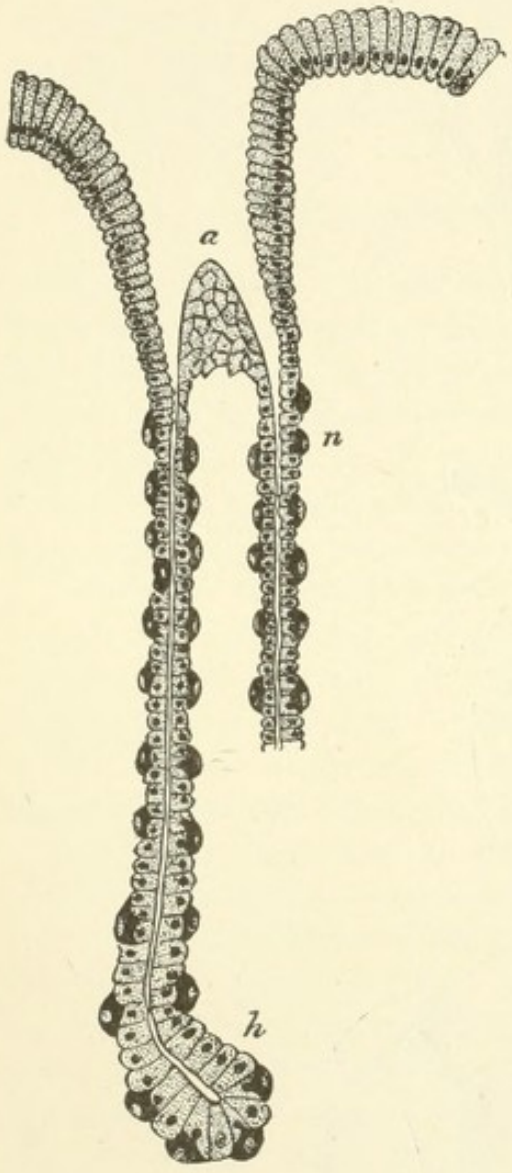


FIG. 254.

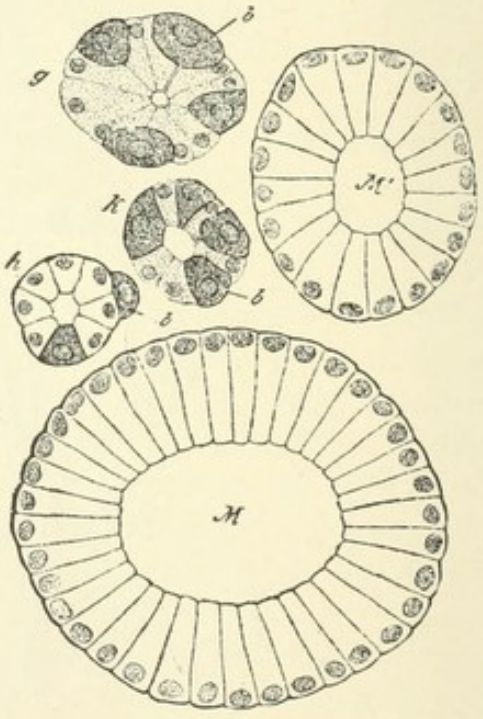


FIG. 255.

FIG. 254.—From a Vertical Section through the Mucous Membrane of the Cardiac End of Stomach. Two peptic glands are shown with a duct common to both, one gland only in part. *a*, Duct with columnar epithelium becoming shorter as the cells are traced downward; *n*, neck of gland tubes, with central and parietal or so-called peptic cells; *h*, fundus with curved cecal extremity—the parietal cells are not so numerous here. × 400. (Klein and Noble Smith.)

FIG. 255.—Cross-sections at Various Levels of Peptic Glands of Stomach. × 400. *M*, Section through gastric pit near surface; *M'*, section through gastric pit near bottom; *h*, mouth of gland; *k*, neck; *g*, body near fundus; the chief cells are shaded lightly; *b*, parietal cells. (Kölliker.)

The parietal cells are absent in the pyloric glands. The pyloric glands become larger as they approach the duodenum, also more convoluted and more

deeply situated. They are directly continuous with Brunner's glands in the duodenum (Watney).

Blood-vessels and Lymphatics. The blood-vessels of the stomach first break up in the submucous tissue and send branches upward between the closely packed glandular tubes, which anastomose around them by a fine capillary network with oblong meshes. Contiguous with this deeper plexus, or prolonged upward from it, so to speak, is a more superficial network of larger capillaries, which branch densely around the orifices of the tubes and

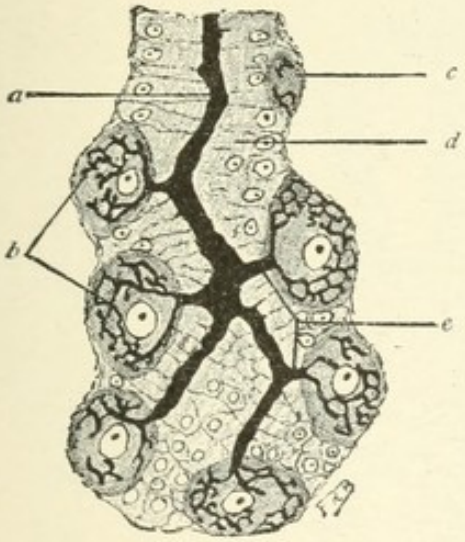


FIG. 256.

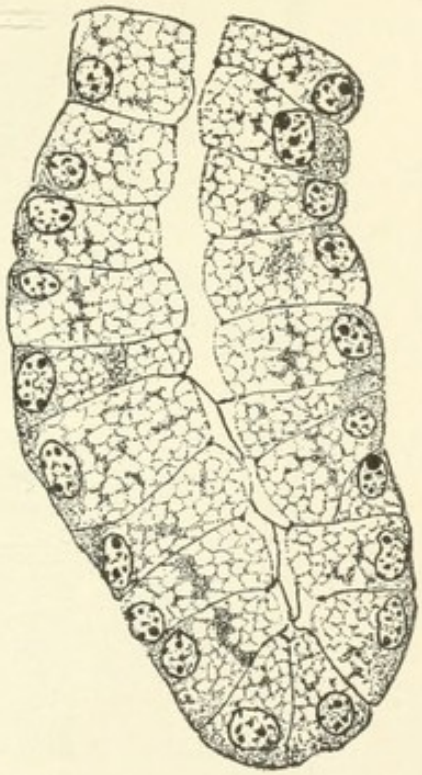


FIG. 257.

FIG. 256.—Longitudinal Section of Fundus of Gland from Dog's Stomach. *a*, Lumen of gland; *b*, intracellular canals in parietal cells; *c*, cut-off portion of parietal cell; *d*, chief cells; *e*, intercellular canals leading from lumen of gland to canals in parietal cells. (Bailey.)

FIG. 257.—Tubule of Pyloric Gland of Man. (Highly magnified.) Note the thin basal layer of cytoplasm; the reticular cell body containing secretion; the subdivision of the latter in some cells into proximal and distal masses.

form the framework on which are molded the small elevated ridges of mucous membrane. From this *superficial* network the veins chiefly take their origin, pass down between the tubes, with no very free connection with the deeper *intertubular* capillary plexus, and open finally into the venous network in the submucous tissue.

The lymphatic vessels surround the gland tubes with a network. Toward the fundus of the peptic glands are masses of lymphoid tissue which may appear as distinct follicles, somewhat like the solitary glands of the small intestine.

Microscopic Changes in the Gastric Glands During Secretion. Langley has made a study of the histological changes in the glandular tissues in the fresh state. He finds that during fasting or when the glands are at rest the chief cells are granular throughout, being crowded with *large* highly refractive granules. During activity these granules gradually disappear progressively from the base toward the border of the cell on the lumen of the tube. They no doubt represent the *zymogen* substances from which the first discharge

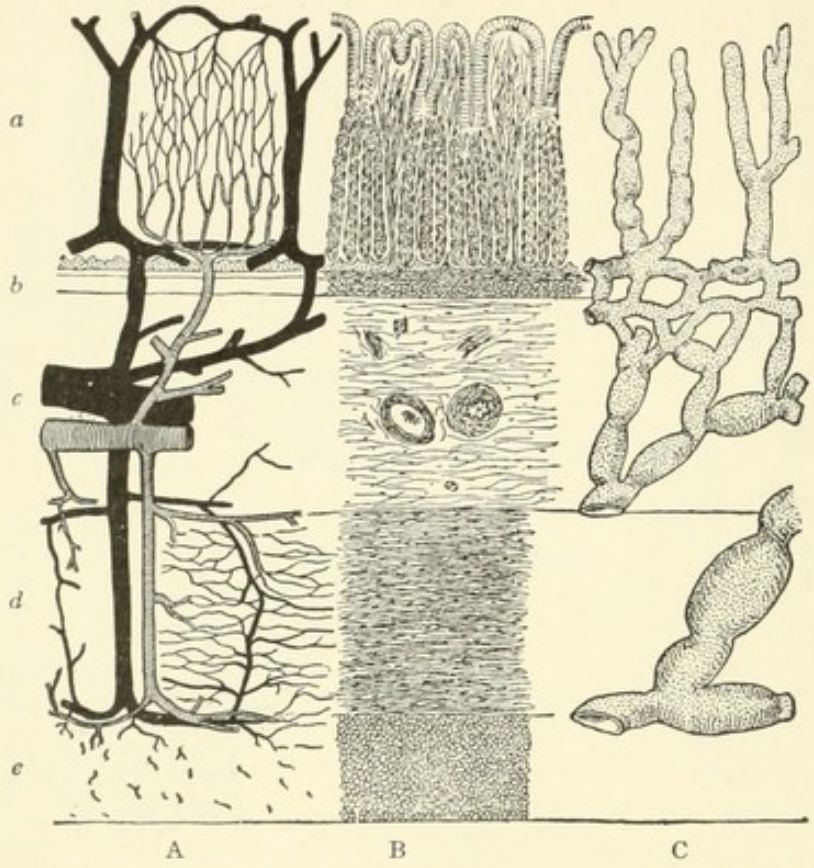


FIG. 258.—Scheme of Blood-vessels and Lymphatics of Stomach. × 70. *a*, Mucous membrane; *b*, muscularis mucosæ; *c*, submucosa; *d*, inner circular muscle layer; *e*, outer longitudinal muscle layer; *A*, blood-vessels; *B*, structure of coats; *C*, lymphatics. (Szymonowicz, after Mall.)

of enzyme is derived during the activity of secretion. The parietal cells are finely granular throughout, though they decrease in size during activity, as in fact do the chief cells. The pyloric cells do not undergo such marked changes, and the mucous cells of the more superficial layers of the mucosa cannot be said to show any special changes at the time of digestional activity of the other layers. During periods of rest the gastric cells increase in size and again become charged with granules as before.

The Act of Secretion of Gastric Juice. The gastric glands undergo periods of rest and activity. The active secretion of normal gastric juice takes place when food is introduced into the mouth, or in fact the mere sight of appetizing food is followed by an abundant secretion of gastric juice as shown by Bidder and Schmidt on a dog with a gastric fistula. Such

observations strongly indicate that the act is a nervous phenomenon, at least under nervous control.

Quite recently Pawlow has proved that secretory fibers are carried to the gastric glands in the vagus trunk. His experiment consisted in establishing a gastric fistula, and some days later in dividing the esophagus in the neck in such a manner that any food swallowed would be diverted to the exterior through the cut end. A "fictitious meal" could then be given to the animal, and the effect upon the stomach noted. As long as the vagi were intact, certain foods (meats) caused a flow of gastric juice, though none of the food reached the stomach. The secretion of gastric juice continued for hours with the production of a large quantity of secretion. When

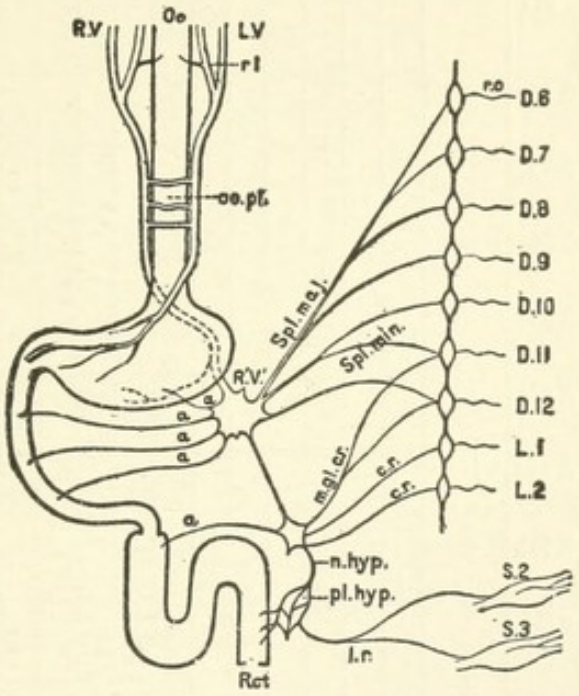


FIG. 259.—Very Diagrammatic Representation of the Nerves of the Alimentary Canal. *Oe* to *Rct*, the various parts of the alimentary canal from esophagus to rectum; *L. V.*, left vagus, ending on front of stomach; *rl*, recurrent laryngeal nerve, supplying upper part of esophagus; *R. V.*, right vagus, joining left vagus in esophageal plexus; *œ. pl.*, supplying the posterior part of stomach, and continues as *R'V'* to join the solar plexus, here represented by a single ganglion, and connected with the inferior mesenteric ganglion, *m. gl.*; *a*, branches from the solar plexus to stomach and small intestine, and from the mesenteric ganglia to the large intestine; *Spl. maj.*, large splanchnic nerve, arising from the thoracic ganglia and rami communicantes; *r. c.*, belonging to dorsal nerves from the 6th to the 9th (or 10th); *Spl. min.*, small splanchnic nerve similarly from the 10th and 11th dorsal nerves. These both join the solar plexus, and thence make their way to the alimentary canal; *c. r.*, nerves from the ganglia, etc., belonging to 11th and 12th dorsal and 1st and 2d lumbar nerves, proceeding to the inferior mesenteric ganglia (or plexus), *m. gl.*, and thence by the hypogastric nerve, *n. hyp.*, and the hypogastric nerve, *n. hyp.*, and the hypogastric plexus, *pl. hyp.*, to the circular muscles of the rectum; *l, r.*, nerves from the 2d and 3d sacral nerves, S. 2, S. 3 (nervi erigentes) proceeding by the hypogastric plexus to the longitudinal muscles of the rectum. (M. Foster.)

the vagi had been cut, no secretion occurred. Moreover, he found that direct stimulation of the vagus produced a flow of gastric juice.

Khigine placed foods in an isolated gastric pouch prepared with care to maintain the nervous relations intact, and it led to secretion of gastric juice in the main part of the stomach. This is undoubtedly a nervous reflex effect.

Recently observations on a case of stricture of the human esophagus which prevented food from reaching the stomach have shown that an abundant flow of gastric juice takes place when food is taken in the mouth.

It seems conclusively established at the present time that the secretion of gastric juice is a reflex act controlled by a definite nervous mechanism. This

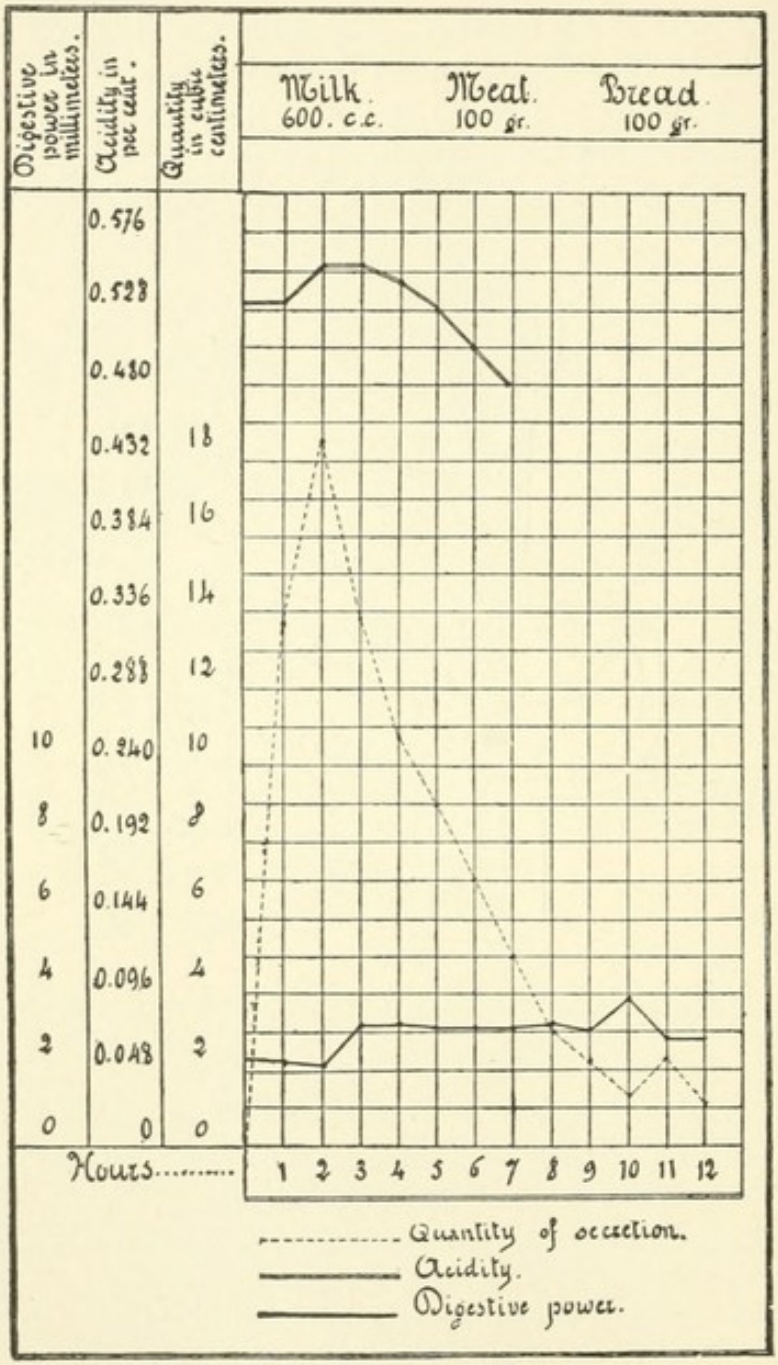


FIG. 260.—Table to Show the Secretion of Gastric Juice by the Dog. (Khigine.)

reflex can be aroused by the sensory stimuli of taste, smell, and even sight. It can also be initiated by stimuli arising in the stomach itself by the effects of ingredients of the food or by the products of digestion. Indeed it has been shown that peptone is a very efficient stimulus for this stomach reflex.

The influence of the higher nerve centers on gastric digestion, as in the case of emotions, is too well known to need more than a reference.

Immediately on the introduction of food or other stimulating substance, the mucous membrane, which was previously quite pale, becomes slightly turgid and reddened with the influx of a larger quantity of blood, and the gastric glands commence actively to secrete. An acid fluid is poured out in minute drops and the secretion may continue for hours.

The Gastric Juice. The first analysis of gastric juice was made by Prout on a small and impure specimen. Beaumont made an elaborate and classic series of observations on the gastric secretion of Alexis St. Martin, in whom there existed, as the result of a gunshot wound, an opening leading directly into the stomach near the upper extremity of the great curvature and three inches from the cardiac orifice. The introduction of any mechanical irritant, such as the bulb of a thermometer, into the stomach through this artificial opening excited the secretion of gastric fluid. This was drawn off, and was often obtained to the extent of nearly an ounce.

The chemical composition of human gastric juice has been also investigated by Schmidt. The fluid in this case was also obtained by means of an accidental gastric fistula. The mucous membrane was excited to action by the introduction of some hard matter, such as dry peas, and the secretion was removed by means of an elastic tube. The fluid obtained was found to be acid, limpid, odorless, with a specific gravity of 1002 to 1010. It contained a few cells and some fine granular matter. The analysis of the fluid obtained in this way is given below. Essentially it is a weakly acid fluid containing hydrochloric acid and two enzymes, *pepsin* and *rennin*, with possibly a third, *maltase*. The gastric juice of dogs and other animals obtained from gastric fistulas shows some difference in composition.

CHEMICAL COMPOSITION OF GASTRIC JUICE.

	Dogs.	Human.
Water	971.17	994.4
Solids	28.82	5.60
Solids—		
Ferment—Pepsin	17.5	3.19
Hydrochloric acid (free)	2.7	0.2
Salts—		
Calcium, sodium, and potassium chlorides; and calcium, magnesium, and iron phosphates	8.57	2.19

The *quantity* of gastric juice secreted daily has been variously estimated; but the average for a healthy adult may be assumed to range from 2,000 to 3,000 cubic centimeters in the twenty-four hours.

The Acid of Gastric Juice. The acidity of the fluid is due to free *hydrochloric* acid, although other acids, *e.g.*, *lactic*, *acetic*, *butyric*, are not infrequently to be found therein as products of gastric digestion or abnormal

fermentation. In healthy gastric juice the amount of free hydrochloric acid is usually about 0.2 per cent, but may be as much as 0.3 per cent. In pathological conditions it may be entirely absent, or may amount to 0.5 per cent, or even more.

Hydrochloric acid is the proper acid of healthy gastric juice, and various tests have been used to prove this. The tests depend upon changes produced in aniline colors by the action of hydrochloric acid even in minute traces, whereas lactic and other organic acids have no such action.

An aqueous solution of *oo-tropeolin*, a bright yellow dye, is turned red on the addition of a minute trace of hydrochloric acid, and aqueous solutions of methyl violet and gentian violet are turned blue under the same circumstances. The lactic acid sometimes present in the contents of the stomach is derived partly from the sarcolactic acid of muscle and partly from lactic-acid fermentation of carbohydrates. Lactic acid ($C_3H_6O_3$), if present, gives the following test. A solution of 10 cubic centimeters of a 4 per cent aqueous solution of carbolic acid, 20 cubic centimeters of water, and one drop of ferric chloride is made; forming a blue-colored mixture. A mere trace of free lactic acid added to such a solution causes it to become yellow, whereas hydrochloric acid even in large amount only bleaches it.

The proteid matter in the food combines to some extent with the hydrochloric acid, which then is known as *combined acid* and does not redden litmus paper. As this combination is immediate, it follows that no free acid is found in the gastric contents until the amount secreted is more than enough to saturate the various albuminous affinities. It is partly for this reason that, as already mentioned, salivary digestion may continue in the stomach for some time after the commencement of gastric digestion. According to Ehrlich the amount necessary to saturate the affinities of 100 grams of various articles of diet is as follows:

Beef (boiled)	2.0	grams	of pure	HCl.
Mutton (boiled)	1.9	"	"	"
Veal (boiled)	2.2	"	"	"
Pork (boiled)	1.6	"	"	"
Ham (boiled)	1.8	"	"	"
Sweetbread (boiled)	0.9	"	"	"
Wheat bread	0.3	"	"	"
Rye bread	0.5	"	"	"
Swiss cheese	2.6	"	"	"
Milk (100 c.c.)	0.32–0.42	"	"	"

The acid is chiefly found at the surface of the mucous membrane, but is in all probability formed by the parietal cells of the cardiac glands, hence called oxyntic, for no acid is formed by the pyloric glands in which this variety of cell is absent. It seems established that the chlorides of the blood are the source of the hydrochloric acid, for when these chloride salts are reduced to the point at which they are tenaciously held the hydrochloric

acid is no longer secreted. One can only guess at the detail by which the parietal cells secrete the acid.

The acid probably results (Maly) from a combination of common salt with monosodic phosphate, $NaH_2PO_4 + NaCl = Na_2HPO_4 + HCl$; the disodic phosphate is then reconverted by the action of carbonic acid and water, $Na_2HPO_4 + CO_2 + H_2O = NaH_2PO_4 + NaHCO_3$. All these salts are found in the blood.

The Pepsin. The *pepsin* of the gastric juice is derived from the activity of the chief cells of the fundic glands. The zymogen *pepsinogen*, which is its immediate precursor, is in all probability represented by the granules of the resting cells. The ferment pepsin does not exist as such in the cells, for an extract of peptic glands in 0.2 per cent soda solution kept at 40° C. retains for hours its power to digest proteid when added to 0.2 per cent hydrochloric acid. If the extract be first treated with acid till it is active, then neutralized and kept, it quickly loses its power to digest. The enzyme is destroyed by the treatment, but the pro-enzyme is not so injured.

Digestive Action of Pepsin and Hydrochloric Acid. The chief function of gastric juice is to alter the proteid food stuffs so that they may be readily absorbed. Less important functions are the antiseptic action of the hydrochloric acid, and the coagulation of milk. The chief digestive power of the gastric juice depends on the pepsin and acid contained in it, both of which are necessary for the process in the stomach.

This action on proteids may be shown by adding a little gastric juice (natural or artificial) to some flakes of fibrin or to diluted egg albumin, and keeping the mixture at a temperature of about 37.8° C. (100° F.). It is soon found that the fibrin goes into solution and that the albumin cannot be precipitated on boiling. If the solution be neutralized with an alkali, a precipitate of acid albumin is thrown down. After a while the acid albumin disappears, so that no precipitate results on neutralization, and proper analysis will show that all the fibrin or albumin has been converted into other proteid substances, viz., *proteoses* and *peptones*. The process, as in the case of salivary digestion, is never complete and the final result is always a mixture of peptones with proteoses which cannot be further peptonized. The relative proportions, of course, depend on the duration of the process. A side product is found (as an insoluble residue) in artificial gastric digestion which gives practically all the proteid reactions and is soluble in dilute alkali, though insoluble in water, sodium chloride, or dilute acid. This is known as *anti-albumid* and may be changed into peptone by prolonged digestion; it does not occur in physiological gastric digestion. The commonest proteose is the one formed from albumin and is known as albumose, or by the more general name *proteose;* this name is used in the subsequent descriptions of the digestive processes.

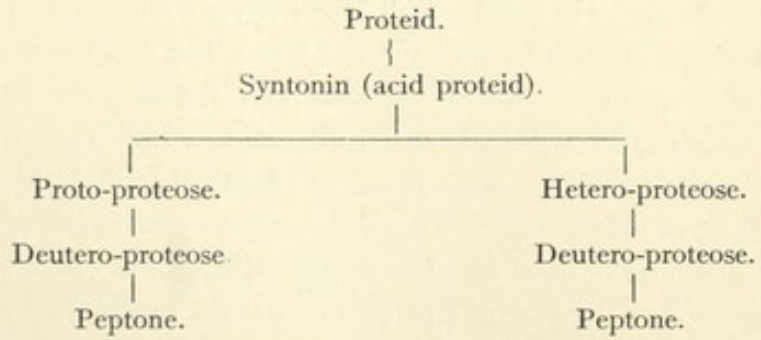
All classes of proteids are digested by gastric juice, leading to the production of proteoses and peptones. The change is indicated best by the characters

of the new proteid formed. Peptones have certain characteristics which distinguish them from other proteids. They are *diffusible*, *i.e.*, they possess the property of passing through animal membranes. In their diffusibility peptones differ remarkably from egg albumin, and on this diffusibility depends one of their chief uses. Egg albumin as such, even in a state of solution, would be of little service as food, inasmuch as its diffusibility renders difficult its absorption or in the case of insoluble proteids effectually prevents absorption into the blood-vessels of the digestive canal. When completely changed by the action of the gastric juice into peptones, albuminous matters *diffuse readily*, and are thus quickly absorbed.

Peptones are not found in the blood, even of the vessels immediately concerned in absorption from the stomach and intestines. In their absorption, therefore, by the epithelial cells, they must undergo a synthetic change, appearing in the blood as albumins and globulins, which are not readily diffusible and which occupy the same plane as the proteids from which the peptones were derived. The previous cleavage to proteoses and peptones is in the nature of preparation for this final act of absorption.

Products at Different Stages of Gastric Digestion. The proteid is first changed into syntonin, or acid proteid, by the combined action of the pepsin and acid. Though the acid alone is capable of accomplishing this step, the fact that it does not do so physiologically is proven by the great length of time required, in laboratory experiments, for the change.

The next change is the conversion of the syntonin into proteoses which, according to Neumeister, occurs in two successive stages. The first of these stages is the conversion of syntonin into the primary proteoses, *i.e.*, proto-proteose and hetero-proteose. The second is the conversion of both proto-proteose and hetero-proteose into the secondary proteoses, *i.e.*, deutero-proteose. The last change is the conversion of the deutero-proteose into the end product peptone. This last change does not occur completely to any great extent and the proteoses always predominate in the digesting mass. Schematically the changes in the proteids may be represented as follows:



The action of pepsin is one of hydrolysis and the products are hydrated forms of proteid. The acid is absolutely essential to the action of pepsin, but it also aids digestion by causing the proteids to absorb water. That this ac-

tion is important is proven, in laboratory experiments, by the decreased length of time required for digestion when fibrin has first been soaked in 0.2 per cent hydrochloric acid and thus caused to swell with the absorption of water before coming in contract with the pepsin.

Circumstances Influencing Gastric Digestion. A temperature of about 40° C. is most favorable to gastric digestion. The pepsin is destroyed by a temperature of 55° (neutral) to 65° C. (acid solution) and its action is retarded and suspended by low temperatures. It is inactive in neutral or alkaline solution, for an acid medium is necessary. Hydrochloric is the best acid for the purpose, but nitric acid or the organic acids may be substituted for the hydrochloric. Excess of peptone delays the action, and the removal of the products of digestion facilitates the process.

Action of Rennin. *Milk* is curdled, the casein being precipitated, and then dissolved. The curdling is due to a special ferment of the gastric juice, rennin, and is not due to the action of the free acid alone. The effect of rennin, which is obtained from the fourth stomach of a calf, has long been known, as it is used extensively to cause precipitation of casein in cheese manufacture. The ferment rennin is active in a neutral solution as well as in acid.

Time Occupied in Gastric Digestion. Under ordinary conditions, from three to four hours may be taken as the average time occupied by the digestion of a meal in the stomach. But many circumstances will modify the rate of gastric digestion. The chief are: The *nature* of the food taken and its *quantity* (the stomach should be fairly filled, not distended); the time that has elapsed since the last meal, which should be at least enough for the stomach to be quite clear of food; the amount of exercise previous and subsequent to a meal (gentle exercise being favorable, over-exertion injurious to digestion); the state of mind; and the bodily health.

Summary of Changes in the Food in Gastric Digestion. Briefly summarizing the action of gastric juice, the facts appear as follows: Gastric juice has a specific digestive action on proteid foods of all kinds, converting them into the more soluble *proteoses* and *peptones*. The action is due to an enzyme, *pepsin*, acting in and with an acid, *hydrochloric acid*. Digestion takes place best at the temperature of the body, is destroyed by high heat and suspended by cold, 0° C. Putrefaction is prevented by gastric juice. Milk is first coagulated by a special enzyme, *rennin*, and then digested as any other proteid. Gastric juice dissolves soluble substances like salts, saccharides, etc. Fats and carbohydrates are not digested by gastric juice, in fact fats tend to hinder the action.

MOVEMENTS OF THE STOMACH.

Attention has been called to the fact that the stomach is a muscular sac capable of holding quite a large mass of food. During a full meal as much

as one to two liters or more of semi-solid food is packed away in the organ in a comparatively short space of time. The gastric juice is secreted by the mucous membrane which surrounds the surface of the food mass. The result is that the secretion begins to soften and digest the food over its surface, thus tending to liquefy and erode away layer after layer of the food mass. The picture is made clearer if one remembers that the food mass is retained almost wholly in the fundus of the stomach. The pyloric portion of the stomach is quite strongly muscular and quite definitely marked off by the strong transverse band at its union with the fundus.

The gastric juice is assisted in accomplishing digestion by the movements of the stomach itself. When digestion is not going on, the stomach is uniformly contracted, its orifices not more firmly than the rest of its walls; but, if examined shortly after the introduction of food, it is found closely encircling its contents, and its orifices are firmly closed like sphincters. The cardiac orifice, every time food is swallowed, opens to admit its passage to the stomach, and immediately closes again. The pyloric orifice, during the taking of food

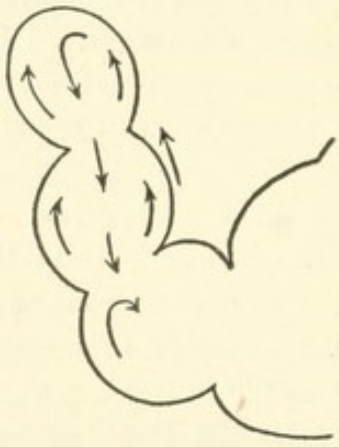


FIG. 261.—Diagram to Show the Movement of Food in the Pylorus at Times when the Pyloric Valve is Closed.

and the first part of gastric digestion, is so completely closed that none of the contents escape.

The character of stomach movements has been admirably determined by recent observers using the Roentgen-ray method. Thus Cannon working with cats has shown that in from five to ten minutes after a meal slight rings or constrictions occur in the pyloric antrum and travel slowly toward the pyloric valve in the form of a peristaltic wave. Successive waves begin a little further back toward the fundus each time and follow over the pyloric antrum with clocklike regularity, in the cat one wave in ten seconds, which requires in each case about twenty seconds for its completion. In man they are doubtless slower. These peristalses continue during the whole period of digestion, for as much as seven or even more hours.

These peristaltic contractions aid the gastric juice in carrying away the

softened layers of food by propelling it into the pylorus. There it is thoroughly mixed with the gastric juice, forming the *chyme*. Figure 261 gives an idea of the movement of the food in the antrum. The peristaltic contractions carry it forward, but if the valve does not open to permit passage to the duodenum, then the pressure will force the *chyme* back through the center toward the fundus. After several minutes the pyloric sphincter will occasionally relax to allow fluid food to pass to the duodenum, but when more solid particles come

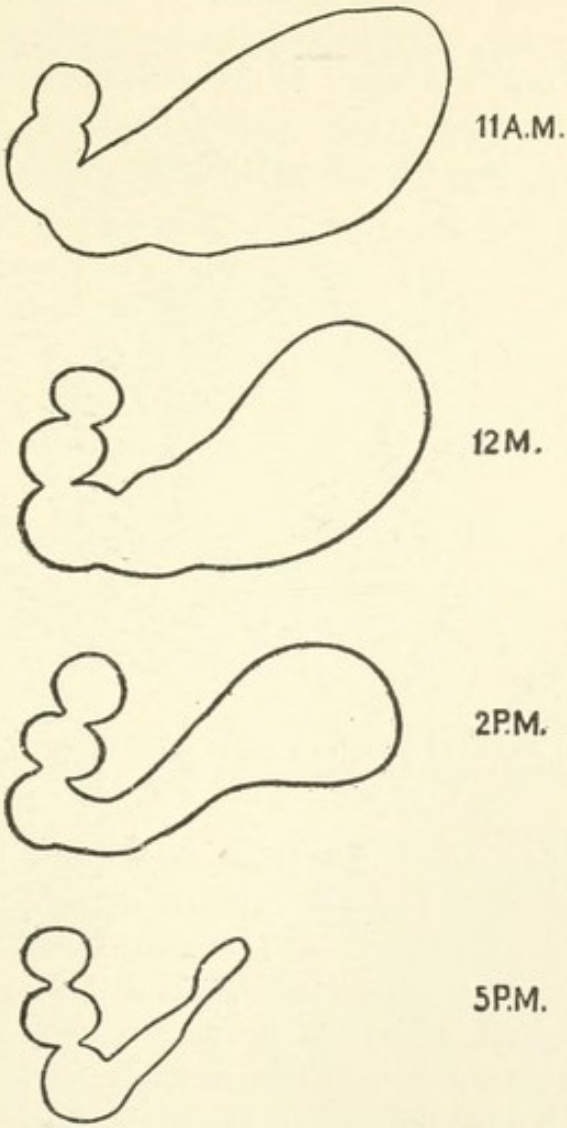


FIG. 262.—Outlines of the Roentgen-ray Shadows of the Stomach Content as Digestion Progresses. (Cannon.)

up against the valve the sphincter promptly contracts and remains so for some time. Toward the completion of digestion even solid undigested particles are carried on into the intestine.

The movements of the stomach are under nervous regulation. Cannon found that the peristalses were promptly inhibited in cats by excitement. Stimulation of the vagi leads to contractions of the stomach, while the splanchnics

bring about relaxation or dilatation. It is also demonstrated that afferent vagus impulses influence the contractions in the stomach.

It seems probable that automatic peristaltic contraction is inherent in the muscular coat of the stomach, and that the central nervous system is only employed to regulate it by impulses passing down by the vagi or splanchnic nerves.

Vomiting. The expulsion of the contents of the stomach in *vomiting* is preceded by a deep inspiration with closure of the glottis, followed immediately afterward by strong contractions of the muscles of the abdomen, diaphragm, and stomach. The diaphragm forms an unyielding surface against which the stomach can be pressed. In this way as well as by its own contraction the diaphragm is *fixed*, to use a technical phrase. At the same time the cardiac sphincter muscle is relaxed, and the orifice which it naturally guards is

FIG. 263.—Horizontal Section of a Small Fragment of the Mucous Membrane, including one entire crypt of Lieberkühn and parts of several others.

actively dilated. The *pylorus* is closed, and, the stomach itself also contracting, the action of the abdominal muscles produces strong compression which expels the contents of the organ through the esophagus, pharynx, and mouth. Reversed peristaltic action of the esophagus probably increases the effect.

It has been frequently stated that the stomach itself is quite passive during vomiting, and that the expulsion of its contents is effected solely by the pressure exerted upon it when the capacity of the abdomen is diminished by the contraction of the diaphragm. It is true that facts are wanting to demonstrate with certainty this action of the stomach in vomiting; but cases of fistulous opening into the organ appear to support the belief that it does take place; and the analogy of the case of the stomach with that of the other hollow viscera, as the rectum and bladder, may also be cited in confirmation.

Vomiting is a reflex act. It can be excited by irritation of the lining of the stomach which is perhaps the normal stimulus. It is excited by stimulation or irritation of other parts of the alimentary tube, *i.e.*, the pharynx, the

uvula, the intestine, etc. Vomiting may occur from stimulation of sensory nerves from many organs, *e.g.*, kidney, testicle, etc., or by impulses arising in the organs of special sense, the eye, olfactory membrane, etc. The sensory impulses are coordinated by a nerve center located in the medulla. The center may also be stimulated by impressions from the cerebrum and cerebellum or by changes arising in the center itself, the so-called central vomiting occurring in disease of those parts. The efferent impulses are carried by the phrenics and other spinal nerves and by the vagus.

DIGESTION IN THE INTESTINES.

The food that enters the small intestine has already been subjected to two digestive enzymes. The ptyalin of the saliva and the pepsin of the gastric juice together with the mechanical processes involved have reduced the food to a pulpy mass, the chyme. This peptonized *food* contains most of the total quantity of food eaten, little having been absorbed as we shall see later, but much of the starch has been changed to soluble maltose and dextrose and the proteid to albumoses and peptones. The discharge from the stomach through the pyloric valve to the duodenum has been going on through three

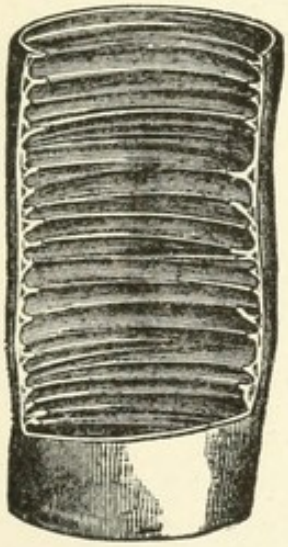


FIG. 264.

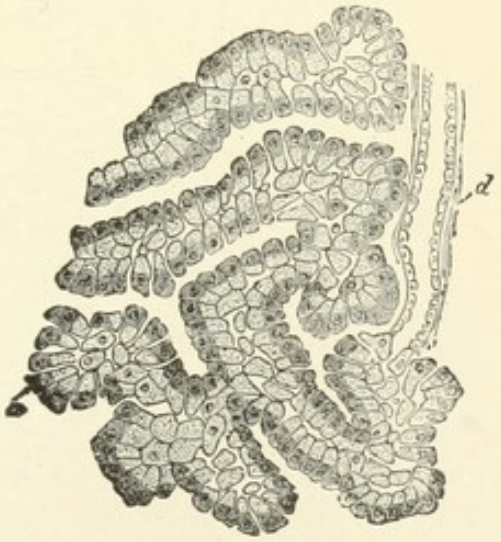


FIG. 265.

FIG. 264.—Piece of Small Intestine (previously distended and hardened by alcohol), Laid open to Show the Normal Position of the Valvulæ Conniventes.

FIG. 265.—Section of the Pancreas of a Dog During Digestion. *a*, Alveoli lined with cells, the outer zone of which is well stained with hematoxylin; *d*, intermediary duct lined with squamous epithelium. × 350. (Klein and Noble Smith.)

or four hours on an average for each full meal. This stream of food passing down the small intestine, slowly because of the valvulæ conniventes, meets a number of secretions which contain enzymes which act on each of the three great food principles, proteids, fats, and carbohydrates. These secretions are the pancreatic fluid, the succus entericus, and the bile.

The Pancreas. The pancreas is situated within the curve formed by the duodenum; and its main duct opens into that part of the small intestine through a duct common to it and to the liver and about two and a half inches from the pylorus.

The pancreas bears some resemblence in structure to the salivary glands. Its capsule and septa, as well as the blood-vessels and lymphatics, are similarly distributed. It is, however, looser, the lobes and lobules being less compactly arranged.

Heidenhain has observed that the alveolar cells in the pancreas of a fasting dog consist of two zones, an inner or central zone which is finely granular,

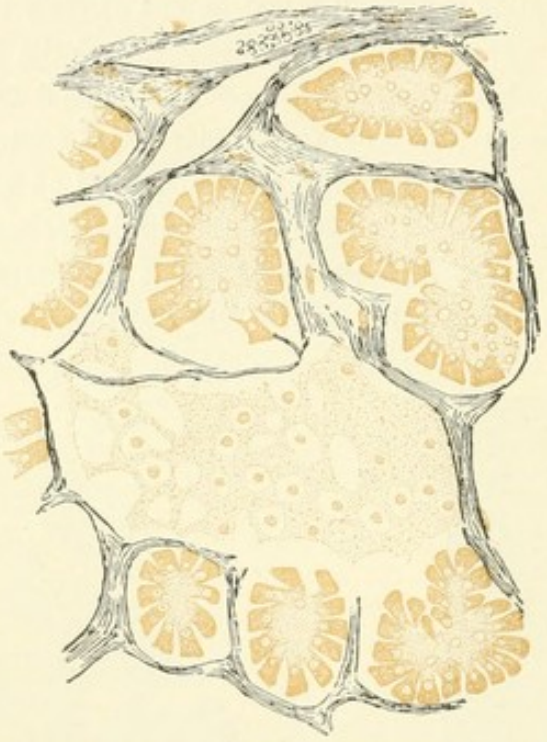


FIG. 266.—Section of the Pancreas of Armadillo, Showing the Two Kinds of Gland-structure. (V. D. Harris.)

and which stains feebly, and a smaller parietal zone of finely striated protoplasm which stains easily. The nucleus is partly in one, partly in the other zone. During secretion it is found that the outer zone increases in size, and the central granular zone diminishes, as in the case of the salivary glands. The pancreatic cell itself becomes smaller from the discharge of the secretion. During a period of rest the granular zone again increases in size and the outlines of the cells become full and indistinct. The granules, as in the salivary cells, are the material from which, under certain conditions, the ferments of the gland are developed, and which are therefore a *Zymogen*. In addition to the ordinary alveoli of the pancreas there are distributed irregularly in the gland other collections of cells of a different character, the *Islands of Langerhans*. These cells are considerably smaller, their protoplasm is more

granular and less easily stained with hematoxylin, and their nuclei are small and stain deeply. The collections of cells vary in size and shape. The special form of nerve terminations, called *Pacinian corpuscles*, are often found in the pancreas. The secretion of the pancreas has been obtained for purposes of experiment from the lower animals and from man in at least one case. A pancreatic fistula is established in the dog by opening the

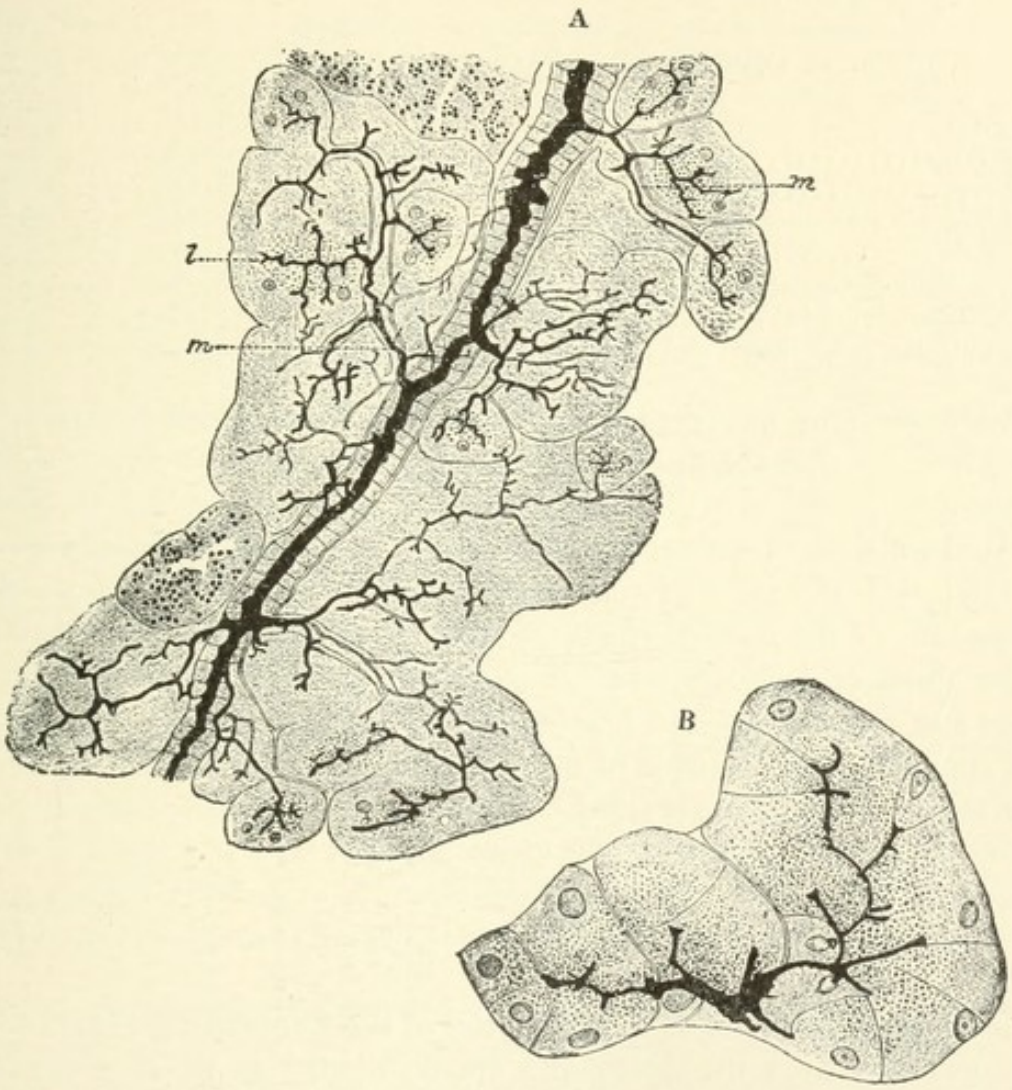


FIG. 267.—Duct with Laterals to the Alveoli. Silver method of Golgi (E. Muller). *A*, Duct with branches; *m*, between the cells. *B*, Laterals more strongly magnified.

abdomen and exposing the duct of the gland which is then made to communicate with the exterior. In Pawlow's method a circular bit of the intestinal mucous membrane around the mouth of the duct in the intestine is brought to the surface and stitched into the wound. The secretion is then easily collected into a vessel suspended under the opening.

The Pancreatic Juice. Pancreatic juice is colorless, transparent, slightly viscid, and alkaline in reaction. It varies in specific gravity from 1010 to 1030, according as it is obtained from a permanent fistula—then more

watery, or from a newly opened duct. The solids vary in a temporary fistula from 80 to 100 parts per thousand, and in a permanent one from 16 to 50 per thousand. It is characterized by having three distinct and important enzymes known as *trypsin*, *amylopsin*, and *steapsin*, whose actions are respectively, proteolytic, amylolytic, and lipolytic (fat-splitting). *Maltase*, which inverts the disaccharides, is also present, and some have stated that *rennin* is found in pancreatic juice.

CHEMICAL COMPOSITION OF PANCREATIC JUICE. (C. SCHMIDT.)

From a dog.	Recent fistula.	Permanent fistula.
Water	900.76	980.45
Solids	99.24	19.55
Organic substances	90.44	12.71
Ash	8.80	6.84
Sodium carbonate	0.58	3.31
Sodium chloride	7.35	2.50
Calcium, magnesium, and sodium phosphates	0.53	0.08

An extract of pancreas made from the gland which has been removed from an animal killed during digestion possesses the active properties of pancreatic secretion. It is made by first dehydrating in absolute alcohol the gland which has been cut up into small pieces. After the entire removal of the alcohol the gland is pulverized and extracted in strong glycerin. The amount of the ferment greatly increases if the gland be exposed to the air for three or four hours before placing in alcohol; indeed, a glycerin extract made from the gland immediately upon the removal from the body often appears to contain none of the ferments. The conversion of zymogen in the gland into the ferment takes place only after the gland stands a while. Dilute acid assists or accelerates the conversion, and if a recent pancreas be rubbed up with dilute acid before dehydration, a glycerin extract made afterward, even though the gland may have been only recently removed from the body, is very active.

Nervous Regulation of the Secretion of the Pancreas. Fibers from the vagus and from the splanchnics are distributed to the pancreas. In Pawlow's laboratory it has been found that stimulation of these nerves leads to the increased secretion of the pancreas. Popielski, in studying the effects of dilute hydrochloric acid solution in the duodenum, which resulted in a marked increase of pancreatic secretion, explained the phenomenon as a local nerve reflex.

Doubt has been cast on the whole question of nervous control by the recent discovery of the fact that acid (0.4 per cent hydrochloric acid) in the duodenum results in the production of a chemical substance, *secretin*, by the duodenal mucous membrane. This secretin is absorbed into the circulation and acts specifically on the pancreas to produce increased activity by the pancreatic cells. Acid extracts of the duodenal mucous membrane produce the same

effects on the pancreas, in fact this is the current method of stimulating the flow of pancreatic juice at the present time, the secretion being collected from a tube introduced into the duct

Under the normal stimulus of food, the flow of pancreatic juice is greatly increased. The increase continues to a maximum in from two to three hours, after which it gradually decreases through the period of digestion. Pawlow

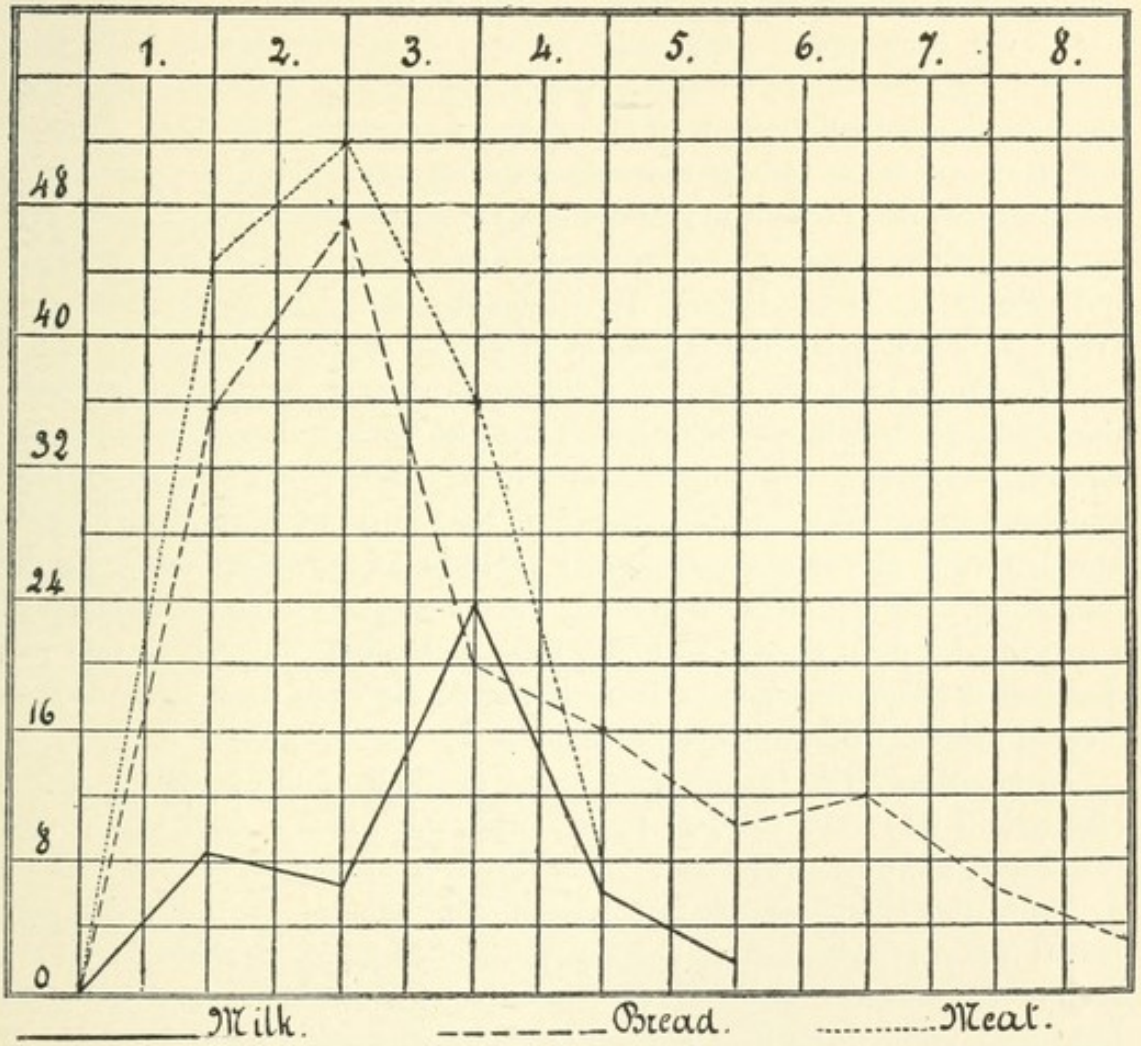


FIG. 268.—Three Curves Showing the Secretion of Pancreatic Juice upon a Diet (1) of 600 c.c. of milk; (2) of 250 gm. of bread; (3) of 100 gm. of meat. The divisions along the abscissa represent hours after the beginning of the meal; the figures along the ordinates represent the quantity of the secretion in cubic centimeters. (Walter.)

has found a certain amount of adaptation not only of the quantity but of the enzyme composition of the pancreatic secretion to the kind and character of the food (in dogs).

Action of the Enzymes of Pancreatic Juice. The secretion of the pancreas accomplishes its digestive action by means of the enzymes given above, viz., *trypsin*, *amylopsin*, *steapsin*, and *maltase*.

Trypsin. Trypsin is a proteolytic enzyme. Strange to say it does not exist in the fresh pancreatic juice as such, but makes its appearance only when there

is an admixture with the secretion of the mucous membrane of the intestine. The succus entericus contains an activating enzyme, *enterokinase*, which converts the inactive and stable trypsinogen of the pancreatic juice into the active but less stable trypsin. This fact is another of the wonderful series of contributions to the exact knowledge of the subject of digestion made from Pawlow's laboratories.

Trypsin converts *proteids into proteoses and peptones.* The process is both more rapid and more complete than in gastric digestion, so that, in the final result, the peptones are greatly in excess of the proteoses. The proteids pass through the same preliminary stages as in gastric digestion, being split at first into alkali-albumin, then into primary proteoses, both proto-proteose and hetero-proteose, and then into deutero-proteose. The first stages are so transient that it is difficult to detect either the alkali-albumin or primary proteose. The deutero-albumoses are easily demonstrated in the earlier stages, but become very scanty later. Anti-albumid is found as a side product in artificial digestion, but is not present in normal digestion.

Trypsin also has the power of splitting a certain proportion of peptones, the hemi-peptones, into simpler bodies such as *leucin* or amido-caproic acid, *tyrosin* or paraoxyphenyl-amido-propionic acid, *lysin*, *lysatinin*, *tryptophan*, and some other bodies. In the cleavage of the proteid molecule there is probably left a complex nucleus which may yet serve as a synthetic center for the rebuilding of the proteid molecule. This nucleus is called a *polypeptid.* Leucin and tyrosin have been found in the intestinal contents, so that this destruction of hemipeptone in artificial tryptic digestion must take place to a certain extent within the body as well.

In laboratory experiments only about one-half of the peptones can be changed in this way. The more stable portion which cannot be changed is usually known as *antipeptone.* There are several theories as to the reason or use of this change into leucin, tyrosin, etc. One of the most plausible is that it saves the body from needless work when too much proteid food has been taken; the breaking down in the intestine of bodies only slightly removed from urea relieves the liver and other glandular organs from the strain of converting an excess of absorbed proteid material into a form in which it can be excreted. Another theory is that leucin, tyrosin, etc., are essential for the physiological working of the body in some unknown way, just as are the products of the thyroid gland. The formation of the decomposition products, indol and skatol, is caused by the action of bacteria on proteids. The albuminous or proteid substances which have not been converted into peptone in the stomach, and the partially changed substances, *i.e.*, the proteoses, are converted into peptone by the pancreatic juice, and then in part into leucin and tyrosin, etc.

The ferment trypsin acts best in an alkaline medium, but will act also in a neutral medium, or in the presence of a small amount of combined acid;

it will not work in the presence of free acid. It therefore differs from pepsin in being able to act without the aid of any other substance than water. In the process of tryptic digestion, proteid matter does not swell up at first, but seems to be corroded at once.

Amylopsin. *Starch* is converted into *maltose* in an exactly similar manner to that which happens with saliva, erythro-dextrin and one or more achroödextrins being the intermediate products. The amylolytic enzyme of the pancreatic juice, which cannot be distinguished from ptyalin, is called *amylopsin.* The maltose thus formed is converted to dextrose by the *maltase,* in which form it is ultimately absorbed.

Pancreatic juice, according to certain observers, possesses the property of curdling milk. It contains a special ferment, rennin, for that purpose. The ferment is distinct from trypsin, and will act in the presence of an acid (W. Roberts). The milk-curdling ferment of the pancreas is, in some pancreatic extracts, said to be quite powerful, insomuch that 1 c.c. of a brine extract will coagulate 50 c.c. of milk in a minute or two.

Steapsin or Lipase. *Oils and fats* are *emulsified* and *saponified* by the pancreatic secretion. The terms emulsification and saponification may need a little explanation. The former is used to signify an important mechanical change in oils or fats, whereby they are made into an emulsion, or in other words are minutely subdivided into small particles. If a small drop of an emulsion be looked at under the microscope it will be seen to be made up of an immense number of minute rounded particles of oil or fat, of varying sizes. The more complete the emulsion the smaller are these particles. An emulsion is formed at once if oil or fat, which when old is slightly acid from the presence of free fatty acid, is mixed with an alkaline solution. Saponification signifies a distinct chemical change in the composition of oils and fats. An oil or a fat being made up chemically of *glycerin,* a triatomic alcohol, and one or more fatty-acid radicles, when an alkali (potassium hydrate) is added to it and heat is applied, two changes take place: first, the oil or fat is split up into glycerin and its corresponding fatty acid; second the fatty acid combines with the alkali to form a soap which is chemically known as stearate, oleate, or palmitate of potassium. Saponification thus means a chemical splitting up of oils or fats into new compounds, and emulsification means merely a mechanical splitting up into minute particles. The pancreatic juice has been for many years credited with the possession of a special ferment, which was called by Claude Bernard *steapsin,* and which is a *lipase* or fat-splitting ferment. This ferment has not been isolated, but its presence may be demonstrated by adding portions of the fresh pancreas to butter or other fat and maintaining the proper temperature. Its action is made manifest by the liberation of butyric acid, which smells like rancid butter.

The generally accepted theory is that only a small portion of the fat which is eaten is thus changed into soap, and that the function of the saponified fat

is to assist in the emulsification of the major part, a process which is favorably influenced by the bile. The proper emulsification of fat is a necessary preliminary to its absorption, for when in disease the entrance of the pancreatic juice and of the bile to the intestine is interfered with, the feces contain a great excess of fat.

Some recent experiments, however, tend to prove that the entire fat of the food is changed in the intestine into fatty acids and glycerin; that the fatty acids are entirely, or in part, changed to soaps; and that these soaps, or mixture of soaps and free fatty acids, are absorbed in solution. The chief facts favoring this view are that: (1) The action of steapsin is sufficiently rapid to allow the saponification of a full fatty meal within the ordinary period of digestion; (2) histological examination has never shown that fat particles can pass into a columnar cell, and none have ever been found in the broad striated border of the cell; (3) the fat globules found in columnar cells after a fatty meal grow steadily larger as the period of absorption progresses, indicating that they are deposited from solution; (4) the fatty acids are easily soluble in bile solutions, and the solubility of the soaps is greatly increased by the presence of bile. The fat constituents, according to this theory, are recombined in the columnar cells to form neutral fats.

Conditions which Influence the Action of the Pancreatic Enzymes. The various pancreatic enzymes are influenced by heat, by the presence of an excess of digestion products, etc., in the same way as ptyalin and pepsin. Pancreatic enzymes act in a neutral but best in an alkaline solution. The trypsin, strange to say, is quickly destroyed by the alkaline solution (Bayliss and Starling). The pancreatic juice offers the special case of a secretion of proenzyme which is stable in alkaline solution until acted on by enterokinase, and the amount of kinase present will, therefore, markedly influence the amount of digestion of proteid per unit of time.

The Secretions of the Liver. The *liver*, the largest gland in the body, situated in the abdomen on the right side chiefly, is an extremely vascular organ, and receives its supply of blood from two distinct sources, viz.,

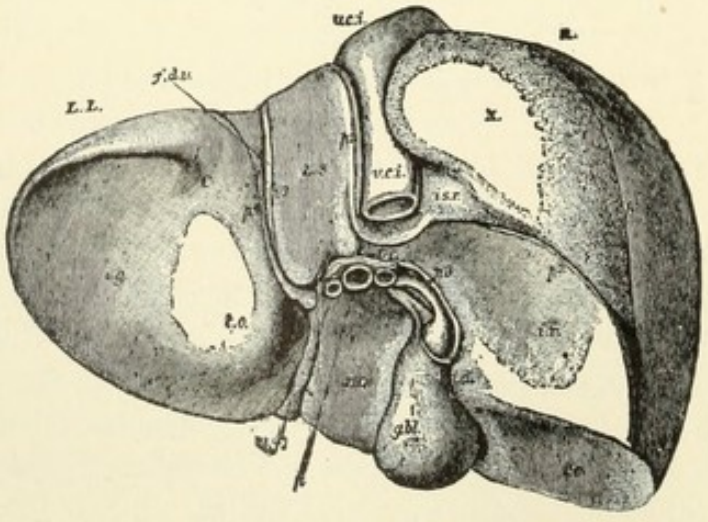


FIG. 269.—The Liver from Below and Behind. *L. S.*, Spigelian lobe; *L. C.*, caudate lobe; *L. Q.*, quadrate lobe; *R. L.*, right lobe; *L.L.*, left lobe; *g. bl.*, gall-bladder; *v.c.i.*, inferior vena cava; *u.f.*, umbilical fissure; *f.d.v.*, fissure of the ductus venosus; *p*, portal fissure with portal vein, hepatic artery and bile-duct. (Wesley, from a His model.)

from the *portal vein* and from the hepatic *artery*, while the blood is returned from it into the vena cava inferior by the *hepatic veins*. Its secretion, the bile, is conveyed from it by the *hepatic duct*, either directly into the intestine, or, when digestion is not going on, into the *cystic* duct, and thence into the gall-

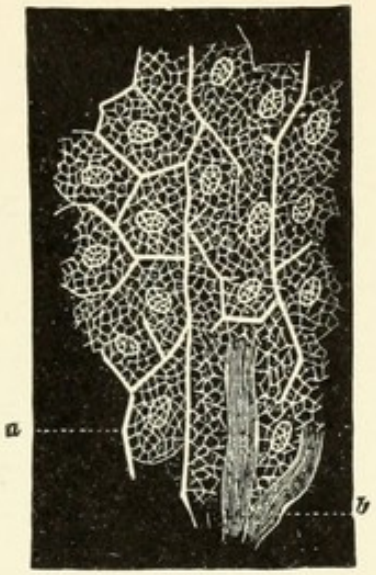


FIG. 270.—Portion of a Lobule of Liver. *a*, Bile capillaries between liver cells, the network in which is well seen; *b*, blood capillaries. × 350. (Klein and Noble Smith.)

bladder, where it accumulates until required. The portal vein, hepatic artery, and hepatic duct branch together throughout the liver, while the hepatic veins and their tributaries run by themselves. The interstices of these vessels are filled by the liver cells.

Structure of the Liver. The liver is made up of small roundish or oval portions called *lobules*, each of which is about $\frac{1}{20}$ of an inch (about

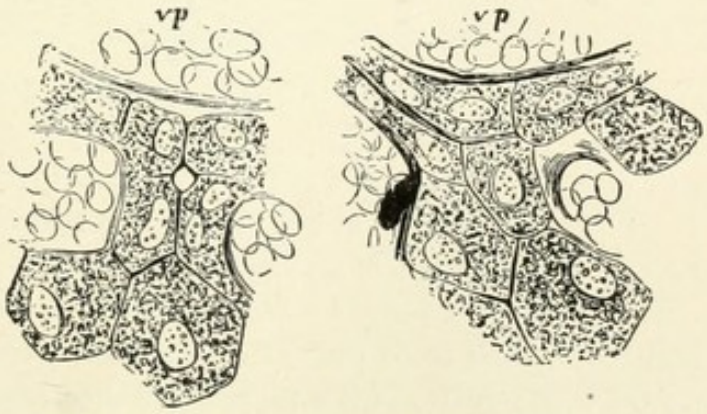


FIG. 271.—Hepatic Cells and Bile Capillaries, from the Liver of a Child Three Months Old. Both figures represent fragments of a section carried through the periphery of a lobule. The red corpuscles of the blood are recognized by their circular contour; *vp*, corresponds to an interlobular vein in immediate proximity with which are the epithelial cells of the biliary ducts. (E. Hering.)

1 mm.) in diameter, and includes the minute hepatic artery and hepatic duct. The hepatic cells, which form the glandular or secreting part of the liver, are of spheroidal form, somewhat polygonal from mutual pressure, about

25 to 30 μ in diameter, and possess one, sometimes two nuclei. The cell-substance contains a variable amount of glycogen and often some fatty molecules, and possibly some granules of bile pigment.

The bile capillaries commence between the hepatic cells, and are bounded by a delicate membranous wall of their own. They appear to be always

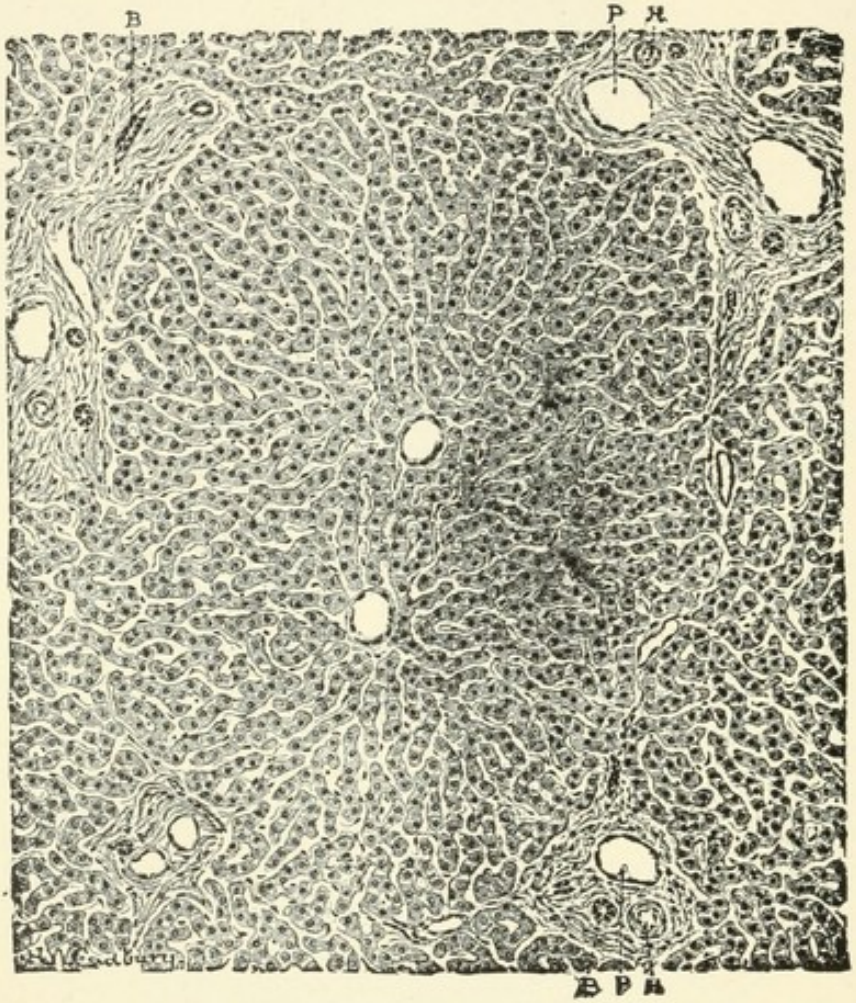


FIG. 272.—Section of Liver. × 80. *P*, Portal vein; *H*, hepatic artery; *B*, bile-duct. (Hendrickson.)

bounded by hepatic cells on all sides, and are thus separated from the nearest blood capillary by at least the breadth of one cell, figures 271 and 272.

The *gall-bladder*, *g. bl*, figure 269, is a pyriform sac attached to the under surface of the liver, and supported also by the peritoneum. The larger end, or *fundus*, projects beyond the front margin of the liver, while the smaller end contracts into the cystic duct. It is a muscular walled reservoir covered with a serous epithelium and lined by mucous membrane. The function of the gall-bladder is to retain the bile during the interval of digestion.

The Bile. The bile is a somewhat viscid fluid, of a yellow, reddish-yellow, or green color, a strongly bitter taste, and, when fresh, with a scarcely perceptible odor; it has a neutral or slightly alkaline reaction, and its specific gravity is about 1020. Its color and consistency vary much, quite independent

of disease; but, as a rule, bile becomes gradually more deeply colored and thicker as it advances along its ducts, or when it remains long in the gall-bladder where it becomes more viscid and ropy, darker, and more bitter. This is on account of its greater degree of concentration, from resorption of its water, and also from being mixed with mucus.

CHEMICAL COMPOSITION OF HUMAN BILE. (FRERICHS.)

Water		859.2
Solids—Bile salts	91.5	
Fat	9.2	
Cholesterin	2.6	
Mucus and coloring matters	29.8	
Salts	7.7	
	140.8	
	1000.0	

Bile salts can be obtained as colorless, exceedingly deliquescent crystals, soluble in water, alcohol, and alkaline solutions, giving to the watery solution the taste and general characters of bile. They consist of sodium salts of glycocholic and taurocholic acids; the formula of the former being $C_{26}H_{42}NaNO_6$, and of the latter $C_{26}H_{44}NaNO_7S$.

The bile acids are easily decomposed by the action of dilute acids or alkalies thus:

$$\underset{\text{Glycocholic Acid.}}{C_{26}H_{43}NO_6} + H_2O = \underset{\text{Glycin.}}{C_2H_5NO_2} + \underset{\text{Cholic Acid.}}{C_{24}H_{40}O_5}$$

$$\text{and } \underset{\text{Taurocholic Acid.}}{C_{26}H_{45}NO_7S} + H_2O = \underset{\text{Taurin.}}{C_2H_7NO_3S} + \underset{\text{Cholic Acid.}}{C_{24}H_{40}O_5}$$

Glycin is amido-acetic acid, *i.e.*, acetic acid $C_2H_4O_2$, with one of the atoms of H replaced by the radical amidogen $NH_2C_2H_3(NH_2)O_2$, $C_2H_5NO_2$. Taurin likewise is amido-isethionic acid. Isethionic acid is sulphurous acid H_2SO_3, in which an atom of H is replaced by the monatomic radicle oxy-ethylene, C_2H_4OH, viz., $H(C_2H_4OH)SO_3$, and in amido-isethionic acid, the OH hydroxyl in this radicle is replaced by amidogen NH_2, thus $H(C_2H_4NH_2)SO_3 = C_2H_7NSO_3$. The proportion of these two salts in the bile of different animals varies, *e.g.*, in the ox bile the glycocholate is in great excess, whereas the bile of the dog, cat, bear, and other carnivora contains taurocholate alone. In human bile the glycocholate is in excess (4.8 to 1.5).

The yellow *coloring matter* of the bile of man and the Carnivora is termed *Bilirubin*, $C_{16}H_{18}N_2O_3$, is crystallizable and insoluble in water, and soluble in chloroform or carbon disulphide. A green coloring matter, Biliverdin, $C_{16}H_{18}N_2O_4$, which always exists in large amount in the bile of Herbivora, is formed from bilirubin on exposure to the air, or by subjecting the bile to any other oxidizing agency, as by adding nitrous acid. Biliverdin is soluble in alcohol, glacial acetic acid, and strong sulphuric acid, but insoluble in water, in chloroform, and ether. It is usually amorphous, but may sometimes crystallize in green rhombic plates.

There is a close relationship between the coloring matters of the blood and of the bile, and it may be added, between these and that of the urine,

urobilin, and of the feces, *stercobilin*. It is probable they are, all of them, varieties of the same pigment, or derived from the same source. Cholesterin, $C_{27}H_{45}OH$, and lecithin, $C_{42}H_{84}NPO_9$ are constant constituents of bile. Iron is found among the salts of the ash.

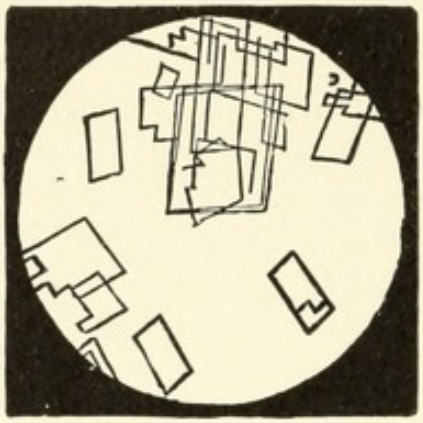


FIG. 273.—Crystalline Scales of Cholesterin.

The Rôle of Bile in Intestinal Digestion. Though it is not a true digestive fluid, in that it has no ferment and digests nothing itself, yet it must be regarded as an important aid to digestion for the following reasons: (*a*) Bile assists in *emulsifying the fats* of the food, and thus renders them capable of passing into the lacteals by absorption. For it has appeared in some experiments in which the common bile-duct was tied, that, although the process of digestion in the stomach was unaffected, chyle was no longer well formed; the contents of the lacteals consisting of clear, colorless fluid, instead of being opaque and white, as they ordinarily are after feeding. It is, however, the combined action of the bile with the pancreatic juice to which the emulsification is due rather than to that of the bile alone. The bile itself has a very feeble emulsifying power. If the theory be accepted that fats are absorbed as fatty acids and soaps, in solution, the action of the bile becomes very important because solutions of bile salts have the power of dissolving the fatty acids. The moistening of the mucous membrane of the intestines with bile, for this very reason, facilitates absorption of fatty matters through it.

(*b*) The bile, like the gastric fluid, has a certain but not very considerable *antiseptic* power, and may serve to prevent the decomposition of food during the time of its sojourn in the intestines. Experiments show that the contents of the intestines are much more fetid after the common bile-duct has been tied than at other times. Moreover, it is found that the mixture of bile with a fermenting fluid stops the process of fermentation.

Bile is also an excretive fluid carrying waste products thrown off by the liver. The liver during fetal life is proportionately larger than it is after birth, and the secretion of bile is active, although there is no food in the intestinal canal upon which it can exercise any digestive property. At birth,

the intestinal canal is full of concentrated bile, mixed with intestinal secretion, and this constitutes the *meconium*, or feces of the fetus. In the fetus, therefore, the main purpose of the secretion of bile must be directly excretive. Probably all the bile secreted in fetal life is incorporated in the meconium, and with it discharged.

Mode of Secretion and Discharge of Bile. The secretion of bile is continually going on, but is retarded during fasting, and accelerated on taking food. This is shown by tying the common bile-duct of a dog, and establishing a fistulous opening between the skin and gall-bladder, whereby all the bile secreted is discharged at the surface. When the animal is fasting, sometimes not a drop of bile is discharged for several hours. In about ten minutes after the introduction of food into the stomach, the bile begins to flow abundantly, and continues to do so during the period of digestion.

The bile is constantly being formed in the hepatic cells; thence, being discharged into the minute hepatic ducts, it passes into the larger trunks, and from the main hepatic duct may be carried at once into the duodenum. This probably happens only while digestion is going on, *i.e.*, for five to seven hours after the introduction of food into the stomach. During fasting, it flows from the common bile-duct through the cystic duct into the gall-bladder, where it accumulates till, in the next period of digestion, it is discharged into the intestine. The gall-bladder thus acts as a reservoir for the bile during the intervals when digestion is not in progress.

The mechanism by which the bile passes into the gall-bladder is simple. The orifice through which the common bile-duct communicates with the duodenum is narrower than the duct, and appears to be closed, except when

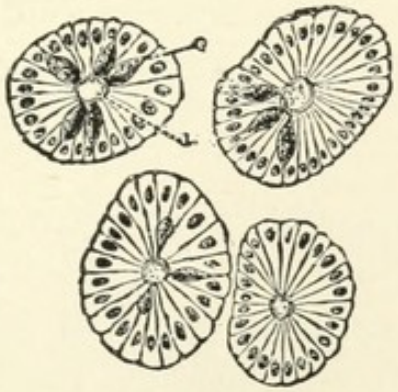


FIG. 274.—Transverse Section through Four Crypts of Lieberkühn, from the Large Intestine of the Pig. They are lined by columnar epithelial cells, the nuclei being placed in the outer part of the cells. The divisions between the cells are seen as lines radiating from L, the lumen of the crypt; G, epithelial cells, which have become transformed into goblet cells. × 350. (Klein and Noble Smith.)

there is sufficient pressure behind to force the bile through it. The pressure exercised upon the bile secreted during the intervals between periods of digestion appears insufficient to overcome the force of the sphincter by which the orifice of the duct is closed; and the bile in the common duct traverses the

cystic duct and so passes into the gall-bladder, being probably aided in this retrograde course by the peristaltic action of the ducts. The bile is discharged from the gall-bladder and enters the duodenum on the introduction of food into the small intestine. It is pressed on by the contraction of the coats of the gall-bladder, and of the common bile-duct. Their contraction is excited by the stimulus of the food in the duodenum acting through a reflex arc to produce contractions, the force of which is sufficient to open the orifice of the common bile-duct.

When the discharge of the bile into the intestine is prevented by an obstruction of some kind, as by a *gall-stone* blocking the hepatic duct, it is reab-

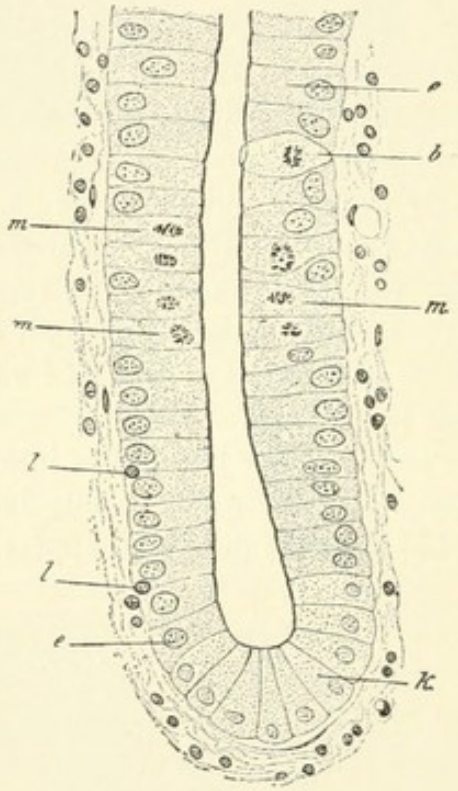


FIG. 275.—Longitudinal Section of Fundus of Crypt of Lieberkühn. *b*, Goblet cell showing mitosis; *e*, epithelial cell; *k*, cell of Paneth; *l*, leucocyte in epithelium; *m*, mitosis in epithelial cell. Surrounding the crypt is seen the stroma of the mucous membrane. × 530. (Kölliker.)

sorbed in great excess into the blood, and, circulating with it, gives rise to the well-known phenomena of jaundice. This is explained by the fact that the pressure of secretion in the ducts, although normally very low, not exceeding 15 millimeters of mercury in the dog, is still higher than that of the portal veins. If the pressure exceeds 15 mm. the secretion continues to be formed but passes into the blood-vessels through the lymphatics.

The Intestinal Secretion, or Succus Entericus. It is impossible to isolate the secretion of the glands of Brunner or of the glands of Lieberkühn, but the total secretion of the intestinal mucosa can be secured by isolating a loop of intestine by the operation known as the Thiry fistula. A few drops

of secretion, the *succus entericus*, can be obtained by this means. Intestinal juice is a yellowish alkaline fluid with a specific gravity of 1011 and contains about 2.5 per cent of solid matters.

Intestinal juice has only slight digestive action. It contains a weak proteolytic enzyme and a weak amylolytic enzyme. Maltase is also present. But the chief and most profound importance is given to the intestinal juice by the discovery of the activating enzyme, *enterokinase*. This specific activating enzyme for the trypsinogen of the pancreatic juice places the intestinal secretion in the rank of necessary secretion for efficient digestion. Enterokinase can be prepared by extracting the superficial scrapings of the intestinal mucous coat. The duodenal region is richest in enterokinase, but the secretion of the lower intestinal lengths also contains the enzyme.

Extracts of the mucosa of the intestine have been found to contain another substance which has the specific action of splitting peptones into simpler amino bodies. This substance has been called *erepsin*.

There are, therefore, three important new substances in the succus entericus (or in the extract of the glands), *secretin*, *erepsin*, and *enterokinase*, in addition to the proteolytic and diastatic enzymes.

Summary of the Digestive Changes in the Small Intestine. The thin chyme which, during the whole period of gastric digestion, is being constantly squeezed or strained through the pyloric orifice into the duodenum, consists of albuminous matter that is broken down, dissolving and half dissolved; of fatty matter broken down and melted, but not dissolved at all; of starch in various stages of the process of conversion into sugar, and as it becomes sugar dissolving in the fluids with which it is mixed; while with these are mingled gastric juice and fluid that has been swallowed, together with such portions of the food as are not digestible.

The chyme in the duodenum is subjected to the influence of the bile and pancreatic juice and also to that of the succus entericus. All these secretions have a more or less alkaline reaction, and neutralize the acid of the gastric chyme.

The special digestive changes in the small intestine are: (1) The *fats* are changed by the bile and pancreatic juice in two ways. (*a*) They are chemically decomposed by the alkaline secretions, and a soap and glycerin are the result. (*b*) They are emulsified, *i.e.*, their particles are minutely subdivided and diffused, so that the mixture assumes the condition of a milky fluid or emulsion. (2) The *albuminous* substances which have been partly dissolved in the stomach are subjected chiefly to the action of the pancreatic juice. The pepsin is rendered inert by the bile. The pancreatic trypsin proceeds with the further conversion of the proteoses into peptones, and part of the peptones (hemipeptones) into leucin, tyrosin, and other amino bodies. (3) The *starchy* portions of the food are now acted on briskly by the pancreatic juice and the succus entericus, and are changed to maltose and dextrose. (4) *Salines*

and *other soluble* matters, such as common salt, are usually in a state of solution before they reach the intestine.

Digestive Changes in the Large Intestine. The changes which take place in the chyme in the *large* intestine are probably only the continuation of the same changes that occur in the course of the food's passage through the upper part of the intestinal canal. No special enzymes have been clearly shown for the mucous membrane of the large intestine. The enzymes of the small intestine may continue their action here, being hindered only by the acid developed from fermentation processes.

Action of Micro-organisms in the Intestines. Certain changes take place in the intestinal contents independent of, or at any rate supplemental to, the action of the digestive ferments. These changes are brought about by the action of micro-organisms or bacteria. We have indicated elsewhere that the digestive ferments are examples of *unorganized* ferments, so bacteria are examples of *organized* ferments. Organized ferments, of which

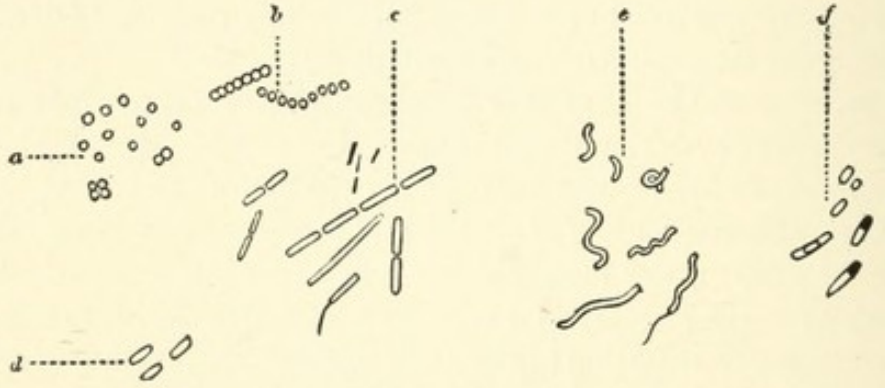


FIG. 276.—Types of Micro-organisms. *a*, Micrococci arranged singly; in twos, diplococci—if all the micrococci at *a* were grouped together, they would be called staphylococci—and in fours, sarcinæ; *b*, micrococci in chains, streptococci; *c*, and *d*, bacilli of various kinds, one is represented with flagellum; *e*, various forms of spirilla; *f*, spores, either free or in bacilli.

the yeast plant may be taken as a typical example, consist of unicellular vegetable organisms, which when introduced into a suitable medium grow with remarkable rapidity. By their growth they produce new substances from those supplied to them as food. Thus, for example, when the yeast cell is introduced into a solution of grape-sugar, it grows, and alcohol and carbon dioxide are produced. These substances probably arise from the formation by the cell activity of some chemical substances which are allied to the unorganized ferments and which greatly increase in amount with the multiplication of the original cell. In all such fermentative processes organisms analogous to the yeast cell are present, and it is not strange that if the ferment cell is introduced into a suitable medium it may by its rapid growth convert an unlimited amount of one substance into another. Speaking generally, a special variety of cell is concerned with each ferment action, thus one variety has to do with alcoholic, another with lactic, and another with acetous fermentation.

A considerable number of species of bacteria exist in the body during life, chiefly in connection with the mucous membranes, particularly of the digestive tract. Many forms of bacteria have been isolated from the mouth, a few varieties from the stomach, and a very large number from the intestines. It is only in the last-named locality that their multiplication has much effect from a physiological point of view. The normal (hydrochloric-acid) acidity of the stomach usually destroys all the micro-organisms taken in with the food, but when the amount of this acid is deficient (and sometimes even when it is normal) some of the spores may escape. On reaching the small intestine these spores begin to develop in its alkaline medium, and may increase to such an extent as to stop all intestinal digestion; the point where this occurs varies from day to day. The large intestine always swarms with micro-organisms, though they do not readily pass the ileo-cecal valve into the small intestine. The bacteria found in the intestine are anaërobic, *i.e.*, they do not develop in the presence of free oxygen.

The changes induced in the intestine by the activity of micro-organisms are of two kinds, fermentation and putrefaction; the former of these results in the breaking down of carbohydrate matter, and the latter in the disintegration of proteid matter. The process of fermentation is the less complex and probably occurs normally in the small intestine to a certain extent. The lactic-acid fermentation is the most important, though the butyric-acid fermentation is next; under their influence the carbohydrates are broken down into lactic and butyric acids, and perhaps into acetic acid also. Carbonic acid gas may be formed at the same time and cause flatulence. Cellulose and other insoluble carbohydrates are decomposed, with the formation of marsh gas and hydrogen, which escape by the rectum.

In putrefaction the process is similar to that in tryptic digestion, the proteids being broken down into peptones, leucin, tyrosin, and a long row of similar substances. It also results in the production of various gases, such as carbon dioxide, sulphureted hydrogen, ammonia, hydrogen and methane (marsh gas), and of a high percentage of the volatile fatty acids, valerianic and butyric. Of the aromatic substances the most important are indol and skatol, though their toxicity has been greatly overestimated. Some undergo oxidation, indol and skatol forming indoxyl and skatoxyl; they are usually carried off in the feces, but when the bowel is obstructed they are absorbed and eventually appear in the urine, indoxyl and skatoxyl forming respectively indoxyl- and skatoxyl-sulphuric acids and their salts. Tyrosin is further broken down into para-oxy-phenol-propionic acid, paracresol, and phenol; para-oxy-phenol-acetic acid is also formed. Experiments have been performed to determine whether or not the intestinal bacteria are neccessary to normal digestion. The weight of evidence is in favor of the view that they are not.

The Feces. The contents of the large intestine, as they proceed toward the rectum, become more and more solid, lose more liquid and nutrient

parts, and gradually acquire the odor and consistency characteristic of *feces*. After a sojourn of uncertain duration in the sigmoid flexure of the colon, or in the rectum, they are finally expelled by the act of defecation. The average quantity of solid matter evacuated by the human adult in twenty-four hours is about 200 to 250 grams, but the amount and character vary exceedingly according to the food eaten. Vegetable foods contain much indigestible matter, while meats and meat diets leave very little unabsorbed material to be expelled in the feces.

Table of Composition of Feces.

The amount of water varies considerably, from 68 to 82 per cent and upward. The following table gives about an average composition:

Water		733.00
Solids, comprising:		
a. Insoluble residues of the food, uncooked starch, cellulose, woody fibers, cartilage, horny matter, mucin, seldom muscular fibers and other proteids, fat, and cholesterin		
b. Certain substances resulting from decomposition of foods, indol, skatol, fatty and other acids; calcium and magnesium soaps		
c. Special excretions,—Excretin, excretoleic acid (Marcet), and stercorin (Austin Flint)		267.00
d. Salts,—Chiefly phosphate of magnesium and phosphate of calcium, with small quantities of iron, soda, lime, and silica		
e. Insoluble substances accidentally introduced with the food		
f. Mucus, epithelium, altered coloring matter of bile, fatty acids, etc		
g. Varying quantities of other constituents of bile and secretions		
		1000.00

Intestinal Gases. Under ordinary circumstances, the alimentary canal contains a considerable quantity of gases. The presence of gas in the

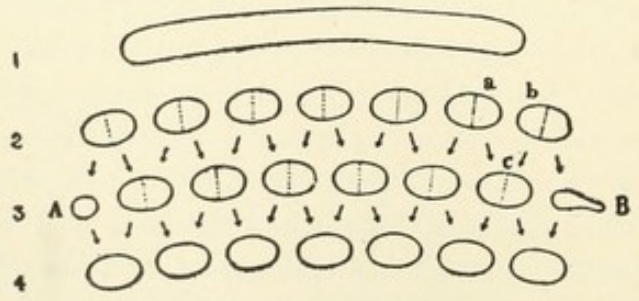


Fig. 277.—Diagram Illustrating the Segmentation of the Food in the Small Intestine. (Cannon.)

intestines is so constant and the amount in health so uniform that there can be no doubt that its existence is a normal condition.

The gas contained in the stomach and bowels is from air swallowed with

either food or saliva, gases developed by the decomposition of foods, or of the secretions and excretions thrown into the intestines. The decomposition of foods is the chief source. The following table, compiled by Brinton, is a collection of analyses that have been made and is chiefly valuable as showing the kinds of gases present:

GASES FOUND IN THE ALIMENTARY CANAL.

Whence obtained.	Composition by Volume.					
	Oxygen.	Nitrog.	Carbon. Acid.	Hydrog.	Carburet. Hydrogen.	Sulphuret. Hydrogen.
Stomach	11	71	14	4	—	—
Small intestines	—	32	30	38	—	Trace.
Cecum	—	67	12	8	13	
Colon	—	35	51	6	8	
Rectum	—	46	43	—	11	
Expelled per anum	—	22	40	19	19	0.5

The amounts of the gases vary with the diet.

An analysis of the intestinal gases (Ruge, copied by Halliburton) in man is as follows:

Gases.	Milk Diet.	Meat Diet.	Vegetable Diet.
Carbon dioxide	9 to 16	8 to 13	21 to 34
Hydrogen	43 to 54	0.7 to 3	1.5 to 4
Carbureted hydrogen	0.9	26 to 37	44 to 55
Nitrogen	36 to 38	45 to 64	10 to 19

The carbon dioxide arises from the carbonates and lactates in food, from fermentation and putrefaction of carbohydrates and proteids, and from butyric-acid fermentation.

The hydrogen is derived from butyric- and lactic-acid fermentations, and carbureted hydrogen comes from the decomposition of acetates and lactates and from cellulose. The nitrogen is derived from the swallowed air.

MOVEMENTS OF THE INTESTINES.

The muscular activity of the intestines accomplishes two important functions, *i.e.*, it thoroughly mixes the digesting food and secretions and it carries the content along the tract. Intestinal peristalses have been described for a long time. These peristalses begin as contractions of the circular muscles, producing ring-like constrictions that are propagated as waves over the intestine

from above downward. Such constrictions carry the intestinal contents forward. The longitudinal muscles by their contraction produce pendular motion of the intestine.

A most instructive contribution to the knowledge of intestinal movements has been made by Cannon. He fed cats food mixed with 10 to 33 per cent of subnitrate of bismuth, and observed the shadows of the food when subjected to the Roentgen rays. A length of food in the intestine was seen to be constricted into a series of oval masses, figure 277. Each of these oval masses is quickly constricted in the middle, and neighboring halves of adjacent masses flow together. After this process is repeated a number of times a peristaltic wave of the type previously described sweeps the whole content of the loop down the intestinal tract.

Peristaltic contractions of the same general type as in the small intestine also occur in the large intestine. Cannon has noted a variation here, also. The ascending and the transverse loops of the colon exhibit rhythmic antiperistalses which keep the content moving against the ileocecal valve for several minutes at a time. From time to time strong general contractions, in the cecum and ascending colon, force some of the food onward. When material has accumulated in the transverse colon, deep successive tonic constrictions appear and force its contents into the descending colon. When sufficient material has accumulated here, it is evacuated by strong peristalses combined with compression by the contracting abdominal muscles.

Reverse or antiperistalsis does not commonly occur in the small intestine, but large nutrient enemata introduced into the rectum and colon may be forced by antiperistaltic waves in the large intestine to and through the ileocecal valve into the small intestine. Here they are treated in the same way as food which has been introduced in the normal way.

Influence of the Nervous System on Intestinal Peristalsis. As in the case of the esophagus and stomach, the peristaltic movements of the intestines may be directly set up in the muscular fibers by the presence of food acting as the stimulus. Few or no movements occur when the intestines are empty. The intestines are connected with the central nervous system both by the vagi and by the splanchnic nerves, as well as by other branches of the sympathetic which come to them from the celiac and other abdominal plexuses. The relations of these nerves respectively to the movements of the intestine and the secretions are probably the same as in the case of the stomach already considered.

The vagus fibers are described as the motor fibers for the intestine, while the sympathetic are said to be at least in part inhibitory. Various states of the central nervous system, such as fear, anger, etc., inhibit the intestinal movements. The intestine carries out peristalses when isolated from the body so that the central connections do not originate, but are only regulative. The intestinal movements are essentially automatic, depending on the rhyth-

mic property of the muscle itself but coordinated by the complex local nervous mechanism.

The innervation of the large intestine is also double in character and the relations are doubtless the same as in the small intestine.

Defecation. The emptying of the rectum is essentially an involuntary act which has acquired a certain amount of voluntary regulation. The act is accomplished wholly reflexly in dogs with isolated lumbar cord, in fact has been observed when the lumbar spinal cord was removed. In the latter case defecation occurs by automatic peristalsis of the rectum, while in the former cases reflexes through the lumbar cord carry out the act. The stimulus of the feces against the rectum and the internal sphincter initiate the movement.

Normally in man the rectal stimulus gives rise to the consciousness of the desire to defecate and the initiation of efferent nerve impulses that may increase the contraction of the external sphincter and inhibit the act temporarily. During defecation, however, the voluntary effort leads to relaxation of the external sphincter, and the normal peristalsis of the rectum is supported by contractions of the abdominal musculature so as greatly to increase the abdominal pressure, thus aiding the involuntary reflex.

LABORATORY EXPERIMENTS IN DIGESTION.

I. SALIVA AND SALIVARY DIGESTION.

1. **Reflex Salivary Secretion.** Saliva, which is the mixed secretion of the salivary and buccal glands, is produced more or less intermittently. Examine, taste, or smell appetizing food, for example, an *apple*, the salivary glands begin to discharge secretion which is poured into the mouth more rapidly than under ordinary conditions. This increased activity is a reflex secretion. It is brought about by the stimulation of sensory structures which lead to afferent nerve impulses reacting on nerve centers in the medulla to cause secretory nerve impulses to the glands. The stimulating effect of food in the mouth causes the most rapid reflex secretion, which may last through several minutes, or even hours. Especially stimulating substances are, beside food, such substances as *tartaric acid, lemon juice, ether, alcohol*, etc., in fact anything that produces strong local irritation will lead to reflex secretion.

2. **The Secretory Nerves of the Salivary Glands of the Dog.** The nervous mechanism for the salivary gland is well known, and the anatomical relations are such as to make this gland a favorable one for studying the nervous mechanism of glands in general.

Anesthetize a dog and bind it to a suitable holder. Expose the nerves to the submaxillary gland as follows: cut through the skin of the lower jaw along the inner border for about 3 inches. Isolate and double ligate the jugular vein and any other veins in the field except the ones coming from the sub-

maxillary gland. Isolate and cut the digastric muscle, also the mylo-hyoid, using pains not to injure the duct of the gland or its arteries. When the muscles are laid back, the artery and accompanying sympathetic nerve branches, the hypoglossal and the lingual nerves, the submaxillary duct and the submaxillary gland, will all be exposed. Isolate and introduce a very fine glass cannula into the submaxillary duct. A small nerve filament branches from the lingual nerve and runs to the hilus of the gland, the *chorda tympani*. Carefully expose the chorda, place a silk ligature under it for convenience in handling. Also expose the sympathetic filaments with the artery.

Stimulate the chorda tympani with a mild induction current for a few minutes at a time at intervals, and note that the secretion which is absent or forming slowly before stimulation now gathers quickly and leaves the end of the cannula in a series of drops. Collect the saliva in a small beaker. One can measure the rate of flow by collecting the saliva in a small graduated cylinder, or, by changing the beaker every ten minutes, making a record of the quantity of secretion formed. Stimulate the sympathetic fibers, cutting the hypoglossal nerve if necessary, and note that the secretion is very slightly increased, but the increase lasts for only a few minutes. If the sympathetic fibers are stimulated before the chorda, then the sympathetic secretion is relatively less than if the order of stimulation is reversed.

During stimulation of the nerves, note the relative flow of blood through the organ. During chorda stimulation the flow is increased; during sympathetic stimulation it is decreased, as these nerves contain vaso-dilator and vaso-constrictor fibers, respectively.

3. **Microscopic Changes in the Gland Cells.** Make a histological preparation (by any standard method of fixing and staining) of the submaxillary gland of the cat, *a*, taken after a period of several hours' fasting when the gland cells may be assumed to be at rest; and *b*, immediately after a period of activity (from eating, or activity secured by the stimulation of the chorda tympani) and note: *a*, The cells from the resting gland are relatively larger, the nuclei are pushed back against the basement membrane, they have sparsely sustaining protoplasm, and the cells are crowded with large granules, which in a fortunate preparation fill the entire cell. The outlines of the cells are relatively indistinct and the lumen of the gland is small. *b*, The cells of the active gland are relatively small, the nuclei are centrally placed, the protoplasm stains more definitely, the granules are usually present but limited to the side of the cell next to the lumen, the outlines of the cells are distinct, and the lumen is often quite large.

4. **The Chemical Composition of Saliva.** Collect several cubic centimeters of saliva as follows: Wash the mouth thoroughly with water, then induce secretion of saliva by chewing a bit of paraffin or a piece of thoroughly washed rubber. The inhalation of ether vapor will often facilitate the reflex secretion. One should avoid strong acids to induce secretion unless their

presence is to be taken into consideration afterward. Make the following tests:

Reaction. A slip of neutral litmus paper when introduced into freshly collected saliva, or for convenience simply taken into the mouth during salivary secretion, shows an alkaline reaction.

Mucin. To 3 or 4 c.c. of saliva add 2 per cent acetic acid drop by drop until distinct acidity is obtained. On stirring the saliva with a glass rod a sticky mucin makes its appearance.

Potassium Sulphocyanide. To 2 c.c. of saliva in a test tube add 2 or 3 drops of ferric-chloride solution, slightly acidulated with hydrochloric acid, a reddish-brown coloration indicates the presence of potassium sulphocyanide. One should run a blank test on distilled water for comparison.

Chlorides. Add silver nitrate to 2 c.c. of saliva after first removing the proteids. A white, cloudy precipitate, which disappears on adding ammonia and reappears on adding nitric acid, indicates the presence of chlorides.

Proteids. Remove the mucin from a sample of saliva, as above, and test by the characteristic proteid reactions. A faint trace of proteid can usually be demonstrated.

5. **Digestive Action of Saliva on Starch.** Review the test for starch, dextrin, and dextrose, as preparation for an identification of these products of salivary digestion. To 50 c.c. of 1 per cent starch paste in the water bath at 40° C. add 5 c.c. of saliva, and mix thoroughly with a glass rod. Immediately begin two series of tests: *a*, for the presence of starch; *b*, for the presence of reducing sugar. The tests for starch can be made by adding to 3 drops of starch, on a porcelain plate, an equal quantity of dilute iodine in potassium iodide solution. Use a glass rod. Make the tests every 2 minutes for 20 minutes. The tests for reducing sugar are best made by placing 2 c.c. of Fehling's solution in each of a series of test tubes and adding, at intervals of 5 minutes, 1 c.c. from a dropping-pipet and boiling. If the tests are set away as fast as they are prepared, a reddish-yellow cuprous oxide will settle out, and the series will give a rough comparison as to the quantity of reducing sugar present.

In the first series the deep blue of the starch reaction quickly changes to a reddish-blue, a red, a reddish-brown, until finally no change in color other than that produced by the mixture of the iodine occurs, showing that the starch has passed the second stage of erythro-dextrin in its disappearance. The indication of reducing sugar in the second series shows that this erythro-dextrin has been transformed into reducing sugar, and also that the amount of sugar is greatly increased during the progress of the test.

6. **The Influence of Temperature on Salivary Digestion.** Prepare three test tubes, *a*, *b*, *c*, containing 4 c.c. each of saliva. Boil *a*, place *b* in a water bath at 40° C., and place *c* in ice water. After *c* has been cooled down to the temperature of the ice bath add to each 2 c.c. of 1 per cent starch solu-

tion and mix. At intervals of 2 to 5 minutes test these 3 samples for the disappearance of starch and appearance of reducing sugar, as in experiment 5. No change will take place in *a*; *b* will be quickly digested; and the digestion in *c* will be slight or suspended. Upon placing *c* in a warm bath digestion will quickly occur.

7. **Influence of Acids and Alkalies on Salivary Digestion.** To each of 5 test tubes, *a*, *b*, *c*, *d*, *e*, add 5 c.c. of saliva. Leave *a* for the normal; make *b* strongly alkaline; *c* exactly neutral; *d* acid to the extent of 0.2 to 0.3 per cent hydrochloric acid; *e* strongly acid. Place all in the water bath at 40° C. Add to each 2 c.c. of 1 per cent starch paste and mix. Test for starch and for reducing sugar at intervals of 20 minutes and compare, noting the results in the following table:

	A	B	C	D	E
Prepare and set in water bath at 40 C.	5 c.c. saliva	5 c.c. saliva and 1 c.c. strong KOH	5 c.c. saliva exactly neutralized	5 c.c. saliva and 1 c.c. 0.2 per cent hydrochloric acid	5 c.c. saliva and 1 c.c. strong hydrochloric acid
Then add.....	2 c.c. 1 per cent starch	2 c.c. 1 per cent starch	2 c.c. 1 per cent starch	2 c.c. 1 per cent starch	2 c.c. 1 per cent starch
Test for starch and sugar immediately.					
After 20 minutes.					
After 40 minutes.					

The results obtained in the experiments 5, 6, and 7 show that starch is converted into reducing sugar, and furthermore that the conditions for its conversion indicate that the change is accomplished by an amylolytic enzyme which in this case is called *ptyalin*.

8. **The Action of Ptyalin is Favored by the Removal of the End Products.** Place 50 c.c. of 2 per cent starch paste in a dialyzing tube or paper, suspend in a beaker of running water. Take 50 c.c. of the same solution in a beaker, to each add 2 c.c. of saliva and mix thoroughly. Test for the disappearance of starch at intervals of 20 minutes. The starch in the dialyzing tube will disappear first because the reducing sugar passes out through the dialyzer, while in the beaker it is retained and hinders the further action of ptyalin.

II. GASTRIC JUICE AND GASTRIC DIGESTION.

9. **The Secretion of Gastric Juice.** The conditions which influence gastric secretion can be readily observed on the dog with a gastric fistula. Take a dog which has had a gastric fistula prepared some weeks before and which is in a condition of hunger, place him in a holder with a cup suspended to collect the gastric juice, and exhibit before the dog some fresh meat or other food which he enjoys, but do not allow him to eat it. After teasing the animal for 5 or 10 minutes, an abundant flow of gastric juice will begin. Pawlow calls this the *psychic secretion.*

If an esophageal fistula has also been performed on the animal the dog may be allowed to eat the meat, of course swallowing it out of the esophageal

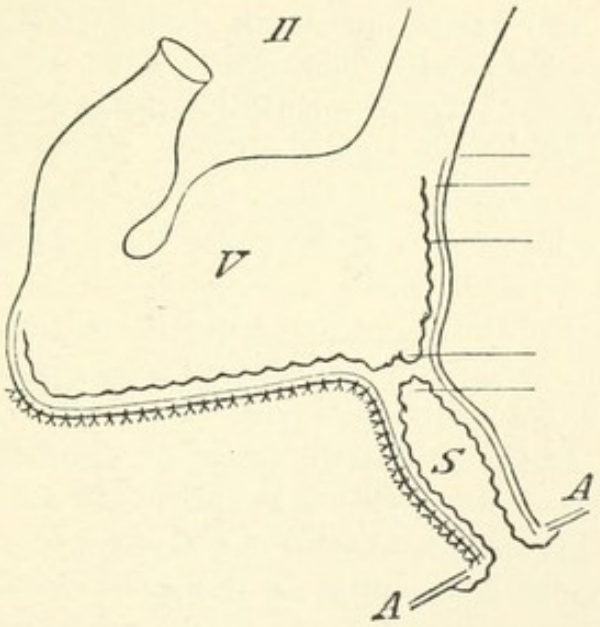


FIG. 278.—Operation on the Stomach to Form an Isolated Pouch with Nerves Intact. *S*, Isolated sac; *V*, cavity of stomach; *A*, *A*, opening at the abdominal wall.

fistula back into the plate. In this experiment an abundant flow of gastric secretion takes place and may continue for an hour or more.

If a gastric pouch has been performed by Pawlow's method, the animal may be allowed to eat the food, swallowing it into the stomach. In this case the reflex secretion just described takes place as usual, but is followed after an hour or an hour and a half by a second increase in the quantity of secretion. This second increase has been ascribed to the reflexes originating in the stomach, possibly from the reflex stimulating action of the digestive products themselves.

10. **Composition of Gastric Juice.** Test a sample of gastric juice obtained from a gastric fistula, as follows:

Reaction. Gastric juice is strongly acid. Test for free hydrochloric acid

as follows: Gastric juice turns congo-red to a blue color. Organic acids produce violet. Gastric juice plus 0.5 per cent alcoholic solution of dimethyl-amido-azobenzol develops a cherry-red color, a reaction that is given by free hydrochloric acid. Combined hydrochloric acids and organic acids do not give the color. Günzburg's reagent, consisting of 2 per cent phloroglucin and 1 per cent vanillin in 80 per cent alcohol, produces a rose-colored mirror on porcelain in the presence of free hydrochloric acid. The test is very delicate.

Proteids. The usual proteid tests can be applied to gastric juice and show that it contains small quantities.

11. **Artificial Gastric Juice.** An active principle, *pepsin*, of gastric juice can be obtained by extracting the gastric mucous membrane of the dog, pig, etc. Scrape off the mucous membrane, grind it to a fine pulp by repeatedly running it through a sausage machine, or by pounding in a mortar with clean sand. The mucous membrane should be allowed to stand for three or four hours before extraction, otherwise the zymogen, and not the enzyme, will be obtained. Extract a portion of this gastric pulp in water, and filter. Or extract with glycerin for several weeks and filter. Either of these extracts contains the enzyme. A solution of the glycerin extract in 0.2 per cent hydrochloric acid contains all the properties of gastric juice. This is known as *artificial gastric juice.*

Commercial pepsin already prepared can be obtained on the market. Artificial gastric juice is made from commercial pepsin by adding 3 to 5 grams to a liter of 0.2 per cent hydrochloric acid.

12. **Digestive Action of Gastric Juice, or Artificial Gastric Juice.** The digestive action of gastric juice is limited to proteids. Shreds of fibrin which permit the gastric juice to come in intimate contact with all parts of the material, form the best proteid for testing the action of this enzyme. Prepare a series of test tubes, *a*, *b*, *c*, *d*, each containing 5 c.c. of artificial gastric juice. Add to *a* some shreds of fibrin; to *b* some boiled white of an egg; to *c* some fibers of boiled meat; to *d* some fibers of raw meat; place in a warm bath at 40° C. and examine at intervals of 20 minutes. Tabulate the results by the plan indicated in experiment 13, noting particularly the rapidity with which the proteid goes into solution.

13. **Conditions Affecting the Enzyme Action of Gastric Juice.** Prepare a series of test tubes containing 5 c.c. each of gastric juice, according to the table on the following page. Add a definite quantity of fibrin to each and note the changes at intervals of 20 minutes.

14. **Cleavage Products of Gastric Digestion.** Add 5 to 10 grams of fibrin to 100 c.c. of artificial gastric juice in a flask and place in a water bath at 40° C. After one hour filter off 40 c.c. Exactly neutralize this filtrate with 1 per cent potassium hydrate. A precipitate makes its appearance, and can be collected on the filter paper, washed with distilled water, and dis-

solved in 1 per cent dilute hydrochloric acid, acid albumin. Test for the proteid reactions.

After two hours filter the remaining 60 c.c., exactly neutralize to remove any traces of acid albumin, and filter. The filtrate contains proteoses. Concentrate the filtrate over a water bath to one-fourth its volume, add an equal quantity of saturated ammonium-sulphate solution, a sticky precipitate of primary proteoses separates out. Collect on a filter paper, wash with half-saturated ammonium sulphate, redissolve in very dilute salt-solution, and test for proteid reactions. The primary proteoses are precipitated by nitric acid.

To the filtrate from the half-saturated ammonium sulphate add crystals of ammonium sulphate until complete saturation with salt. Deutero-albumoses

	A	B	C	D	E
Prepare.....	5 c.c. gastric juice at 40° C.	5 c.c. neutral gastric juice at 40° C.	5 c.c. alkaline gastric juice at 40° C.	5 c.c. boiled gastric juice at 40° C.	5 c.c. gastric juice at 0° C.
Then add.....	Fibrin	Fibrin	Fibrin	Fibrin	Fibrin
Note after 20 minutes.					
After 40 minutes.					
After 60 minutes.					

separate out. Collect on a filter paper, wash, dissolve, and test for proteids. The secondary proteoses are not precipitated by nitric acid.

Finally the filtrate contains peptone. It can be isolated and tested by concentrating over the water bath, adding barium hydrate to slight excess to remove the sulphate, filtering, and precipitating the excess of barium by exact neutralization with 1 per cent sulphuric acid. Test for proteid reactions. Peptone gives a rose color in the biuret reaction. The xanthoproteic reaction gives the color change, but not the usual precipitate. Peptone is redissolved from its alcoholic precipitate without change. It is dialyzable.

15. **Action of Rennin.** Add a solution of commercial rennin (junket powder), or of the extract of gastric mucous membrane of the fourth stomach of a calf, to 5 c.c. of milk and let stand for a few minutes. Repeat the test with artificial gastric juice. Also with neutral gastric juice. In each case the milk will form a jelly-like clot, which is firmer in the test tube containing commercial rennin. In the test tube containing artificial gastric juice,

the milk is first coagulated, then slowly dissolved or digested. This clotting is due to the special coagulating enzyme, rennin.

III. PANCREATIC JUICE AND PANCREATIC DIGESTION.

16. **The Secretion of Pancreatic Juice.** If a dog containing a pancreatic fistula made by Pawlow's method is available, then try the experiment of feeding the animal and noting the rate of secretion of pancreatic juice through a period of two hours. When the gastric digestion has proceeded to the point where the acid chyme may be supposed to have entered the duodenum, then a sharp increase in the flow of pancreatic juice takes place. This increased activity will last through a period of two or three hours or more. It is produced either by nerve reflexes (Pawlow) or by the influence of the secretion produced by the gastric mucous membrane when stimulated by acid.

17. **Influence of Secretin on the Rate of Secretion.** Make an extract of the intestinal mucous membrane, preferably from the duodenum, by scraping off the membrane, grinding it to a pulp, and extracting it over a water bath in 0.2 per cent hydrocholoric acid, and filtering.

Anesthetize a large dog, open the abdomen, isolate the pancreatic duct, introduce a cannula, and arrange for the collection of pancreatic juice. Introduce a cannula into the saphenous vein and connect it with a buret containing the extract of secretin already prepared. Inject 5-c.c. quantities of the secretin solution into the vein at intervals of ten minutes. Measure the rate of secretion of pancreatic juice by counting the drops per minute, or if the secretion is rapid enough, by collecting it at intervals of five or ten minutes and measuring it in a graduated pipet.

This method will often yield enough pancreatic juice in the course of a couple of hours to make the pancreatic experiments which follow. Bayless and Starling call it secretin juice.

18. **Chemical Characters of Pancreatic Juice.** Test the reaction, proteid, salt, etc., content of the sample of pancreatic juice collected in the last experiment.

19. **Artifical Pancreatic Juice.** Artificial pancreatic juice can be prepared from the pancreas by grinding and macerating and extracting a pancreas with water or glycerin, as described for the gastric glands in experiment 11 above. Commercial preparations of pancreatic enzyme can be obtained on the market. A solution of glycerin extract of pancreatic gland or of commerical pancreatin in 0.2 per cent sodium carbonate is known as artificial pancreatic juice.

20. **The Enzymes of Pancreatic Juice.** The pancreatic juice contains enzymes which have exerted a digestive action on starches, fats, and proteids. This fact can be tested as follows: *a*, To 5 c.c. of artificial pancreatic juice add 2 c.c. of 1 per cent starch paste, mix and set in the water bath at 40° C.

b, To 1 c.c. of pancreatic juice (artificial juice is not active), collected in experiment 17, add 0.5 c.c. of neutral olive oil, and place over a water bath. *c*, To 5 c.c. of artificial pancreatic juice add a few flocks of fibrin. Test the digestive action on starch by the iodine test for the disappearance of starch, or by the copper-reduction test for the presence of reducing sugar. Test the fat by its reaction, noting that the neutral or slightly alkaline solution has become acid, also by the fact that an emulsion has been formed. Note that the proteid has gone into solution.

The digestive action on starch is due to the enzyme *amylopsin*, or pancreatic *diastase*, as it is sometimes called. The fat-splitting effect is due to the enzyme *lipase*, and the solution of the fibrin is accomplished by the proteolytic enzyme, *trypsin*.

21. **Conditions which Influence the Action of the Enzymes of Pancreatic Juice.** To each of 5 test tubes, *a*, *b*, *c*, *d*, *e*, add 5 c.c. of artificial pancreatic juice. Place *a*, *b*, *c*, *d* in the water bath at 40° C., and *e* into an ice bath. Leave *a* normal, make *b* exactly neutral, add to *c* 1 c.c. of 2 per cent hydrochloric acid, and boil *d*. Add to each tube 2 c.c. of 1 per cent starch paste. Follow the digestive changes by the tests previously outlined. Tabulate according to the following scheme:

	A	B	C	D	E
Take.....	5 c.c. pancreatic juice 40° C.	Neutralize 5 c.c. pancreatic juice 40° C.	5 c.c. pancreatic juice and 1 c.c. of 2 per cent hydrochloric acid 40° C.	5 c.c. pancreatic juice and boil.	5 c.c. pancreatic juice at 0° C.
Then add.....	2 c.c. of starch	2 c.c. of starch	2 c.c. of starch	2 c.c. of starch	2 c.c. of starch
Note after 20 minutes.					
After 40 minutes.					
After 60 minutes.					

Repeat this experiment with a second set of test tubes containing fibrin. Lipase is not very active in artificial pancreatic juice and may be omitted. If pancreatic juice is available make a third set containing fat.

22. **Cleavage Products of Pancreatic Digestion.** To 200 c.c. of arti-

ficial pancreatic juice add 25 grams of moist fibrin and place in a water bath at 40° C., add 7 c.c. of chloroform to prevent putrefactive changes. After three or four hours filter off 80 c.c. and place the remainder on the water bath for two or three days. Test the filtrate for alkali albumin, albumoses, and peptones, by the method outlined in experiment 14 above.

Filter the second portion and concentrate to a syrupy mass on the water bath. Crystals make their appearance. Pour off the fluid, wash the crystals with cold water, and examine under the microscope for sheaves of *tyrosin*. The filtrate contains *leucin*.

If the digestion had been allowed to proceed without the chloroform, bacteria would have appeared in the solution, and proteid cleavage products, due to their action, would be found, notably *indol*.

IV. BILE AND INTESTINAL JUICE.

23. **Bile.** Secure bile from the gall-bladder of a pig or dog, or, if it is possible, a sample of human bile. Test the reaction which, in fresh bile, is neutral. Test for *mucin; albumin;* and for *iron;* hydrochloric acid and ferrocyanide of potassium give a blue color when iron is present.

Bile Salts. Evaporate 10 c.c. of bile to complete dryness, mix with animal charcoal, add 50 c.c. of absolute alcohol, filter; add an excess of ether to the filtrate, which gives a white precipitate of bile salts. Crystals will form on standing in a well-stoppered flask for a day or two.

Bile Acids. A drop of syrup of cane-sugar in a test tube of bile forms a deep red-purple color at the line of separation from concentrated sulphuric acid. Furfur aldehyde with cholalic acid gives the color.

Bile Pigments. With 1 c.c. of bile in a test tube strong nitroso-nitric acid produces a play of colors beginning with green, blue, red, and yellow—Gmelin's test.

Bile does not contain digestive enzymes, but the bile wets the mucous surface of the intestine and facilitates the solution of fats and fatty acids.

24. **Intestinal Juice.** The secretion of the mucous membrane of the small intestine has been proven to have a weak digestive action on proteids and perhaps on starches. It can be obtained from an intestinal fistula. Its chief digestive importance consists in the presence of the activating enzyme, *enterokinase*. Enterokinase can be prepared by extracting the mucous membrane of the small intestine by the method outlined for making a pancreatic extract.

To two test tubes containing 5 c.c. of artificial pancreatic juice, or preferably containing secretin pancreatic juice, add flocks of fibrin. Keep one for the control, to the other add 2 c.c. of enterokinase solution. The test tube containing enterokinase will digest more rapidly and more effectively than the other.

CHAPTER IX

ABSORPTION

Absorption in its restricted use means the process by which the digested foods pass through the walls of the alimentary canal and into the circulation. In its more general meaning absorption is the process by which substances pass from one part of the body to another by means other than the blood- and lymph-vessels. Usually the absorption takes place from a free surface, such as the alimentary canal, the skin, and the lungs.

The alimentary canal is lined throughout with a continuous layer of epithelial tissue. This layer is only a single cell thick in most of its extent, but nevertheless it effectively separates the food inside the canal from the lymph in the tissue interspaces on the outside of the mucous membrane. These spaces are separated from the blood in the adjacent blood-vessels by a second continuous layer, the endothelial walls of the capillaries. The food, therefore, in its absorption, must pass through two layers of tissue to reach the blood stream. But the submucous lymphatic spaces and vessels furnish channels which may carry substances into the blood by way of the thoracic duct. The mucous membrane is, therefore, the one strict barrier through which the food must pass in the act of absorption.

The exact methods by which absorption takes place have long been a subject of controversy and of research. But this problem is of such difficulty that it is yet, in the main, unsolved. Known physical and chemical laws were thought to explain the facts of absorption. Some of the known physical factors concerned in absorption and elimination have already been considered in a former chapter, *osmosis* and *diffusion*, Chapter IV. A third factor, *filtration*, consists in the passage of a fluid under pressure through a membrane. These factors undoubtedly play an important rôle in the passage of solutions through the alimentary mucous membrane and the walls of the blood-vessels. The part which the physical factors play is probably more pronounced in the absorption of water and crystalloids. The nature of the fluid within the digestive tract, and the movements of the walls of the stomach and intestines by means of which the material to be absorbed is brought into intimate contact with the absorbing membrane, are additional factors which influence absorption.

But the mechanical and physical factors do not fully explain the observed facts of absorption. It becomes more and more evident that there is an

unexplained factor bound up in the characteristics of the living protoplasm of the epithelial cells themselves. When isotonic blood serum is introduced into the intestine the salts and water are at once absorbed, also the albumins, but more slowly. In this experiment the osmotic conditions are in balance and the pressure is greater on the side of the blood-vessels, so that absorption takes place with the actual expenditure of energy. The important fact here is that the absorption through a living membrane is influenced by the membrane in ways that we cannot yet explain. It is this factor which determines the different rate of absorption and the so-called selective absorption in different regions of the alimentary canal.

As a rule, the current of absorption is from the stomach or intestine into the blood; but the reversed action may occur, as, for example, when sulphate of magnesium is taken into the alimentary canal. In this case there is a rapid discharge of water from the blood-vessels into the canal. The rapidity with which matters may be absorbed and diffused through the textures of the body has been found by experiment. It appears that lithium chloride may be diffused into all the vascular textures of the body, and into some of the non-vascular, as the cartilage of the hip joint, as well as into the aqueous humor of the eye, in a quarter of an hour after being given by way of the mouth and on an empty stomach. Lithium carbonate, when taken in five- or ten-grain doses on an empty stomach, may be detected in the urine in five or ten minutes; or, if the stomach be full at the time of taking the dose, in twenty minutes.

Absorption in the Mouth. The epithelial lining of the mouth is of the thicker stratified type and the conditions are otherwise unfavorable for absorption. Little, if any, absorption normally takes place in the mouth, and the same is true for the esophagus.

Absorption in the Stomach. The mucous and submucous coats of the stomach, see figure 258, are well supplied with blood-vessels and lymphatics. The mucous membrane is, however, so crowded with the peptic glands that the relative amount of absorbing surface is small. It is limited to the mucous membrane around the mouths of the glands.

Recent experiments have shown that though absorption does take place in the stomach, it is not as active as was formerly supposed, even in the case of water. Von Mering has found that water begins to pass from the stomach into the intestine almost as soon as it is swallowed, and that very little of it is absorbed from the stomach. Of 500 c.c. given by the mouth to a large dog with a duodenal fistula, only 5 c.c. were absorbed in 25 minutes, the rest having passed into the intestine. Peptones, sugars, and salts are absorbed in the stomach, but only to a limited extent. Peptones are not absorbed in appreciable amount unless present to as much as 5 per cent or more. Examination of the mucous membrane during the stage of active digestion has revealed the presence of albumoses. Sugars, like peptones, are

absorbed by the stomach only to a slight extent in the weaker solutions, but are readily absorbed when the more concented solutions are introduced into the stomach, five per cent and over (von Mehring). Fats are not absorbed at all in the stomach. Even salts in the stomach are not readily absorbed until this concentration is from three to four times that of the blood. This fact is in direct opposition to the popular views on the subject.

While some absorption does take place in the stomach it is evidently not of any great importance under normal conditions. The presence of alcohol has been shown to increase the amount of absorption, and pepper, mustard, and such drugs as produce mild local irritation accomplish the same result.

Absorption in the Intestines. The products of digestion are all absorbed in the small intestine, as is abundantly shown by experiments.

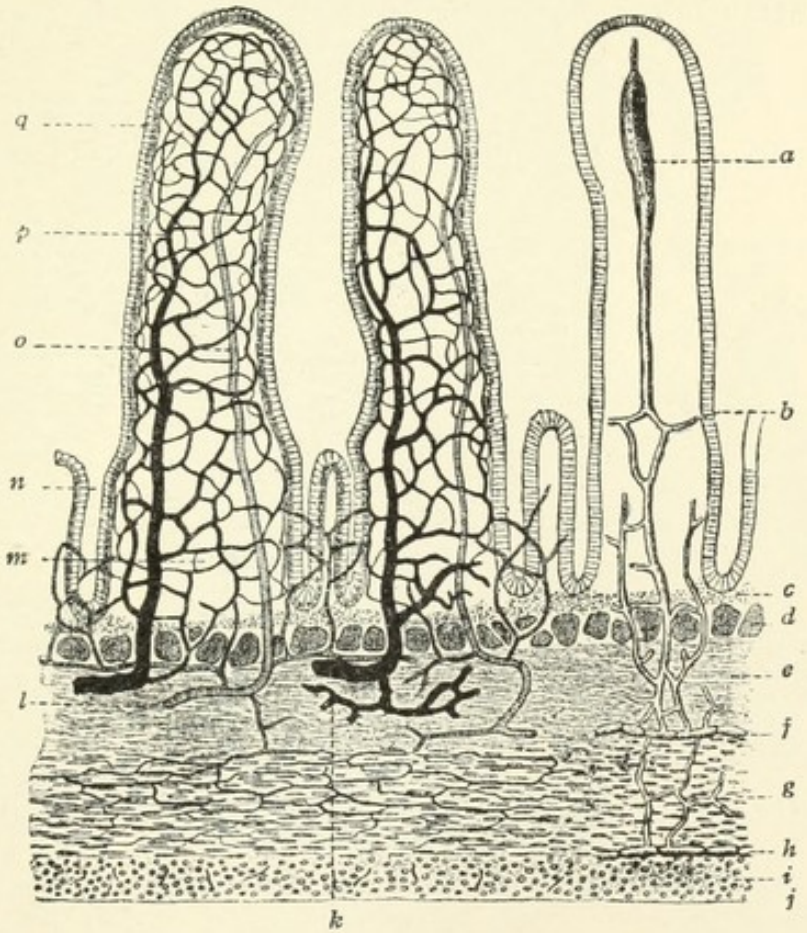


FIG. 279.—Scheme of Blood-vessels and Lymphatics of Human Small Intestine. *a*, Central lacteal of villus; *b*, lacteal; *c*, stroma; *d*, muscularis mucosæ; *e*, submucosa; *f*, plexus of lymph-vessels; *g*, circular muscle layer; *h*, plexus of lymph-vessels; *i*, longitudinal muscle layer; *j*, serous coat; *k*, vein; *l*, artery; *m*, base of villus; *n*, crypt; *o*, artery of villus; *p*, vein of villus; *q*, epithelium. (Mall.)

Absorption from the small intestine has been studied in the human subject in the case of a patient who had a fistulous opening in the lower part of the ileum. For example, 85 per cent of the proteid of a test meal was absorbed before the food reached the fistula. The food passes slowly down the length

of the small intestine, and the digestive changes produce a series of cleavages which have known osmotic and diffusion properties. The question has been to determine which of the cleavage products are most favorable for absorption and the details of the mechanism.

The mucous membrane of the small intestine possesses special structures for absorption, the villi. Each villus projects as a finger-like process into the lumen of the intestine. Its single-layered covering of epithelial cells supported by a connective-tissue framework brings a relatively large extent

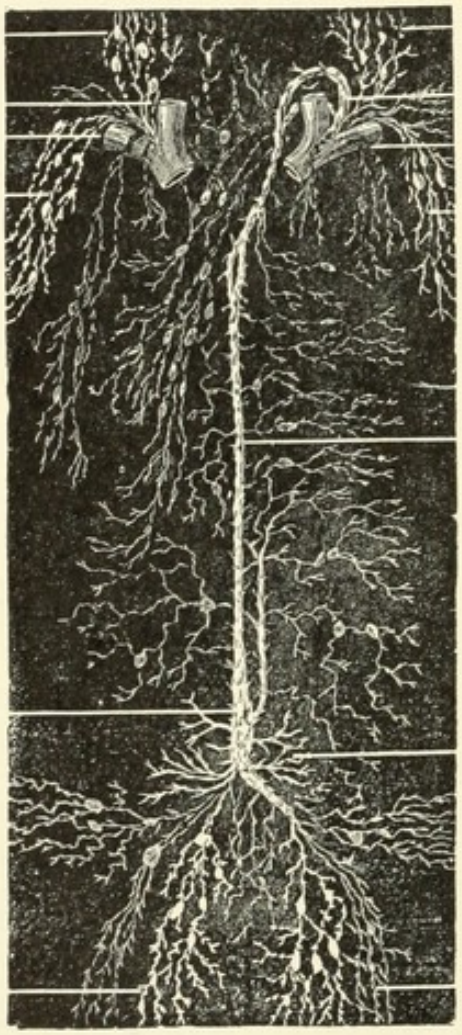


FIG. 280.—Diagram of the Principal Groups of Lymphatic Vessels. (From Quain.)

of surface into contact with the digesting food, which is thus separated from a loop of capillaries and lymphatic radicals.

The capillaries of the villus are connected with the veins which contribute to the portal vein, hence carry blood to the liver. The lacteals of the villus contribute to the mesenteric lacteal system, hence the chyle and lymph pass through the mesenteric glands and the portal duct to the subclavian vein in the neck. There are thus two routes by which absorbed foods may reach the general circulation. These paths can be independently isolated; and a

study of the composition of their discharge during active absorption contributes to our knowledge of the course taken by the different absorption products.

Absorption of Proteids from the Intestines. Proteid is absorbed chiefly in the small intestine, though just exactly how cannot at present be affirmed. In the preceding chapter the cleavage products of proteid diges-

FIG. 281.

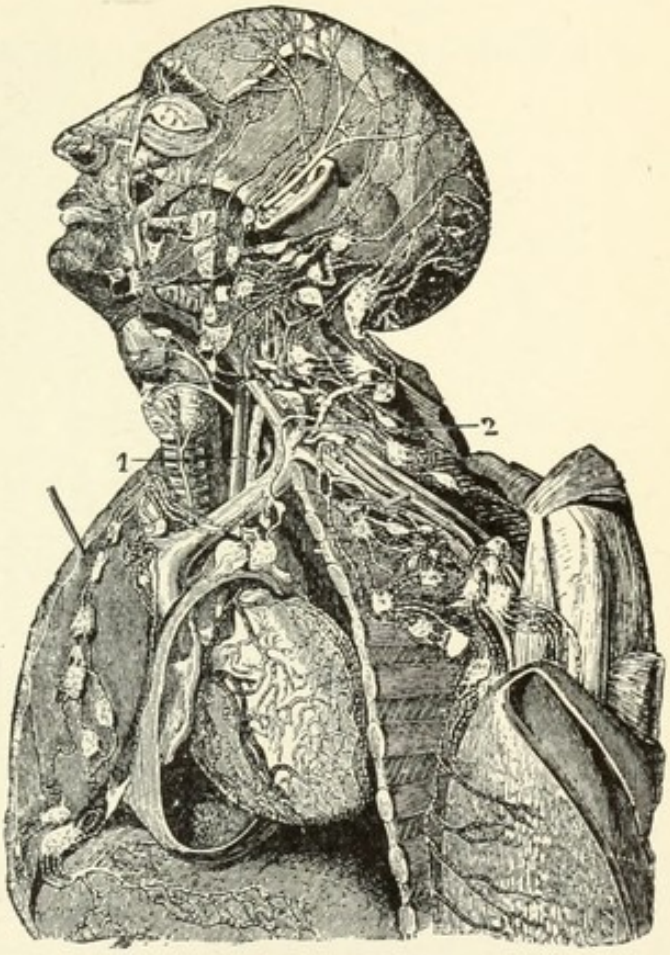


FIG. 282.

FIG. 281.—Superficial Lymphatics of the Forearm and Palm of the Hand, ⅛.—5, Two small glands at the bend of the arm; 6, radial lymphatic vessels; 7, ulnar lymphatic vessels; 8, 8, palmar arch of lymphatics; 9, 9′, outer and inner sets of vessels; *b*, cephalic vein; *d*, radial vein; *e*, median vein; *f*, ulnar vein. The lymphatics are represented as lying on the deep fascia. (Mascagni.)

FIG. 282.—Lymphatic Vessels of the Head and Neck and the Upper Part of the Trunk. (Mascagni.) ⅛.—The chest and pericardium have been opened on the left side, and the left mamma detached and thrown outward over the left arm, so as to expose a great part of its deep surface. The principal lymphatic vessels and glands are shown on the side of the head and face, and in the neck, axilla, and mediastinum. Between the left internal jugular vein and the common carotid artery, the upper ascending part of the thoracic duct marked 1, and above this, and descending to 2, the arch and last part of the duct. The termination of the upper lymphatics of the diaphragm in the mediastinal glands, as well as the cardiac and the deep mammary lymphatics, is also shown.

tion have been discussed. It was shown there that albumoses, peptones, peptids, and the amido-acids are derived from the proteids as digestion products. It has, in the past, been assumed that peptone represents the form most freely absorbed. No peptone has, however, been isolated from the blood or lymph on the vascular side of the epithelial membrane. But the same may be said with equal truth of the other cleavage products. The present supposition is that the proteids are taken up by the epithelium and synthesized into other and more complex forms before being discharged into the blood; or that the digestion cleavages are further broken down in

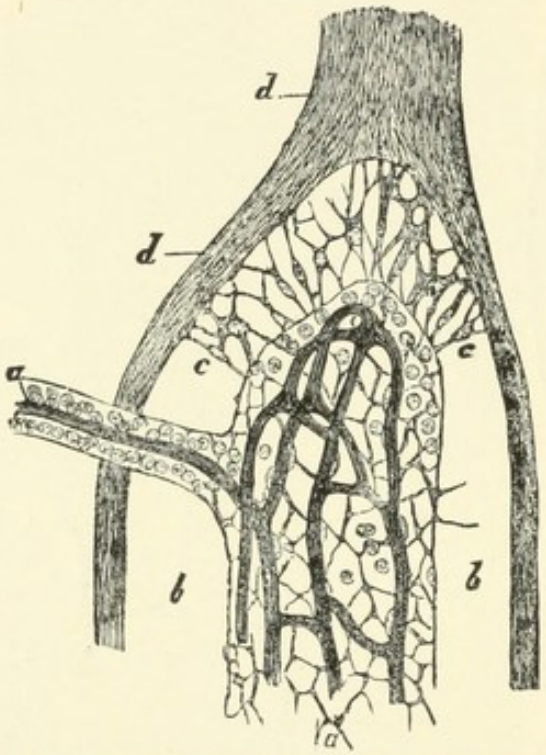


FIG. 283.—A Small Portion of Medullary Substance from a Mesenteric Gland of the Ox. *d, d*, Trabeculæ; *a*, part of a cord of glandular substances from which all but a few of the lymph-corpuscles have been washed out to show its supporting meshwork of retiform tissue and its capillary blood-vessels (which have been injected and are dark in the figure); *b, b*, lymph-sinus, of which the retiform tissue is represented only at *c, c*. × 300. (Kölliker.)

the liver into elimination forms, such as urea, ammonium carbonate, etc. If the intestinal epithelium produces change in the proteid on its passage through, then it is evident that absorption of proteids is more than mere osmosis and filtration. This idea is further strengthened by the known power of the intestines to absorb certain albumins, egg albumin for example, which is non-diffusible and non-dialyzable.

In animal foods, such as eggs, meat, etc., it is estimated that about 98 per cent of the proteid is absorbed; whereas in vegetable foods, where the proteid is often protected from the action of the digestive enzymes, there may be 10 to 15 per cent loss. Analysis of the total lymph discharge of the thoracic duct fails to show any increase of proteids during active digestion, from which it is inferred that proteids pass by way of the liver.

From 12 to 15 per cent of the proteid remains in the food as it passes the ileocecal valve. This amount, less the loss in the feces, is absorbed in the large intestine.

Absorption of Carbohydrates by the Intestines. Carbohydrates are broken down to dextrose, levulose, etc., and are absorbed as such. Even the soluble cane-sugar is split by the invertase of the intestine into the monosaccharides, dextrose and levulose. Starch is the source of most of the 500 grams of dextrose absorbed in an average diet per day. During the absorption of a carbohydrate meal the percentage of dextrose in the blood of the portal vein is increased over the normal which is 0.1 to 1.5 per cent. This excess of dextrose passes through the liver and is temporarily stored in the

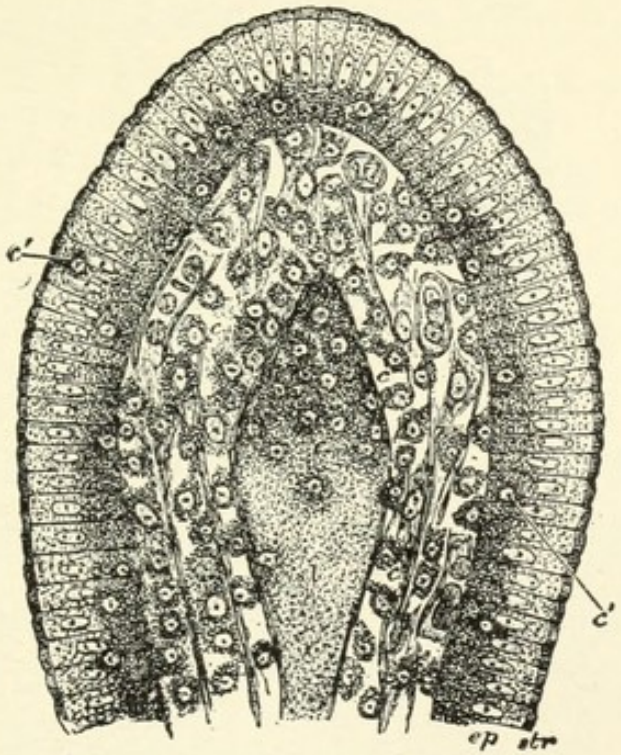


FIG. 284.—Section of the Villus of a Rat Killed during Fat Absorption. *ep*, Epithelium; *str*, striated border; *c*, lymph-cells; *c'*, lymph-cells in the epithelium; *l*, central lacteal containing disintegrating lymph-corpuscles. (E. A. Schäfer.)

liver cells as glycogen. In the case of a fistula in the receptaculum chyli, the chyle contained less than a half per cent of the total dextrose absorbed.

Experiments on the rate of absorption of the different sugars seem to indicate that their absorption does not follow known physical laws and that we must assume an unknown chemical factor in the living protoplasm.

Dextroses are absorbed readily by the large intestine.

Fermentation process from bacterial growth produces certain acids from the carbohydrates, chiefly in the large intestine. These are readily absorbed.

Absorption of Fats by the Intestines. Fats reach the absorbing epithelium in two forms, as soluble glycerin and soaps and as finely emulsified fats. The first two are taken up by the epithelium readily enough,

but in the last the process of absorption is not so clear. It is comparatively easy to demonstrate the presence of microscopic globules of fat, both in the intercellular substance and in the epithelial cells themselves. But it has been constantly noticed that there is a clear zone along the free borders of the cells. Fat drops exist in the adjacent digesting mass, and in the deeper parts of the cells, but not in this border zone. Since the demonstration of the reversible action of lipase, the view has been strengthened that in the very act of absorption the emulsified fats are decomposed and passed through the cell border only to be resynthesized in the cell protoplasm. This is of course against the strictly mechanical view. The decreasing efficiency of fats when the bile, which wets the mucous surface and dissolves the fatty acids, is withheld from the intestine also supports this view. As absorption progresses the size of the fat drops in the epithelial cells increases, a fact

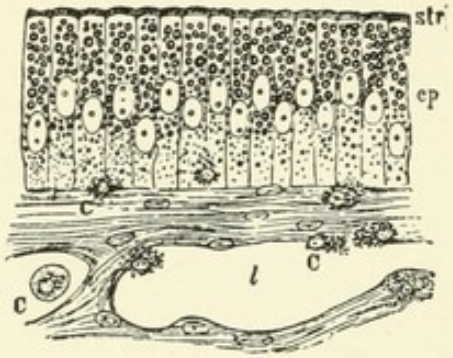


FIG. 285.—Mucous Membrane of Frog's Intestine during Fat Absorption. *ep*, Epithelium; *str*, striated border; *C*, lymph-corpuscles; *l*, lacteal. (E. A. Schäfer.)

that is readily explained by supposing a continued synthesis and accumulation of fat.

The fat drops are ultimately discharged into the connective-tissue spaces and finally pass into the lymph channels, the thoracic duct, and into the blood of the subclavian vein. This is the course taken by the larger percentage of the fat. However, some of the fat is absorbed into the capillaries of the villi and passes through the liver. The presence of fat drops in the liver cells at certain times can be ascribed to storage of this absorbed fat.

It is said that the more readily emulsified fats, those that melt readily at the body temperature, are the more completely absorbed. The efficiency of absorption is as high as 96 to 98 per cent for the oils, and decreases sharply for such fats as the tallows.

The large intestine is capable of absorbing fats, though not so readily as the small intestine.

Absorption of Minerals and Water in the Intestines. The salts common in the foods are most of them readily soluble, dissociate quite completely in the dilute solutions, and diffuse and dialyze readily. Of the salts of the foods, the sodium and potassium cations and chlorine anion are the most readily dissociated and are most diffusible, while the calcium and

magnesium cations and the sulphate anion are least diffusible. These substances pass through the intestinal epithelial cells and the intercellular substance; at least salts easily recognized by microchemical means have been found in both localities during absorption. It seems probable that the forces concerned are largely osmosis and diffusion.

Yet observers have not been able to show that the rate and character of the absorption of even the salines obey the known physical laws. In fact there is evidence that some of the salts, iron for example, are taken up as organic compounds (hematogens of Bunge). The activity of the epithelial cells is to be taken into account, even in the absorption of salts.

Water, which we have seen is not absorbed in the stomach, is readily absorbed in the small intestine. Perhaps the bulk of the water taken into the system is absorbed in the upper part of the small intestine. In the large intestine, too, it is absorbed with facility and in considerable quantities. The content of the bowel is still quite fluid when it enters the ascending colon, but the feces are quite firm on discharge from the rectum. There are many analogies by which we may suppose a controlling influence of the epithelium over the process of water-absorption. Among the fishes there are species, the salmon for example, in which the blood maintains a relatively constant osmotic pressure, and therefore salt content. In the salmon this is about the same as that of human blood. The blood is separated in the gills by an extremely thin epithelium from the water in which the animals live, yet these fishes go with impunity from sea water, with two and a half times more salt than the blood, to fresh water with practically no salt at all. The epithelium of the gills permits the passage of oxygen, but it does not permit the diffusion or dialysis of the salts or the water in either direction. It is possible that there is a certain amount of resistance to the passage of water through the walls of the stomach, while the intestinal epithelium permits water to pass readily.

The factors active in absorption are under searching investigation at the present time, so that it is reasonable to hope that the near future will give a more exact understanding of this intricate subject.

ABSORPTION FROM THE SKIN, THE LUNGS, ETC.

The dry corneous stratified epithelium covering the human body possesses great resistance to the absorption of most substances. The sebaceous secretion keeps the surface slightly oily. Watery solutions do not readily wet the surface and therefore do not penetrate. There is some absorption of water on prolonged contact with the skin, but the amount is insignificant. Medicated baths, especially hot baths, may be accompanied by some slight absorption of the substances dissolved in the waters; though it must be confessed that the good effects of such treatment come from other sources.

On the other hand, oily substances come in more intimate contact with the skin and penetrate deeper and more readily. Therefore lotions containing medicines are occasionally applied to the skin, and slow but gradual absorption occurs. The volatile oils penetrate the skin readily.

The epithelial lining of the lungs seems peculiarly adapted to the quick absorption of all gases and volatile substances. This is illustrated by the rapidity with which anesthesia may be accomplished by breathing the vapors of ether or chloroform.

Solutions injected into or otherwise brought into contact with the subdermal connective tissue, the body of a muscle, or the peritoneal or thoracic cavity, very quickly pass into the general circulation. They are practically injected into the lymphatic intercellular spaces in these instances and, of course, are very readily carried through the lymphatic vessels, figures 280 and 282, to the thoracic duct and into the blood. Comparing the rapidity of absorption in the cases mentioned, that from the muscle is most rapid, a fact of medical importance in the use of the hypodermic needle for the giving of medicines in emergency.

CHAPTER X

EXCRETION

EVERY substance taken into the body, in whatever form, must, in the end, be cast off again, no matter how great the change that may be wrought during its sojourn. We have already found that in the lungs the expired air, and in the intestine the feces, carry from the body waste matters of no further use. We have now to find that the urine separated by the kidney and the sweat and sebum of the skin are likewise channels by which the body throws off water, salts, and broken-down organic matters of no further use to the organism. Of these two organs, the skin and the kidney, the latter is by far the more important in so far as the quantity and complexity of its secretion is concerned.

STRUCTURE AND FUNCTION OF THE KIDNEYS.

General Structure. The kidneys are two in number, and are situated deeply in the lumbar region of the abdomen on either side of the spinal column behind the peritoneum. They correspond in position to the last two dorsal and two upper lumbar vertebræ, the right slightly below the left in consequence of the position of the liver on the right side of the abdomen. They are about 4 inches long, 2½ inches broad, and 1½ inches thick. The weight of each kidney is about 4½ ounces, 140 grams.

On dividing the kidney into two equal parts by a section carried through its long convex border, figure 286, the main part of its substance is seen to be composed of two chief portions called respectively *cortical* and *medullary*, the latter being also sometimes called *pyramidal*, from the fact of its being composed of about a dozen conical bundles of uriniferous tubules, each bundle forming what is called a pyramid. The upper part of the *ureter*, or duct of the organ, is dilated into the *pelvis;* and this, again, after separating into two or three principal divisions, is finally subdivided into 8 to 12 smaller portions, *calyces*, each of which receives the pointed extremity or papilla of a pyramid. Sometimes, however, more than one *papilla* is received by a calyx.

The kidney is a compound tubular gland. Both its cortical and its medullary portions are composed essentially of numerous tubes, the *tubuli uriniferi*,

which begin at the opening on the Malpighian pyramid and, after a devious course, end in the capsule of the glomerulus.

Tubuli Uriniferi. The tubuli uriniferi, figure 287, are composed of a nearly homogeneous membrane, and are lined internally by epithelium. They vary considerably in size in different parts of their course, but are, on an average, about 40 μ in diameter, and are found to be made up of several distinct sections. The first section or part to be identified is the *Malpi-*

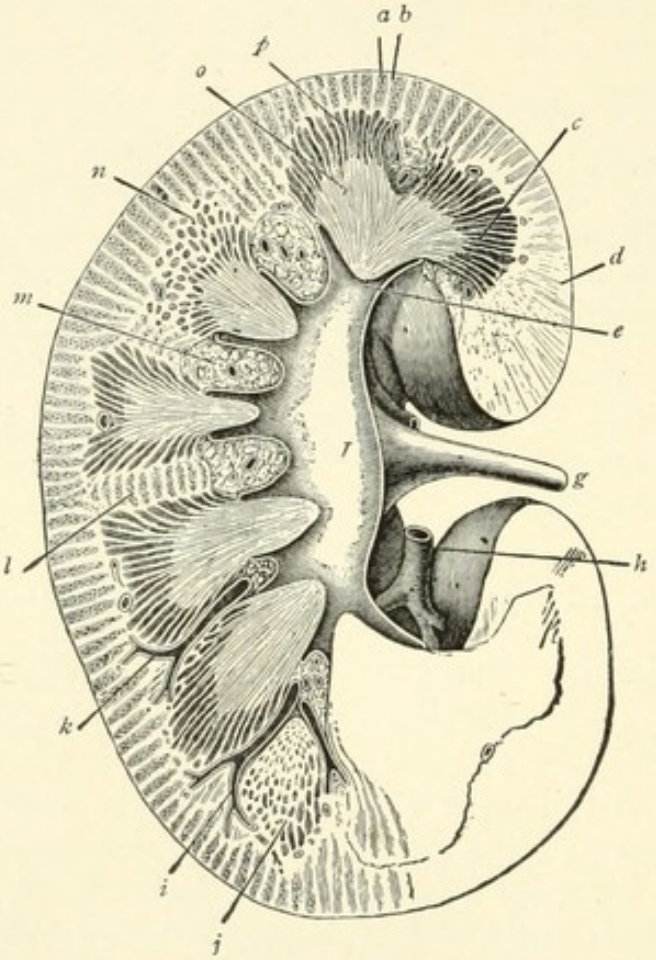


FIG. 286.—Longitudinal Section of Kidney through Hilum. *a*, Cortical pyramid; *b*, medullary ray; *c*, medulla; *d*, cortex; *e*, renal calyx; *f*, hilum; *g*, ureter; *h*, renal artery; *i*, obliquely cut tubules of medulla; *j* and *k*, renal arches; *l*, column of Bertini; *m*, connective tissue and fat surrounding renal vessels; *n*, medulla cut obliquely; *o*, papilla; *p*, medullary pyramid. (Merkel-Henle.)

ghian, or Bowman's, *capsule*, figure 287. It is composed of a hyaline membrana propria, thickened by a varying amount of fibrous tissue, and lined by *flattened nucleated epithelial* plates. This capsule is the dilated extremity of the uriniferous tubule which is invaginated to receive the glomerulus of convoluted capillary blood-vessels. The invaginated portion of the tubule is of particular importance since it is the membrane through which a large part of the urine is secreted. The glomerulus is connected with an efferent and an afferent blood-vessel. The Malpighian capsule is connected by a constricted neck, figure 287, *N*, with the *proximal convoluted tubule*. This forms

several distinct curves and is lined with short columnar cells. The tube next passes almost vertically downward toward the medulla, forming the *spiral tubule*, still within the cortex of the kidney, which is of much the same diameter. The *loop of Henle*, *L*, in the medulla, is a very narrow tube lined with flattened nucleated cells. Passing vertically upward from the loop of

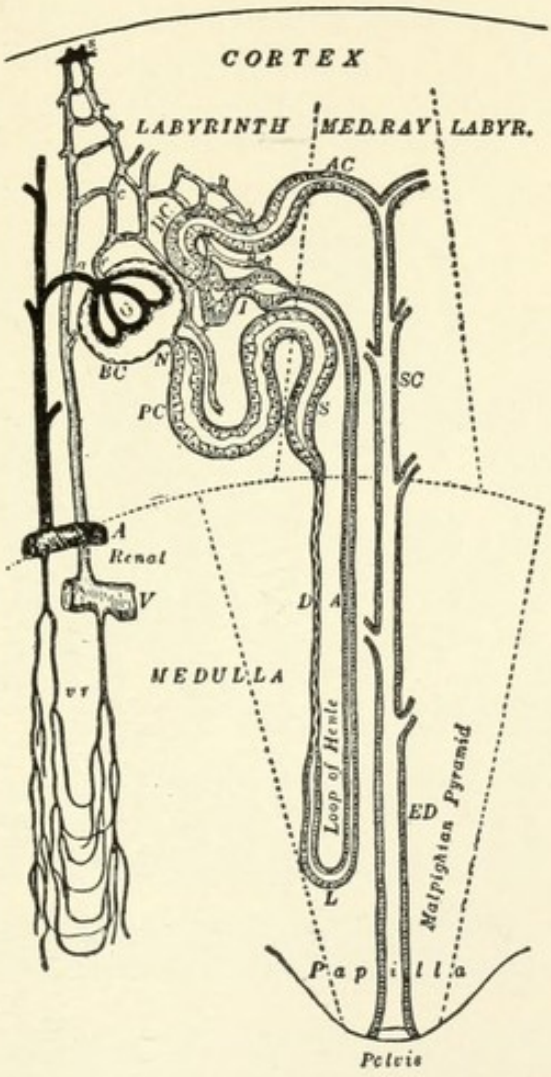


FIG. 287.—Scheme of Uriniferous Tubule and of the Blood-vessels of the Kidney, Showing Their Relation to Each Other and to the Different Parts of the Kidney. *G*, Glomerulus; *BC*, Bowman's capsule; *N*, neck, *PC*, proximal convoluted tubule; *S*, spiral tubule; *D*, descending arm of Henle's loop; *L*, Henle's loop; *A*, ascending arm of Henle's loop; *IDC*, distal convoluted tubule; *AC*, arched tubule; *SC*, straight collecting tubule; *ED*, duct of Bellini; *A*, arcuate artery, and *V*, arcuate vein, giving off interlobular vessels to cortex and vasa recta to medulla; *a*, afferent vessel of glomerulus; *e*, efferent vessel of glomerulus; *c*, capillary network in cortical labyrinth; *s*, stellate veins; *vr*, vasa recta and capillary network of medulla. (Pearsol.)

Henle, the tubule varies somewhat in histological character, but the *irregular tubule* and the distal convoluted tube, identical in all respects with the proximal convoluted tube, are to be noted. The proximal convoluted tube passes into the curved and straight collecting tubes, the latter running vertically downward to the papillary layer, and, joining with other collecting tubes, form larger ducts which finally open at the apex of the papilla. These collecting tubes are lined with nucleated columnar or cubical cells.

Renal Blood Supply. The renal artery divides into several branches which pass in at the hilus of the kidney and are covered by a fine sheath of areolar tissue derived from the capsule. They enter the substance of the organ chiefly in the intervals between the papillæ and at the junction between the cortex and the boundary layer. The main branches then pass almost horizontally, forming more or less complete arches and giving off branches upward to the cortex and downward to the medulla. The former are for the most part straight; they pass almost vertically to the surface of the kidney, giving off laterally in all directions longer and shorter branches, which ulti-

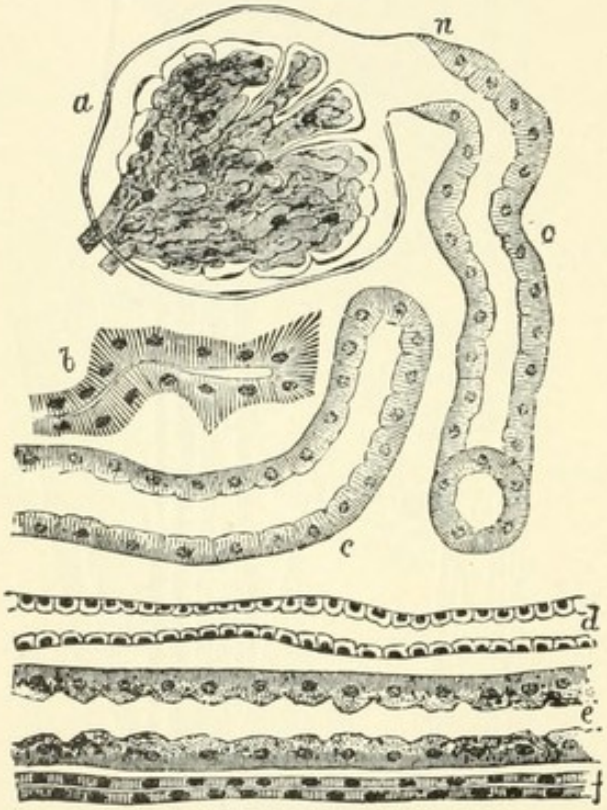


FIG. 288.—From a Vertical Section through the Kidney of a Dog, the Capsule of which is Supposed to be on the Right. *a*, The capillaries of the Malpighian capsule, the glomerulus, are arranged in lobules; *n*, neck of capsule; *c*, convoluted tubes cut in various directions; *b*, irregular tubule: *d*, *e*, and *f* are straight tubes running toward capsules forming a so-called medullary ray; *d*, collecting tube; *e*, spiral tube; *f*, narrow section of ascending limb. × 380. (Klein and Noble Smith.)

mately supply the glomerulus. The small *afferent* artery, figures 287, *a*, 290, *d*, which enters the Malpighian capsule, breaks up in the interior into a dense convoluted and looped capillary plexus, which is ultimately gathered up again into several small *efferent* vessels, comparable to minute veins, which leave the capsule at one or more places near the point at which the afferent artery enters it. On leaving, they do not immediately join other small veins as might have been expected, but again break up into a second set of capillary vessels which form an interlacing network around the uriniferous tubules. This second capillary plexus terminates in small veins which, by union with others, help to form the radicles of the renal vein.

These form venous arches corresponding to the arterial arches situated between the medulla and cortex.

Thus, in the kidney, the blood entering by the renal artery traverses two sets of capillaries before emerging by the renal vein, an arrangement which may be compared to the portal system.

The tuft of vessels within the Malpighian capsule in the course of development has been thrust into the dilated extremity of the urinary tubule, which finally completely invests it. Thus within the Malpighian capsule there are two layers of squamous epithelium, a parietal layer lining the capsule proper, and a visceral or reflected layer immediately covering the vascular tuft, figure 290, and sometimes dipping down into its interstices. This

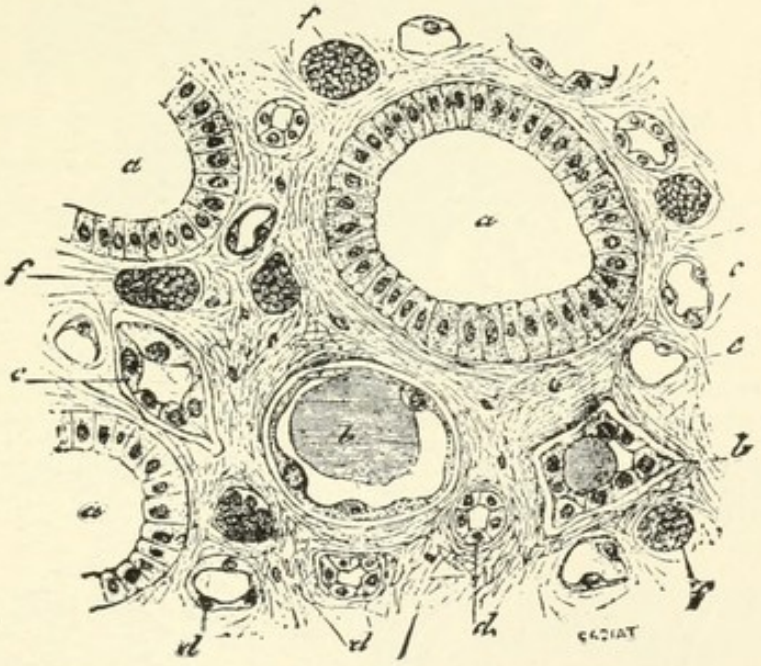


FIG. 289.—Transverse Section of a Renal Papilla. *a*, Large tubes or papillary ducts; *b*, *c*, and *d*, smaller tubes of Henle; *e*, *f*, blood capillaries, distinguished by their flatter epithelium. (Cadiat.)

reflected layer of epithelium is readily seen in young subjects, but cannot always be demonstrated in the adult, figures 290 and 291.

The vessels which enter the medullary layer break up into smaller arterioles, which form a fine arterial meshwork around the tubes of the papillary layer and end in a similar plexus from which the venous radicles arise. The vessels do not form a double set of capillaries.

Besides the small *afferent* arteries of the Malpighian bodies there are, of course, others which are distributed in the ordinary manner, for the nutrition of the different parts of the organ; and there are numerous straight vessels, the *vasa recta*, in the pyramids between the tubes. Some of these are branches of the *vasa efferentia* from Malpighian bodies, and therefore comparable to the venous plexus around the tubules in the cortical portion, while others arise directly as small branches of the renal arteries.

Renal Nerves. Vaso-constrictor and vaso-dilator nerves are supplied to the blood-vessels of the kidney, but no clearly defined secretory nerves have yet been demonstrated for the organ. The vascular nerves arise out of the anterior spinal roots (Bradford), chiefly the eleventh to the

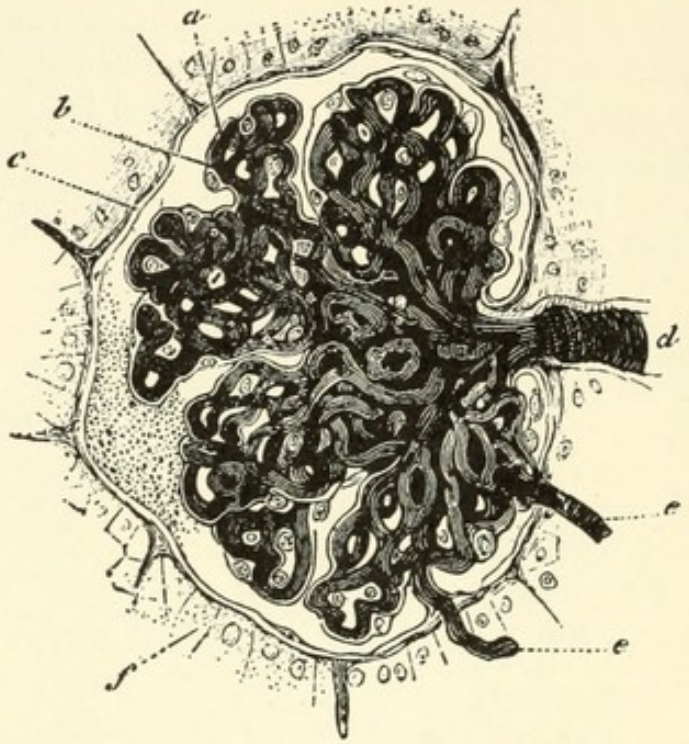


FIG. 290.—Malpighian Capsule and Tuft of Capillaries, Injected through the Renal Artery with Colored Gelatin. *a*, Glomerular vessels; *b*, capsule; *c*, anterior capsule; *d*, glomerular artery; *e*, efferent veins; *f*, epithelium of tubes. (Cadiat.)

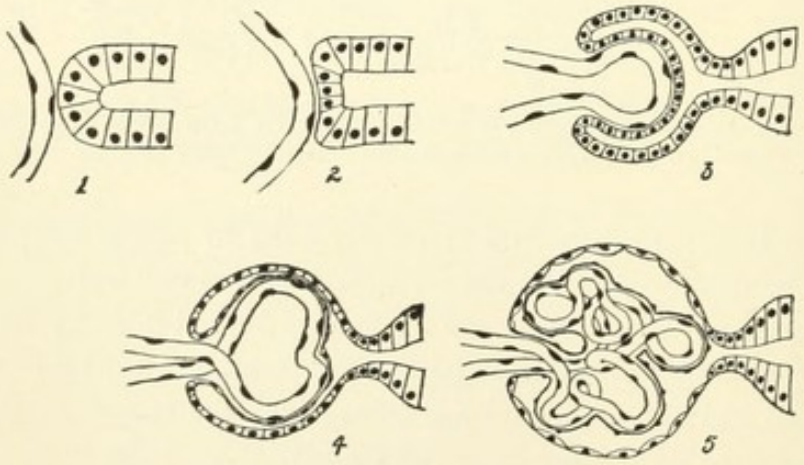


FIG. 291.—Diagrams Illustrating Stages in the Development of the Malpighian Capsule. In 1 and 2 the developing blood-vessel is approaching the blind end of the capsule. In 3 the tubule is beginning to invaginate and enclose the capillary. In 4 and 5 later stages are shown. The cells forming the two layers of the capsule grow very thin. (Bailey.)

thirteenth dorsal nerves. They reach the kidney by way of the splanchnic nerves and the renal plexus to the renal artery along which they run into the substance of the kidney. Berkeley has demonstrated nerve plexuses about the arterioles and around Bowman's capsule. Terminal knob-like

endings of nerve fibrils were shown. Some authors have claimed renal vasoconstriction following vagus stimulation, but the fact seems not to be universally admitted.

The Ureters and Urinary Bladder. The duct of each kidney, the ureter, is a tube about the size of a goose-quill and from twelve to sixteen inches in length. It is continuous above with the pelvis of the kidney, and ends below by obliquely perforating the walls of the bladder and opening on its internal surface. It has three principal coats, an outer fibrous, a middle muscular, of which the fibers are unstriped and arranged in three layers. The fibers of the central layer are circular, and those of the other two layers longitudinal in direction. It has an internal mucous lining continuous with that of the pelvis of the kidney above and the lining of the urinary bladder below. The urinary bladder, which forms a receptacle for the temporary lodgment of the urine in the intervals of its expulsion from the body, is more or less pyriform. Its widest part, which is situated above and behind, is termed the *fundus;* and the narrow constricted portion in front and below, by which it becomes continuous with the urethra, is called its cervix or neck. It is constructed of four principal coats: serous, muscular, areolar or submucous, and mucous. The fibers of the muscular coat deserve special mention. They are unstriped, are arranged in three principal layers, of which the external and internal have a general longitudinal, and the middle layer a circular, direction. The latter are especially developed around the cervix of the organ, and are described as forming a sphincter vesicæ. The mucous membrane is provided with mucous glands, which are more numerous near the neck of the bladder.

The bladder is well provided with blood- and lymph-vessels, and with nerves. The latter are from the sacral plexus (spinal) and hypogastric plexus (sympathetic). Ganglion-cells are found, here and there, in the course of the nerve fibers.

THE URINE.

Quantity and General Properties. Healthy urine is a perfectly transparent amber-colored liquid, with a peculiar but not disagreeable odor, a bitterish salty taste, and a specific gravity of from 1020 to 1025. The urine consists of water holding in solution certain organic and saline matters as its ordinary constituents, and occasionally various other matters. Some of the latter are indications of diseased states of the system, and others are derived from unusual articles of food or drugs taken into the stomach.

The total quantity of urine passed in twenty-four hours is influenced by numerous circumstances. In adults of average size and medium activity the daily amount of urine may be given as from 1,200 c.c. to 1,500 c.c. In Chittenden's recent observations on nine athletic students and on eight

soldiers the average daily output of urine through a period of about five months was for the students 1,215 c.c. with average specific gravity of 1020, and for the soldiers 1,042 c.c. with specific gravity of 1023.

General Chemical Composition of the Urine.

Water		967
Solids:		
Urea	14.230	
Other nitrogenous crystalline bodies:		
Uric acid, principally in the form of alkaline Urates, a trace only free	10.635	
Kreatinin, Xanthin, Hypoxanthin		
Hippuric acid		
Mucus, Pigments, and ferments		
Salts:		
Inorganic:		
Principally Sulphates, Phosphates, and Chlorides of Sodium and Potassium, with Phosphates of Magnesium and Calcium, traces of Silicates	8.135	
Organic:		
Lactates, Hippurates, Oxalates, Acetates, and Formates, which appear only occasionally		33
Sugar	a trace sometimes.	
Gases (nitrogen and carbonic acid principally).		
		1,000

Reaction. The normal reaction of the urine is slightly acid. This acidity is due to carbonic acid and to acid phosphate of sodium, and is less marked soon after meals. After standing for some time the acidity increases from a kind of acid fermentation, due in all probability to the presence of mucus and fungi, and acid urates or free uric acid is deposited. After a time, varying in length according to the temperature, the reaction becomes strongly alkaline from the change of urea into ammonium carbonate, due to the presence of one or more specific micro-organisms (*micrococcus ureæ*). In the process of fermentation the urea takes up two molecules of water, a strong ammoniacal and fetid odor appears, and there are deposits of triple phosphates and alkaline urates. This does not occur unless the urine is freely exposed to the air, or, at least, until air has had access to it.

In most herbivorous animals the urine is alkaline and turbid. The difference depends not on any peculiarity in the mode of secretion, but on the difference in the food on which the two classes of animals subsist; for when carnivorous animals, such as dogs, are restricted to a vegetable diet, their urine becomes pale, turbid, and alkaline like that of herbivorous animals, while the urine voided by the Herbivora, *e.g.*, rabbits, fed for some time exclusively upon animal substances, presents the acid reaction and other qualities of the urine of Carnivora, and its ordinary alkalinity is again restored only on the substitution of a vegetable for the animal diet. Human urine is not usually rendered alkaline by vegetable diet, but it becomes so

after the free use of alkaline medicines, or of the alkaline salts with carbonic or vegetable acids; for these latter are changed into alkaline carbonates previous to elimination by the kidneys.

Specific Gravity of Urine. The average specific gravity of the human urine is about 1020 to 1025. The relative quantity of water and of solid constituents of which it is composed is materially influenced by the condition and occupation of the body during the time at which it is secreted; by the length of time which has elapsed since the last meal; by the amount of water taken; and by several other less important circumstances. The morning urine is the best adapted for analysis in health, since it represents the simple secretion unmixed with the elements of food or drink. If it is not used the whole of the urine passed during a period of twenty-four hours should be taken. The specific gravity of the urine may thus, consistently with health, range widely on both sides of the usual average. It may vary from 1015 in the winter to 1025 in the summer; but variations of diet and exercise, and many other circumstances, may make even greater differences than these. The variations may be extreme in disease, sometimes decreasing in albuminuria to 1004, and frequently increasing in diabetes, when the urine is loaded with sugar, to 1050 or even to 1060.

AVERAGE DAILY QUANTITY OF THE CHIEF URINARY CONSTITUENTS. (MODIFIED FROM PARKES.)

		Per Kilo of Body Weight.
Water	1,500. c.c.	23.0000 grams
Solids	72. grams	0.8800 "
Urea	33.180 "	.5000 "
Kreatinin	.910 "	.0140 "
Uric Acid	.555 "	.0084 "
Hippuric Acid	.400 "	.0060 "
Pigment and Extractives	10.000 "	.1510 "
Sulphuric Acid	2.012 "	.0480 "
Phosphoric Acid	3.164 "	.0305 "
Chlorine	7.000 "	.1260 "
Ammonia	.770 "	
Potassium	2.500 "	
Sodium	11.090 "	
Calcium	.260 "	
Magnesium	.207 "	

Variations in the Constituents of Urine. Most of the constituents are, even in health, liable to variations from the proportions given in the above table. The variations of the quantity of water in different seasons, and according to the quantity of drink and exercise, have just been mentioned. The water of the urine is also liable to be influenced by the condition of the nervous system, being sometimes greatly increased, *e.g.*, in hysteria and in some other nervous affections, and at other times diminished. The increase in water may be either attended with an augmented quantity of solid matter in some diseases, as in ordinary diabetes, or may be nearly the sole

change, as in the affection termed diabetes insipidus. A febrile condition almost always diminishes the quantity of water; and a like diminution is caused by any affection which draws off a large quantity of fluid from the body through any other channel than that of the kidneys, *e.g.*, the bowels or the skin.

In disease or after the ingestion of special foods, various abnormal substances occur in urine, of which the following may be mentioned. Serum-albumin, Globulin, Ferments (apparently present in health also), Proteoses, Blood, Sugar, Bile acids and pigments, Casts, Fats, various Salts taken as foods or as medicines, Micro-organisms of various kinds.

The Nitrogenous Substances in Urine. The nitrogenous waste products which are formed in the body in the metabolism of the proteid foods are ultimately eliminated chiefly through the kidney, to some extent through the bowel, and slightly through the skin. The total nitrogen in the urine and in the feces multiplied by the factor 6.25 is a measure of the nitrogenous

FIG. 292.—Crystals of Urea.

foods, *i.e.*, proteids, metabolized by the body. The nitrogen excreted in the urine is in the form of urea 87.5 per cent, ammonia 4.3 per cent, kreatinin 3.6 per cent, uric acid 0.8 per cent, and undetermined forms 3.73 per cent, according to Folin. The total quantity of nitrogen eliminated in all these forms per day is given as about 18 grams. In Chittenden's recent experiments this quantity is reduced to as low as 6 grams or even less per day.

Urea. Urea, CON_2H_4, is the principal solid constituent of the urine, forming nearly one-half of the total quantity. It is also the most important ingredient, since it is the chief form in which the waste nitrogen which is derived from proteid metabolism is excreted from the body.

Properties. Urea, like other solid constituents of the urine, exists in a state of solution. When in the solid state, it appears in the form of delicate silvery acicular crystals, which, under the microscope, are seen as four-sided prisms, figure 292. It readily combines with some acids, like a weak base, and may thus be conveniently procured in the form of crystals of nitrate or oxalate of urea, figures 293 and 294.

Urea is colorless when pure; when impure it may be yellow or brown. It is without smell and of a cooling niter-like taste. It has neither an acid nor an alkaline reaction, and deliquesces in a moist and warm atmosphere. At 15° C. it requires for its solution less than its own weight of water. It is soluble in all proportions of boiling water, and requires five times its weight of cold alcohol for its solution. It is insoluble in ether. At 120° C. it melts without undergoing decomposition; and at a still higher temperature ebullition takes place, and carbonate of ammonium sublimes.

Urea is decomposed by sodium hypochlorite of hypobromite or by nitrous acid, with evolution of nitrogen. It forms compounds with acids, of which the chief are urea hydrochloride, $CON_2H_4.HCL$; urea nitrate, $CON_2H_4.HNO_3$; and urea phosphate, $CON_2H_4.H_3PO_4$. It forms compounds with

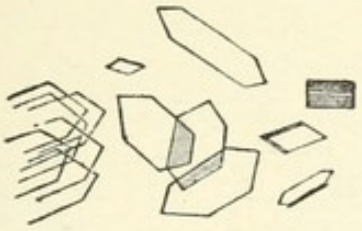


FIG. 293.—Crystals of Urea Nitrate.

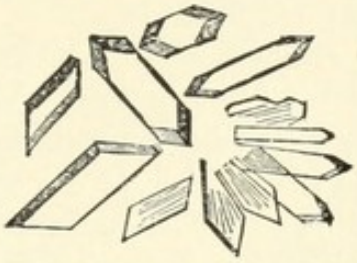
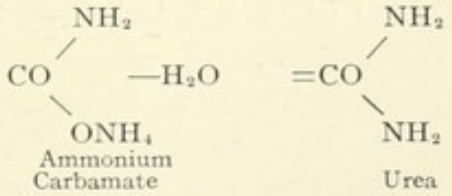


FIG. 294.—Crystals of Urea Oxalate.

metals such as $HgO.CON_2H_4$, with silver, $CON_2H_2Ag_2$. Urea is isomeric with ammonium cyanate, NH_4CNO, and was first prepared artificially from that substance.

The Formation of Urea. Proteids in the body have their nitrogenous moiety broken down to ammonia, by what Folin considers essentially a series of hydrolytic cleavages, which is then built up into urea, as described more fully in the chapter on Metabolism. This last step is essentially a synthetic process which, from the fact that ammonium carbonate introduced into the blood is eliminated as urea, may be supposed to occur as follows:



Urea is present in varying amounts in all organs and fluids of the body, as shown by the following determinations of Schoendorff on the dog:

Organ.	Per cent of Urea.
Blood	0.116
Muscle	0.080
Kidney	0.670
Liver	0.112
Heart	0.173
Brain	0.128
Spleen	0.122

It has been proven that the kidney does not form urea; in fact the kidneys may be removed from the body, and urea will continue to accumulate in the blood. Urea is formed chiefly in the liver, but may in part be constructed in other organs, as described more fully on page 411. It follows that the kidney is only the channel for the elimination of this nitrogenous compound.

Decomposition of the urea with development of ammonium carbonate takes place from the action of bacteria (micrococcus ureæ) when urine is kept for some days after being voided, which explains the ammoniacal odor then evolved. The urea is sometimes decomposed before it leaves the bladder, when the mucous membrane is diseased and the mucus secreted by it is abundant; but decomposition does not occur unless atmospheric germs have had access to the urine.

Quantity Excreted. The quantity of urea excreted is, like that of the urine itself, subject to considerable variation. For a healthy adult about 30 grams per day may be taken as rather a high average. Its percentage in healthy urine is from 2 to 2.5. Its amount is materially influenced by diet, being greater on a diet of high proteid content. The quantity of urea excreted by children, relatively to their body-weight, is much greater than by adults; thus the quantity of urea execreted per kilogram of weight was found to be, in a child, 0.8 gram; in an adult only 0.4 gram. Regarded in this way, too, the excretion of carbonic acid gives similar results, the proportions in the child and adult being as 82 to 34.

Uric Acid. Uric acid, $C_5H_4N_4O_3$, is rarely absent from the urine of man or animals, though in the feline tribe it seems to be sometimes entirely replaced by urea. In birds and reptiles uric acid or its salts is the chief form in which nitrogen is eliminated from the body.

Properties. Uric acid is a colorless, crystalline compound of the purin group, figure 295. It is odorless and tasteless. It is very slightly soluble in water, quite insoluble in alcohol and ether, and freely soluble in solutions of the alkaline carbonates and other salts.

A study of the elimination of nitrogen in birds, *i.e.*, geese, has shown that uric acid, like urea in mammals, is formed largely in the liver from antecedent proteid nitrogen. In man the elimination of uric acid increases or decreases with the proteid content of the daily diet. It does not, however, follow the variations of the food nitrogen so closely as in the case of urea. Any food with a rich nuclein content increases the excretion of uric acid. This observation has led to the inference that uric-acid nitrogen is derived from nuclear metabolism, page 413.

Other representatives of the purin group are adenin, guanin, xanthin, hypoxanthin, etc. Chemically, caffeine from coffee is a trimethyl xanthin.

The most common form in which uric acid is deposited in urine is that of a brownish or yellowish powdery substance, consisting of granules of

ammonium or sodium urate. When deposited in crystals, it is most frequently in rhombic or diamond-shaped laminæ, but other forms are not uncommon, figure 295. When deposited from urine, the crystals are generally more or less deeply colored, from being combined with the coloring principles of the urine.

Hippuric Acid. This compound, $C_9H_9NO_3$, has long been known to exist in the urine of herbivorous animals in combination with soda. It also exists naturally in the urine of man, in a quantity equal to or rather ex-

FIG. 295.—Various Forms of Uric Acid Crystals.

FIG. 296.—Crystals of Hippuric Acid.

ceeding that of the uric acid. The quantity excreted is increased by a vegetable diet.

Hippuric acid appears to be formed in the body from benzoic acid or from some allied substance. The benzoic acid unites with glycin, and hippuric acid and water are formed thus:

$$\underset{\text{Benzoic Acid}}{C_6H_5.COOH} + \underset{\text{Glycin}}{CH_2.NH_2.COOH} = \underset{\text{Hippuric Acid}}{C_6H_5.CO.NH.CH_2.COOH} + H_2O.$$

Hippuric acid is the one substance which has been clearly demonstrated to be formed by the kidney itself.

Kreatinin. This substance is present in urine in a remarkably constant quantity, as shown recently by Folin's analyses. Its daily excretion quantity is from 1 to 15 grams according to the amount of active tissue in the individual. It is of especial importance as a measure of the metabolism of muscle protoplasm.

Ammonia. A considerable daily quantity of ammonia in combination is found in the urine, showing that this is an important method of nitrogen elimination.

Pigments. The pigments of the urine are the following: 1, *Urochrome*, a yellow coloring matter, giving no absorption band; of which but little is known. Urine owes its yellow color mainly to the presence of this body. 2, *Urobilin*, an orange pigment, of which traces may be found in nearly all urines, and which is especially abundant in the urines passed by

febrile patients. It is characterized by a well-marked spectroscopic absorption band at the junction of green and blue. Those who believe urobilin to be identical with hydrobilirubin suppose that the bilirubin is reduced by the putrefactive processes in the intestines, and is conveyed in its reduced form by the blood stream to the kidneys. 3, *Uroerythrin*, occasionally found. And, 4, *Uromelanin*.

Mucus. Mucus sediment in the urine consists principally of the epithelial débris from the mucous surface of the urinary passages. Particles of epithelium, in greater or less abundance, may be detected in most samples of urine, figure 297. As urine cools, the mucus is sometimes seen suspended in it as a delicate opaque cloud, but generally it falls. In inflam-

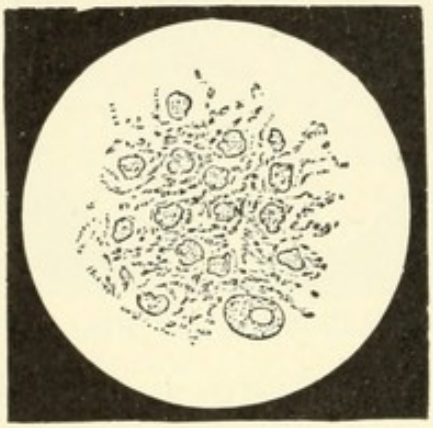


FIG. 297.

FIG. 298.

FIG. 297.—Urinary Deposit of Mucus, etc.

FIG. 298.—Urinary Sediment of Triple Phosphates (large prismatic crystals) and Urate of Amonium, from urine which had undergone alkaline fermentation.

matory affections of the urinary passages, especially of the bladder, mucus is secreted in large quantities and speedily undergoes decomposition.

Saline Matter. *Sulphuric acid*, in the form of salts, is taken in very small quantity with food. Sulphur is also a constituent part of the proteid molecule; hence its elimination, like that of nitrogen, gives a certain measure of proteid metabolism. It is excreted as inorganic sulphates of sodium and potassium, and as ethereal sulphates, compounds of phenol, cresol, skatol, *i.e.*, cresol sulphuric acid ($C_7H_7OSO_2OH$), etc.

The *phosphoric acid* in the urine is combined partly with the alkalies, partly with the alkaline earths—about four or five times as much with the former as with the latter. In blood, saliva, and other alkaline fluids of the body phosphates exist in the form of alkaline, neutral, or acid salts. In the urine they are acid salts, viz., the sodium, ammonium, calcium, and magnesium phosphates, the excess of acid being (Liebig) due to the appropriation of the alkali with which the phosphoric acid in the blood is combined, by the several new acids which are formed or discharged at the kidneys, namely the uric, hippuric, and sulphuric acids, all of which are neutralized with soda.

The phosphates are taken largely in both vegetable and animal food. Some are excreted at once; others only after being transformed and incorporated with the tissues. Calcium and magnesium phosphates form the principal earthy constituents of bone, and from the decomposition of the osseous tissue the urine derives a quantity of this salt. The decomposition of other tissues also furnishes large supplies of phosphorus to the urine, which phosphorus is supposed, like the sulphur, to be united with oxygen, and then combined with bases. The quantity is, however, liable to considerable variation. The earthy phosphates are more abundant after meals, whether of animal or vegetable food, and are diminished after long fasting. The alkaline phosphates are increased after animal food, diminished after vegetable

FIG. 299.—Crystals of Cystin.

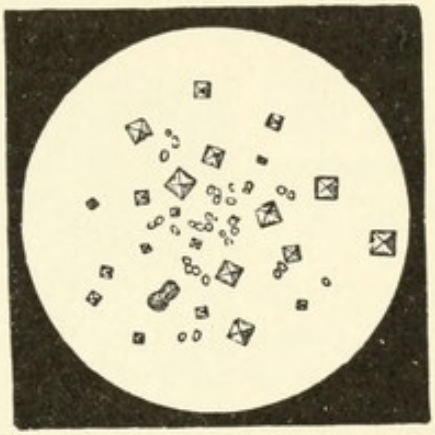


FIG. 300.—Crystals of Calcium Oxalate.

food. Phosphorus uncombined with oxygen appears, like sulphur, to be excreted in the urine. When the urine undergoes alkaline fermentation phosphates are deposited in the form of a *urinary sediment*, consisting chiefly of ammonio-magnesium phosphates (triple phosphate), figure 298.

The *Chlorine* of the urine occurs chiefly in combination with sodium. Next to urea, sodium chloride is the most abundant solid constituent of the urine. As the chlorides exist largely in food, and in most of the animal fluids, their occurrence in the urine is easily understood.

Occasional Constituents of Urine. *Cystin*, $C_3H_7NSO_2$, figure 299, is an occasional constituent of urine. It resembles taurin in containing a large quantity of sulphur—more than 25 per cent. It does not exist in healthy urine.

Another common morbid constituent of the urine is *Oxalic acid*, which is frequently deposited in combination with calcium, figure 300, as a urinary sediment. Like cystin, but much more commonly, it is the chief constituent of certain calculi.

Dextrose and *albumin* are sometimes present in pathological urine, and are of particular interest from the clinical point of view. See the subject Glycosuria, page 418.

THE METHOD OF EXCRETION OF URINE.

The secretion of urine is an act the complexity of which can be profitably discussed only after a clear understanding of three main factors which have already been presented, viz., the chemical composition of the urine secreted, the structure of the kidney tubule as a secreting organ, and, finally, the chemical composition of the blood which supplies the materials to the kidney for the formation of the urine. The substances found in the urine are for the most part also to be found in the blood-plasma. But the relative percentage composition is very different. The amount of urea in the blood is only a fractional part as concentrated as in the urine, while albumins and sugars, which are so plentiful in the blood, are normally present in the urine only in traces. The presence of the glomerulus with its special vascular supply, and the different loops of the tubule, with its gland-like epithelial wall, would, *a priori*, lead one to suspect special functions for each.

Theories of the Secretion of Urine. Bowman in 1842, wholly on structural grounds, advanced a theory of urinary secretion which has more recently been restated and given an experimental basis by Heidenhain. This view as given by Heidenhain is as follows:

1, The secretion in the kidney depends upon the physiological activity of special secreting cells which are of two kinds. 2, The first type of cell is represented by the single layer of epithelium covering the glomerular capillaries. These cells secrete especially water and salts. 3, The second type of cell is represented by the gland-like epithelial cells which form the convoluted tubules and the loop of Henle. These cells secrete the urea, uric acid, and other specific constituents of the urine. 4, The activity of each kind of cell is influenced by the chemical composition of the blood and by the flow of blood through the kidney. 5, The relative secretory activity of the glomerular cells and the tubule cells is sufficient to account for the variation in the chemical composition of the urine.

Ludwig in 1844 advanced a strictly mechanical theory of urine secretion based on his own experiments. He considered the glomerulus and Bowman's capsule as a filtering apparatus in which substances present in the blood are driven through the epithelium of the capsule into the renal tubule by the positive pressure of the blood in the glomerular capillaries. This very dilute urine in the capsule is supposed to be concentrated by the resorption of water as it flows down the tubule. Ludwig originally considered this resorption of water an imbibition process in which the greater saturation of salts in the blood caused water to be taken up through the renal tubule walls, an osmotic process. At present most observers who accept the view that filtration takes place at the glomerulus explain the resorption of water down the tubules as an act of cellular resorption or secretion.

Experimental Observations. There are numerous nerves to the

kidney, but no proven secretory influence has been shown. The variations in the secretion of urine that follow nervous stimulation are quite satisfactorily explained by the changes in the blood flow.

The kidney can be placed in an onkometer and its variation in volume measured directly, figures 301 and 302. This volume measurement, when taken with the arterial pressure, gives a very good index of the volume of blood flowing through the kidney. Now when the kidney is inserted in an onkometer and the urine collected from the ureter, it is found in general that the greater the pressure and flow of blood the greater the secretion of urine, as would follow if the glomerulus were a filtering mechanism. However, if the renal vein is partially obstructed, even though the blood pressure be increased, the amount of urine secreted is sharply decreased. If the vein is

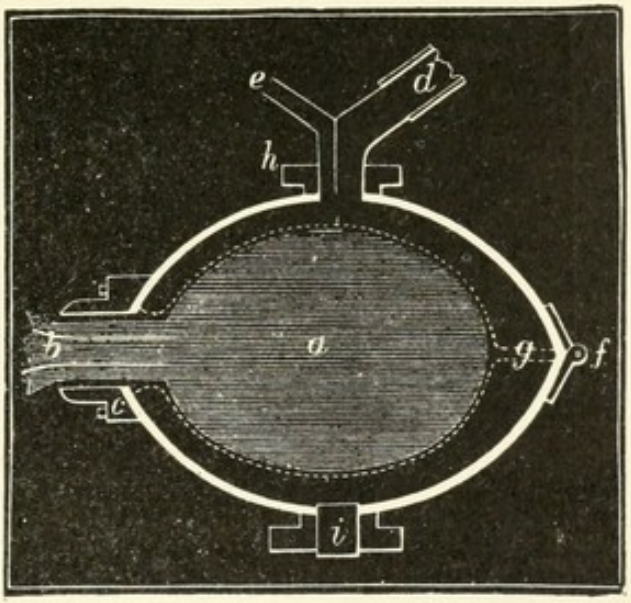


FIG. 301.—Diagram of Roy's Onkometer. *a* Represents the kidney enclosed in a metal box, which opens by hinge *f*; *b*, the renal vessels and ducts. Surrounding the kidney are two chambers formed by membranes, the edges of which are firmly fixed by being clamped between the outside and inside metal capsules (the latter not represented in the figure), the two being firmly screwed together by screws at *h*, and on the opposite side. The membranous chamber below is filled with a varying amount of warm oil, according to the size of the kidney experimented with, through the opening then closed with the plug *i*. After the kidney has been enclosed in the capsule, the membranous chamber above is filled with warm oil through the tube *e*, which is then closed by a tap (not represented in the diagram); the tube *d* communicates with a recording apparatus, and any alteration in the volume of the kidney is communicated by the oil in the tube to the chamber *d* of the Onkograph, figure 302.

completely occluded, the secretion of urine not only ceases for the time but does not immediately begin again when the blood pressure and flow are reestablished. The closure of the vein for only one or two minutes is said to stop the flow of urine for as much as forty-five minutes. This short interruption of the circulation is sufficient to bring about other changes in the glomerular epithelium, for it now excretes albumin, which it did not previously let pass. Therefore, it is not pressure merely that favors the secretion, but there must be an efficient flow of blood. The secretion is influenced especially by the amount of blood flowing through the kidney in a given time.

In the frog the kidney has a double blood supply. The renal artery supplies the glomeruli, while a branch of the renal-portal vein supplies the tubules. Nussbaum ligated the renal artery in one kidney of the frog, while leaving the circulation of the other kidney undisturbed. He found that the operated kidney secreted little or no urine, but that it could be made to secrete by injections of urea, but not by injections of albumin or sugar as in the normal kidney. Ligation of the renal-portal vein, which supplies the tubules in the frog, caused a decrease in the quantity of the secretion, whereas, according to Ludwig's view, it ought to have increased the quantity, since obviously resorption could not take place with any degree of efficiency. In the main, the evidence is in favor of the view that even the glomerular epithelium does

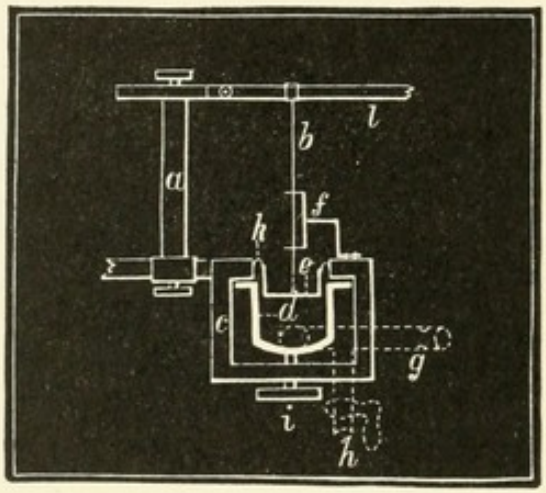


FIG. 302.—Roy's Onkograph, or Apparatus for Recording Alterations in the Volume of the Kidney, etc., as shown by the onkometer. *a*, Upright, supporting recording lever *l*, which is raised or lowered by the needle *b*, which works through *f*, and which is attached to the piston *e*, working in the chamber *d*, with which the tube from the onkometer communicates. The oil is prevented from being squeezed out as the piston descends, by a membrane, which is clamped between the ring-shaped surfaces of the cylinder by the screw *i* working upward; the tube *h* is for filling the instrument.

not filter merely, but that it, as living protoplasm, regulates and controls the quantity and kind of material passing through it.

Micro-chemical observations have been enlisted to demonstrate more fully, if possible, the activity of the different parts of the epithelial tubule. Heidenhain, by injections of indigo-blue into the blood stream, followed by rapid fixation of the kidney in alcohol at the proper stage of elimination, has demonstrated crystals of the pigment in the renal epithelial cells and in the lumen of the tubule. He concluded that these cells were actively eliminating the pigment by a secretory process. This observation has been questioned. But Heidenhain's view is strengthened by Bowman's observation that in birds crystals of uric acid are to be seen in the cells of the convoluted tubules, and in the lumen adjacent.

Only traces of the sugars and proteids of the blood are found in normal urine, but when either cane sugar, peptone, or egg albumin is introduced into the blood it is rapidly eliminated by the kidney. Egg albumin is not essen-

tially different from the serum albumin of the blood, but the serum albumin is not excreted. These are both non-dialyzable compounds. Sugar and urea, both readily dialyzable, present the same comparison, *i.e.*, urea is excreted, while sugar is not. If, however, the percentage of sugar is high, 0.25 per cent or more, it is then eliminated. The excretion of the highly diffusible sodium chloride bears a similar quantitative relation to excretion. If present in the blood in relatively low amounts it is not secreted, while if the concentration is slightly greater it may be quickly eliminated. Other inorganic salts, present only in traces, are meanwhile rapidly eliminated. Even the rapid elimination of a slight excess of water in the blood can scarcely be explained on purely physical grounds. To discharge the water across the glomerulus from the blood to the urine requires an expenditure of osmotic pressure much greater than that balanced by the blood pressure. That is, the epithelial cells must do work, and the energy is dependent on metabolism in the cells. At

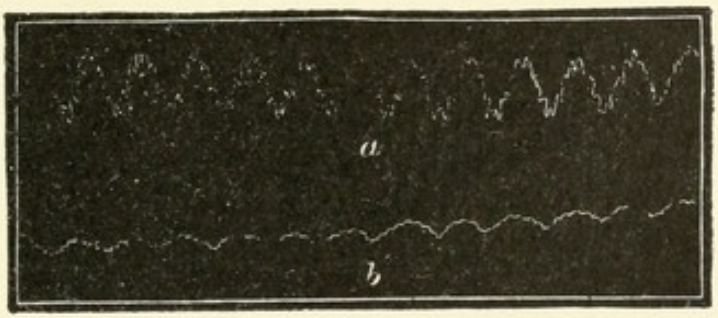


FIG. 303.—Curve Taken by Renal Onkometer Compared with that of an Ordinary Blood-pressure Curve. *a*, Kidney curve; *b*, blood-pressure curve. (Roy.)

least one substance, hippuric acid, is built up chemically by the renal cells and secreted as such.

It would seem, therefore, that the separation of urine in the kidney is a secretory process dependent on the protoplasmic activity of the living renal cells, that the apparent selective property of the cells is a manifestation of such activity, and that even water is secreted.

Diuretics. Certain substances increase the flow of urine and are called diuretics. They act directly on the renal epithelium, for example, urea, or indirectly on the circulatory system to increase the flow of blood. Digitalis is a well-known diuretic which increases the efficiency of the circulation. It also stimulates the renal epithelium with the production of a marked increase in the flow of urine. Caffeine diuresis can best be explained on an assumed stimulating action on the renal epithelium. Urea introduced into the blood produces a copious secretion of urine. Both urea and the saline diuretics induce a flow of urine out of all proportion to the osmotic changes produced, and they may be regarded as direct stimulators of the renal epithelium.

THE DISCHARGE OF THE URINE.

As each portion of urine is secreted, it propels that which is already in the uriniferous tubes onward into the pelvis of the kidney. Thence it passes through the ureter into the bladder, from which at intervals it is discharged to the exterior. The rate and mode of entrance of urine into the bladder has been watched in cases of ectopia vesicæ, *i.e.*, cases in which fissures in the anterior or lower part of the walls of the abdomen and of the front wall of the bladder expose to view the orifices of the ureters. The urine does not enter the bladder at any regular rate, nor is there a synchronism in its movement through the two ureters. Ordinarily two or three drops enter the bladder every minute, each drop as it enters first raising up the little papilla on which the ureter opens, and then passing through the orifice, which at once again closes like a sphincter. Its flow is aided by the peristaltic contractions of the ureters, and is increased in deep inspiration or by straining. The urine collected in the bladder is prevented from regurgitation into the ureters by the mode in which these pass through the walls of the bladder, namely, by their lying a half to three-quarters of an inch between the muscular and mucous coats before they turn rather abruptly forward and open through the latter into the interior of the bladder.

Micturition. The contraction of the muscular walls of the bladder may by itself expel the urine with little or no help from other muscles. The vesicular pressure is increased in the voluntary act by the contraction of the abdominal and other expiratory muscles which bear on the abdominal viscera, thus aiding in the expulsion of the contents of the bladder. The diaphragm is at the same time fixed in contraction and the sphincter of the bladder relaxes. The pressure within the bladder under the combined contractions of these expulsive muscles sometimes amounts to 8 to 10 cm. of mercury. The act is completed by the accelerator urinæ muscle, which, as its name implies, quickens the stream and expels the last drop of urine from the urethra. The act is under the regulative control of a nervous center in the lumbar spinal cord, through which, as in the case of the similar center for defecation, the various muscles concerned are coordinated in their action. It is well known that the act may be reflexly induced, *e.g.*, in children who suffer from intestinal worms or other such irritation. Generally the afferent impulses which set up the reflexes leading to the desire to micturate are excited by overdistention of the bladder, or sometimes by a few drops of urine passing into the urethra. This impulse passes up to the lumbar center or centers, and reflexly produces on the one hand inhibition of the sphincter and on the other contraction of the necessary muscles for the expulsion of the contents of the bladder. In the voluntary act these motor centers are stimulated to activity by impulses coming from the higher cerebral centers.

THE STRUCTURE AND EXCRETORY FUNCTIONS OF THE SKIN.

The skin serves, 1, as an external integument for the protection of the deeper tissues, and 2, as a sensitive organ in the exercise of touch, a subject to be considered in the chapter on the Special Senses. It is also, 3, an important secretory and excretory organ; and 4, an absorbing organ. 5, It plays an important part in the regulation of the temperature of the body by controlling the loss of heat, *i.e.*, a temperature-regulating function, discussed in the chapter on Animal Heat.

Structure. The skin consists principally of a vascular tissue named the *corium*, *derma*, or *cutis vera*, and of an external covering of epithelium termed the *epidermis* or *cuticle*. Within and beneath the corium are embedded several organs with special functions, namely, *sudoriferous* glands,

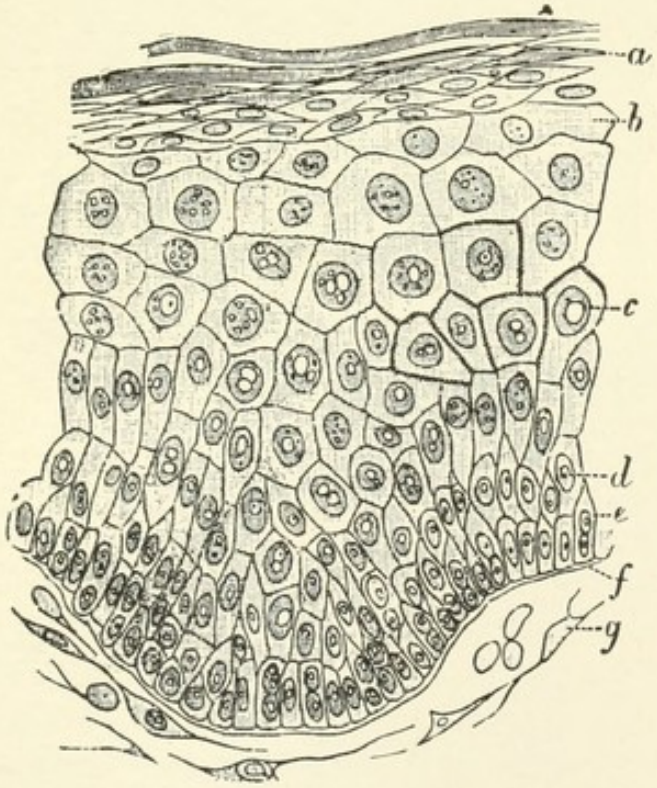


FIG. 304.—Vertical Section of the Epidermis of the Prepuce. *a*, Stratum corneum, of very few layers, the stratum lucidum and stratum granulosum not being distinctly represented; *b*, *c*, *d*, and *e*, the layers of the stratum Malpighii, a certain number of the cells in layers, *d*, and *e* showing signs of segmentation; layer *c*, consists chiefly of prickle or ridge and furrow cells; *f*, basement membrane; *g*, cells in cutis vera. (Cadiat.)

sebaceous glands, and *hair follicles;* and on its surface are sensitive *papillæ*. The so-called appendages of the skin—the *hair* and *nails*—are modifications of the epidermis.

The epidermis is composed of several strata of cells of various shapes and sizes; it closely resembles in its structure the epithelium of the mucous membrane that lines the mouth or covers the cornea. The following four layers may be distinguished:

The *Stratum lucidum*, a bright homogeneous membrane, consisting of squamous cells closely arranged, in some of which a nucleus can be seen. *Stratum granulosum*, consisting of one layer of flattened, fusiform, distinctly nucleated cells. *Stratum Malpighii* or *Rete mucosum* consists of many strata of cells. The deepest cells, placed immediately above the cutis vera, are columnar with oval nuclei, succeeded by a number of layers of more or less

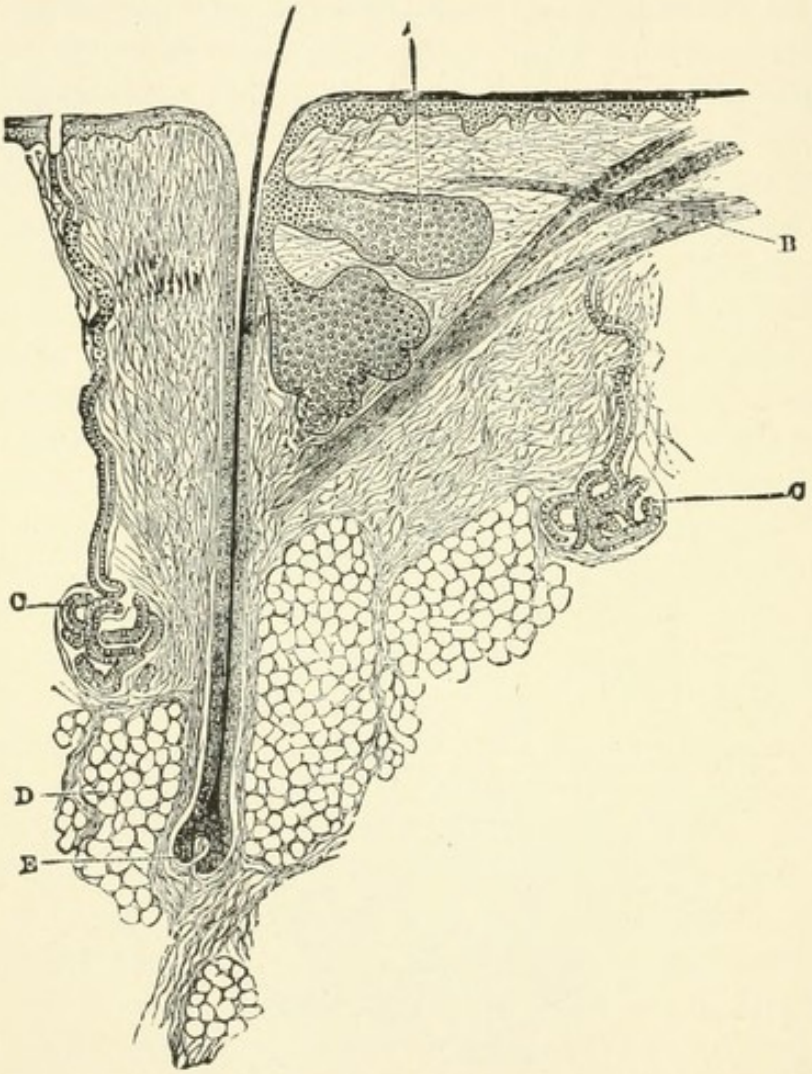


FIG. 305.—Vertical Section of Skin. *A*, Sebaceous gland opening into hair follicle; *B*, muscular fibers; *C*, sudoriferous or sweat gland; *D*, subcutaneous fat; *E*, fundus of hair-follicle, with hair-papillæ. (Klein.)

polyhedral cells with spherical nuclei; the more superficial layers are considerably flattened. The deeper surface of the rete mucosum is accurately adapted to the papillæ of the true skin, being, as it were, moulded on them. It is very constant in thickness in all parts of the skin. The cells of the middle layers of the stratum Malpighii are connected by processes, and thus form prickle cells, figure 28. The pigment of the skin, in the deeper cells of rete mucosum, causes the various tints observed in different individuals and different races. The epidermis maintains its thickness in spite of the constant wear

and tear to which it is subjected. The columnar cells of the deepest layer of the rete mucosum elongate, multiply by division, the new cells produced being pushed toward the free surface of the skin. There is thus a constant production of fresh cells in the deeper layers, and a constant throwing off of old ones from the free surface. When these two processes are accurately balanced, the epidermis maintains its thickness. When by intermittent pressure a more active cell-growth is stimulated, the production of cells exceeds their waste and the epidermis increases in thickness, as we see in the horny hands of the laborer.

The dermis, or cutis vera or true skin, is a dense and tough, but yielding and highly elastic structure supporting the epidermis. It is composed of areolar connective tissue interwoven in all directions and forming numerous spaces by its interlacements. These areolæ in the deeper layers of the cutis are usually filled with little masses of fat, figure 305. Unstriped muscu-

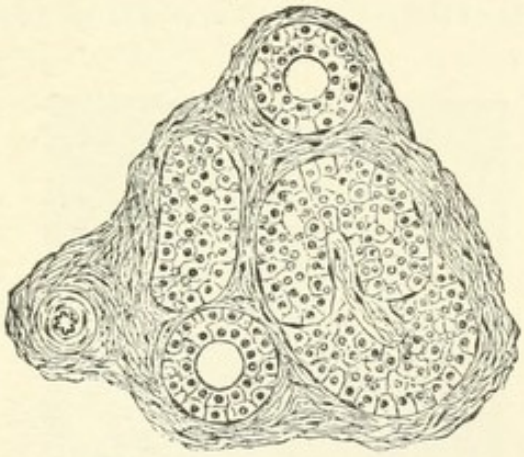


FIG. 306.—Terminal Tubules of Sudoriferous Glands, Cut in Various Directions. From the skin of the pig's ear. (V. D. Harris.)

lar fibers are also abundantiy present, especially in the skin of animals which erect the hairs with greater ease than is usually the case with man.

There is a rich network of blood-vessels to the dermis. In the dermal papillæ and about the sweat glands there are special loops of capillaries. Nerve fibers are also distributed to the papillæ.

The special *nerve terminations* in the skin have been described on page 72.

Glands of the Skin. The skin possesses glands of two kinds: Sudoriferous or Sweat Glands, and the Sebaceous or Oil Glands.

A *Sudoriferous or Sweat Gland* consists of a small lobular mass, formed of a coil of tubular gland-duct, surrounded by blood-vessels, and embedded in the subcutaneous adipose tissue, figure 305, *C*. The duct ascends from this coiled mass for a short distance in a spiral manner through the cutis and the epidermis, and then opens on the surface of the skin. In the parts where the epidermis is thin, the ducts themselves are thinner and more nearly straight in their course.

The duct is lined with a layer of columnar epithelium continuous with the epidermis. The coiled or secreting portion of the gland is lined with at least two layers of short columnar cells with very distinct nuclei, figure 306. The lumen is distinctly bounded by a special lining of cuticle.

The sudoriferous glands are abundantly distributed over the whole surface of the body; but are especially numerous, as well as very large, in the skin of the palm of the hand and of the sole of the foot. The glands by which the peculiarly odorous matter of the axillæ and groin is secreted form a nearly complete layer under the cutis, and are like the ordinary sudoriferous glands, except in being larger and having very short ducts.

The peculiar bitter yellow substance secreted by the skin of the external auditory passage is named *cerumen*, and the glands themselves *ceruminous* glands; but they do not much differ in structure from the ordinary sudoriferous glands.

The sebaceous glands, figures 305 and 306, like sudoriferous glands, are abundant in most parts of the surface of the body, particularly in parts largely

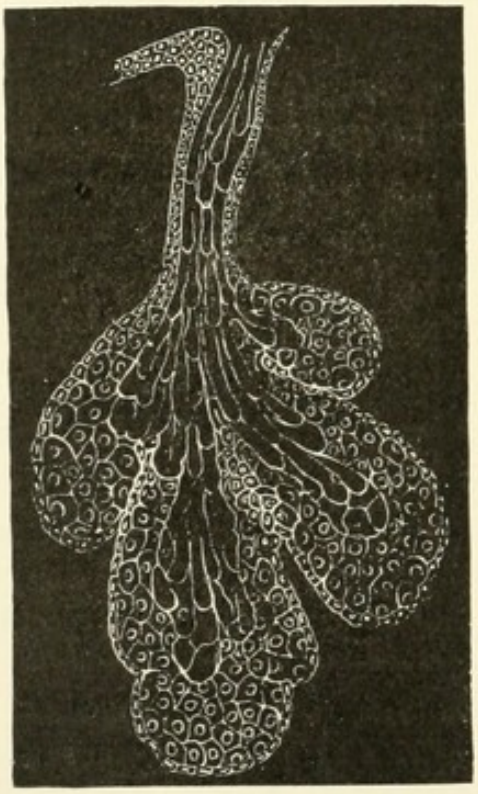


FIG. 307.—Sebaceous Gland from Human Skin. (Klein and Noble Smith.)

supplied with hair, as the scalp and face. They are thickly distributed about the entrances of the various passages into the body, as the anus, nose, lips, and external ear. They are entirely absent from the palmar surface of the hand and the plantar surface of the foot. They are racemose glands composed of an aggregate of small tubes or sacculi lined with columnar epithelium

and filled with an opaque white substance, like soft ointment, which consists of broken-up epithelial cells which have undergone fatty degeneration. Minute capillary vessels overspread them; and their ducts open on either the surface of the skin, close to the hair, or, which is more usual, directly into the follicle of the hair. In the latter case, there are generally two or more glands to each hair, figure 306.

The story of the structure and development of such epithelial structures as the hair and the nails is best left to the histologist, to whom the student is referred.

The Excretory Function of the Skin. The function of the skin which is of special interest to this chapter is that of the excretion of the sweat. The fluid secreted by the sweat glands is usually formed so gradually that the watery portion of it escapes by evaporation as fast as it reaches the surface. But during strong exercise, exposure to great external warmth, in some diseases, and when evaporation is prevented, the secretion becomes more sensible and collects on the skin in the form of drops of fluid.

The *perspiration*, as the term is sometimes employed in physiology, includes all that portion of the secretions and exudations from the skin which are thrown on the surface by the sweat glands. As a matter of fact, this is mingled with various substances lying on the surface of the skin. The contents of the sweat are, in part, matters capable of assuming the form of vapor, such as carbonic acid and water, and in part other matters which are deposited on the skin, and mixed with the sebaceous secretions.

The secretion of the sebaceous glands and hair-follicles consists of cast-off epithelium cells, with nuclei and granules, together with an oily matter, extractive matter, and stearin. In certain parts, also, it is mixed with a peculiar odorous principle, which contains caproic, butyric, and rutic acids. It is similar in composition to the unctuous coating, or vernix caseosa, which is formed on the body of the fetus while in the uterus, and which contains ordinary fat. This sebaceous secretion serves the purpose of keeping the skin moist and supple, and, by its oily nature, of both hindering the evaporation from the surface and guarding the skin from the effects of the long-continued action of moisture. But while it thus serves local purposes, its removal from the body entitles it to be listed among the excretions of the skin.

CHEMICAL COMPOSITION OF SWEAT.

Water		995
Solids:		5
Organic acids (formic, acetic, butyric, propionic, caproic, caprylic)	0.9	
Salts, chiefly sodium chloride	1.8	
Neutral fats and cholesterin	0.7	
Extractives (including urea), with epithelium	1.6	
		1 000

The sweat is a colorless, slightly turbid fluid, alkaline, neutral or acid in reaction, of a saltish taste, and peculiar characteristic odor.

Of the several substances it contains, however, only the *carbonic acid* and *water* need particular consideration.

The quantity of watery vapor excreted from the skin is, on an average, between 750 and 1,000 cubic centimeters daily. This subject has been very carefully investigated by La visier and Sequin. The latter chemist enclosed his body in an air-tight bag provided with a mouthpiece. The bag was closed by a strong band above, and the mouthpiece adjusted and gummed to the skin around the mouth. He was weighed, then remained quiet for several hours, after which time he was again weighed. The difference in the two weights indicated the amount of loss by pulmonary exhalation. Having taken off the air-tight dress, he was immediately weighed again, and a fourth time after a certain interval. The difference between the two weights last ascertained gave the amount of the cutaneous and pulmonary exhalation together; by subtracting from this the loss by pulmonary exhalation alone, while he was in the air-tight dress, he ascertained the amount of cutaneous transpiration. The average loss by cutaneous and pulmonary exhalation in a minute during a state of rest is eighteen grains,—the minimum eleven grains, the maximum thirty-two grains. Of the eighteen grains, eleven pass off by the skin and seven by the lungs.

The quantity of watery vapor lost by transpiration is of course influenced by all external circumstances which affect the exhalation from evaporating surfaces, such as the temperature, the hygrometric state, and the stillness of the atmosphere. But, of the variations to which it is subject under the influence of these conditions, no calculation has been exactly made.

The quantity of *carbonic acid* exhaled by the skin on an average is said to be about one-two-hundredth of that eliminated by the pulmonary respiration.

The cutaneous exhalation is most abundant in the lower classes of animals, more particularly the naked amphibia, as frogs and toads, whose skin is thin and moist, and readily permits an interchange of gases between the blood circulating in it, and the surrounding atmosphere. Bischoff found that, after the lungs of frogs had been tied and cut out, from 3 to 4 c.c. of carbonic-acid gas was exhaled by the skin in eight hours. And this quantity is very large, when it is remembered that a full-sized frog will generate only about 10 c.c. of carbonic acid by his lungs and skin together in six hours.

The importance of the respiratory function of the skin, which was once thought to be proved by the speedy death of animals whose skins, after removal of the hair, were covered with an impermeable varnish, has been shown by further observations to have no foundation in fact. The immediate cause of death in such cases is the loss of temperature. A varnished animal is said to have suffered no harm when surrounded by cotton padding, and to have died when the padding was removed.

Influence of the Nervous System on Sweat Secretion. The secretion of sweat is closely connected with the quantity of blood flowing through the cutaneous vessels. The quantity of sweat increases with vaso-dilatation and diminishes with vaso-constriction. The sweat glands are also under the control of efferent impulses passing to them from the special sweat centers in the brain and spinal cord through special sweat nerves. Thus, if the sciatic nerve be divided in a cat and the peripheral end be stimulated, beads of sweat are seen to appear upon the pad of the corresponding foot. The sweat appears even though at the same time the blood-vessels are constricted, or the blood flow entirely stopped by compression of the aorta, whereas if atropin is injected previously to the stimulation, no sweat appears, although dilatation of the vessels may be present. Secretion of sweat, too, may be brought about reflexly.

The circulation of venous blood in the spinal bulb causes the sweating of phthisis and of dyspnea generally, by stimulating the sweat center. If the cat whose sciatic nerve is divided be rendered dyspneic, abundant sweat occurs upon the foot of the uninjured, and none on the injured, side. The effect of heat in producing sweating may be both local and general, and, again, the various drugs which produce an increased secretion of sweat do not all act in the same way; thus, there is reason for thinking that *pilocarpine* acts upon the local apparatus, that *strychnine* and *picrotoxin* act upon the sweat centers, and that *nicotine* acts both upon the central and upon the local apparatus.

The special sweat-nerves appear to issue from the spinal cord, in the case of the hind limb of the cat, by the last two or three dorsal and first two to four lumbar nerves, pass to the abdominal sympathetic, and from thence to the sciatic nerve, the general course of the autonomic nerves for this region. In the case of the fore limb, the nerves leave the cord by the first to the sixth dorsal nerves, pass into the thoracic sympathetic, and then join the brachial plexus, reaching the arm through the median and ulnar nerves.

It will be as well to repeat here the other functions which the skin subserves. In addition to its excretory office, we have seen that it acts as a channel for absorption. It is also concerned with the special senses, that of touch and temperature, to the consideration of which as well as to its function of regulating the temperature of the body we shall presently return. By its general impermeability it prevents the loss of moisture of the body by direct evaporation from the tissues. It should be recollected, however, that apart from these special functions, by means of its toughness, flexibility, and elasticity, the skin is eminently qualified to serve as the general integument of the body, for defending the internal parts from external violence, while readily yielding and adapting itself to their various movements and changes of position.

LABORATORY EXPERIMENTS IN EXCRETION.

PHYSIOLOGICAL REACTIONS

1. **The Relation of Blood Flow through the Kidney to the Secretion of Urine.** Properly to check this experiment one should make three determinations: 1, the general blood pressure; 2, the volume of the kidney; 3, the amount of urine secreted. Anesthetize a dog and arrange the apparatus for taking the blood pressure as directed in experiment 19. Prepare a renal onkometer, see figures 301 and 302, and an onkograph for recording the variations in the volume of the kidney. The renal onkometer consists of a double metal box to fit the form of a kidney. The inner halves of this box should be covered so loosely with very thin sheet rubber that the rubber can be fitted into the bottom of the cup without undue tension. The rubber must be sealed to the outer edges of this inner cup with rubber cement and allowed to dry. When it is completely dried the inner cup should be adjusted to the outer, and the spaces enclosed by the rubber sheet filled with water. Or the onkometer may be closed with parchment and filled with oil as described in experiment 23 on the Circulation. The half of the onkometer that comes against the wall of the body cavity of the animal should be completely closed with a stopper before the instrument is adjusted to the kidney. Now adjust the onkometer to the kidney, taking care to place the renal arteries, veins, and ureter in the tube in such a way as not to compress them. Fill the outer cup with water and connect this cavity by a two-way cannula with the recording onkograph. In practice it is more satisfactory if one introduces between the onkometer and onkograph an overflow bottle or bulb, adjusted to maintain the constant pressure on the kidney. This direction varies from the usual one in that rubber sheeting instead of parchment is used to cover the inner cup of the onkometer, a method that permits the use of water instead of oil.

Isolate and insert a small cannula into the ureter. This cannula should be clamped in a stand at a level as little above that of the kidney as possible. The urine secreted may be collected in a 10 c.c. graduated cylinder and measured at intervals of 5 or 10 minutes. Or, if the outflow is scanty, it may be allowed to drop on a tambour recording apparatus, the rate of dropping being indicative of the rapidity of secretion.

Determine the normal rate of secretion of a dog under constant anesthesia. The anesthesia should be medium to light, but should be kept very uniform so as to maintain a strong blood pressure. Note the effect on secretion and the corresponding effect on blood pressure and the kidney volume produced by vagus inhibitions. Section the vagus nerves and produce inhibition by stimulating the peripheral end of the vagus. In this instance there are no reflexes to complicate the experiment, so that the fall in blood

pressure is a direct cardiac effect. Stimulate the central end of the vagus which produces a fall of blood pressure through the vaso-motor system. There should be a normal period of at least ten minutes following each experiment to allow the secretion of the kidney to return to the normal.

Expose the splanchnic nerves at the point where they pass beneath the diaphragm into the abdominal cavity. Adjust a pair of shielded electrodes, close the cavity, and, when the animal has returned to the normal uniform rate of secretion and of blood pressure, stimulate the splanchnic nerves. The splanchnics contain vaso-constrictor nerves for the kidney. The onkometer experiment should, therefore, demonstrate a sharp decrease in the volume of the organ, while the blood pressure is only slightly changed. The rate of secretion should be followed for at least twenty minutes after stimulation of the splanchnics. This test should be repeated two or three times.

In this connection demonstrate the influence of deep chloroform anesthesia on urinary secretion. The chloroform should be pushed to the danger limit and maintained there for a couple of minutes or more. Compare the rapidity of the recovery of blood pressure with the recovery of the rate of secretion.

2. **Secretory Nerves for the Sweat Glands.** Langley has mapped out the paths of the secretory nerves for the sweat glands. He has shown that in the cat these fibers are distributed to the hind limb through the sciatic. Anesthetize a half-grown cat, isolate the sciatic nerve, cut it and stimulate the peripheral end with a medium to strong induction current. After a few moments beads of perspiration will appear on the pads of the foot, which should therefore be carefully examined before the experiment.

URINE ANALYSIS.

3. **Daily Quantity.** Determine the total quantity, for 24 hours, of urine secreted through a period of 3 or 4 days, beginning and ending the period at a definite hour in the day, preferably on rising in the morning. The daily secretion varies through wide extremes, depending upon the quantity of liquid taken in the food, the daily exercise, the temperature, etc., etc. In the analysis of urine it is always better to take a mixed 24-hour sample.

4. **Specific Gravity.** Determine the specific gravity of 24-hour urine. This is done by the instrument known as the urinometer which carries a graduated scale at the neck. Care should be taken to float the urinometer so that it does not come in contact with the measuring cylinder. The scale should be read at the bottom of the meniscus.

5. **Reaction.** Determine the reaction of perfectly fresh urine, using litmus paper. The normal urine is slightly acid under ordinary conditions, due to the presence of acid phosphates or perhaps in some cases to traces of free organic acid.

After standing some time the reaction is usually alkaline, owing to fer-

mentation processes. The reaction may vary also according to the food, vegetable foods tending to produce alkaline urine, while with animal foods the reaction is acid.

6. **The Total Quantity of Solids.** Determine the solids of urine by evaporating 25 c.c. of a mixed sample of urine to dryness in a weighed platinum or porcelain dish over a water bath. The residue should be dried to constant weight in a drying oven at 105° C.

Fig. 308.—The Urinometer.

A useful rule for approximately estimating the total solids in any given specimen of healthy urine is to multiply the last two figures representing the specific gravity by 2.33. Thus, in urine of specific gravity 1025, $2.33 \times 25 = 58.25$ grains of solids are contained in 1,000 grains of the urine. Or the total solids are 5.825 per cent. In using this method it must be remembered that the limits of error are much wider in diseased than in healthy urine.

The solids of urine consist of inorganic salts of sodium, potassium, and calcium, and of a long list of organic compounds, chiefly nitrogenous.

7. **Chlorides.** Large quantities of sodium chloride are always present in the normal urine. Add ammonia to 25 or 50 c.c. of albumin-free urine and heat to precipitate earthy phosphates, filter. To a sample of the filtrate add an excess of strong nitric acid and a few drops of 1 per cent silver nitrate. A white flocculent precipitate of silver chloride comes down. This precipitate is soluble in an excess of ammonia. Reprecipitate by adding nitric acid again. The test may be made without removing the phosphates, though in this case, upon adding ammonia, the disappearance of the silver precipitate is complicated by the appearance of insoluble phosphates.

The chlorides may be estimated quantitatively by Volhard's method, or some one of its modifications, which depends upon the determination of the amount of chlorine precipitated by the silver. The student is referred to chemical text-books for this and other quantitative methods.

8. **Sulphates.** Sulphates exist in the urine both in inorganic and organic compounds, chiefly the former. Add a few drops of hydrochloric acid to a sample of urine in a test tube, then a solution of barium chloride, the insoluble barium sulphate settles out. If the test is made on the normal urine without the addition of the acid, the inorganic sulphate will be precipitated, while the ethereal or compound sulphate will remain in solution and can be filtered off. This filtrate, when boiled with strong hydrochloric acid to 10 per cent over a water bath for a short time, will have the sulphates

split off from the organic radicle and may be precipitated by the addition of barium chloride in hot solution.

9. **Phosphates.** The phosphates of urine consist of the earthy and alkaline salts, the latter predominating. Take a 50 c.c. sample of urine, add strong ammonia, and heat. The phosphates of calcium and magnesium separate out, as they are insoluble in aikaline solution. Filter.

To the filtrate add a solution of magnesium sulphate. This precipitates the sodium and potassium phosphates as a triple phosphate of magnesium, which is insoluble. Tests for phosphates in general are:

Add nitric acid to a sample of urine, warm gently, then add a few drops of 10 per cent ammonium molybdate; a yellow precipitate of ammonium phospho-molybdate is formed. Or, add acetic acid, then a few drops of

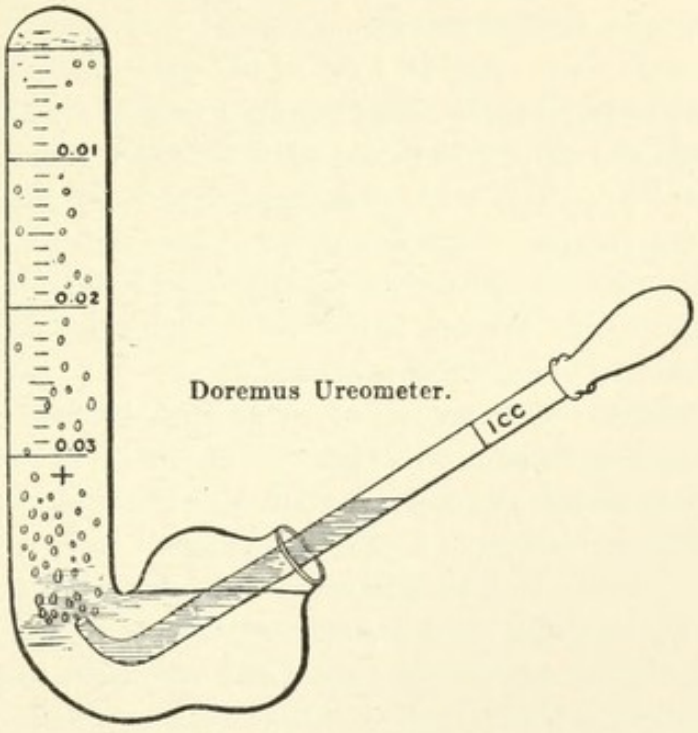


FIG. 309.—Doremus' Ureometer.

uranium acetate; a bright yellow precipitate of uranium ammonium phosphate is formed. These two reactions are used as the basis for a quantitative determination of phosphorus.

10. **The Preparation of Urea.** Take 100 c.c. of normal urine, evaporate to one-half its quantity, and precipitate the phosphates and sulphates by adding a mixed solution of barium hydrate and nitrate. Filter, evaporate the filtrate to dryness, take up in warm 95 per cent alcohol, and refilter. Crystals of urea separate out when the alcohol is evaporated off.

Evaporate a large sample, 200 c.c., of urine to a syrupy mass, add nitric acid. Crystals of urea nitrate are formed. Wash the crystals in dilute nitric acid, then dissolve in water. The urea is set free by adding barium carbonate

until the carbon dioxide ceases to come off. Filter, evaporate over a water bath to dryness, and dissolve the urea in 95 per cent alcohol; decant, and recrystallize by evaporating off the alcohol.

11. **Urea Determination by Doremus' Ureometer.** Fill the ureometer with hypobromite of sodium solution. Take a sample of urine in the pipet which accompanies the instrument, drawing it in exactly to the mark. Insert the pipet past the bend of the ureometer and slowly empty the urine carefully so as not to lose any of the liberated nitrogen. The instrument is graduated to read off the percentage of urea directly.

12. **Uric Acid.** Concentrate over a water bath 500 c.c. of urine to 100 c.c. and boil with 10 c.c. or more of strong hydrochloric acid. Upon cooling, crystals of uric acid are formed. Decant the supernatant liquid and wash the crystals with a few cubic centimeters of 10 per cent hydrochloric acid. Dissolve the crystals and test.

The Murexide Test. Add to 2 c.c. of uric acid solution in a test tube an equal quantity of nitric acid. Heat gently, a reddish ring forms at the point of contact between the nitric acid and uric acid solution. Cool and add ammonia carefully. The color ring deepens to a purple color. This test succeeds well by evaporating a few drops of uric acid on a porcelain plate. Add to the stain a drop of concentrated nitric acid and evaporate. Concentric rings of reddish color will be formed. This color deepens to reddish-purple when a drop of ammonia is added.

13. **Creatinin.** Test 20 c.c. of urine in a beaker for creatinin by adding a cubic centimeter of dilute solution of sodium nitroprusside and then weak sodium hydrate. A ruby-red color, which quickly turns yellow, indicates the presence of creatinin. (Weyl's reaction.) If the yellow solution has an excess of acetic acid added and is then boiled, it turns first green and later blue, forming ultimately a precipitate of Prussian blue.

Urine mixed with picric acid gives a red coloration when made alkaline with caustic alkali solution.

14. **Total Nitrogen in Urine.** Determine the total nitrogen in a sample of urine by the Kjeldahl method. This method depends upon the conversion of all the nitrogen to ammonia, the distillation of this ammonia into a known quantity of sulphuric acid, and the final titration of the excess of sulphuric acid when the distillation is complete. The computation is made on the basis that 1 c.c. of a normal sulphuric acid is equivalent to 1 c.c. normal sodium hydrate, and that in turn to 1 c.c. of ammonium hydrate. The ammonia neutralizes a portion of the sulphuric acid in the distillation. One c.c. of normal ammonium hydrate contains 0.014 gram nitrogen, from which the total nitrogen in the sample used can be readily computed.

15. **Pigments of Urine.** The normal color of the urine is due to the presence of a pigment, *urobilin*. Prepare urobilin by adding lead acetate

to a 200 c.c. sample of urine. A precipitate forms which carries down the coloring matter. Filter. Add acid alcohol to the precipitate to extract the coloring matter, refilter, which gives a deep yellow solution. Shake up with a few cubic centimeters of chloroform which dissolves the pigment. Draw off the chloroform solution and allow to evaporate. The residue is a brownish mass of urobilin.

ABNORMAL CONSTITUENTS OF URINE.

Many abnormal constituents may appear in the urine under pathological conditions, only two of which will be mentioned here.

16. **Albumin in the Urine.** The detection of the presence of albumin, albuminuria, is of considerable clinical importance. The following are the standard tests which present no special difficulty except when traces only are present.

Heat Coagulation. To a half test tube of urine add a drop of dilute acetic acid and boil. A white coagulum indicates the presence of albumin. A faint cloudy appearance indicates traces.

Nitric Acid Test. To 5 c.c. of strong nitric acid in a conical test tube add 10 or 15 c.c. of urine, pouring it gently down the inclined side of the glass. Allow the glass to stand for a few minutes, when a white coagulum appears just above the line of contact of the acid with the urine. This test, known as Heller's test, will usually indicate the presence of traces of albumin.

Picric Acid Test. Add picric acid to a sample of urine. A whitish precipitate of albumin will appear at the line of contact, as in the preceding test.

Citric acid two parts and picric acid one part, when boiled with urine will coagulate minute traces of the proteid.

17. **Detection of Sugar in the Urine.** *Trommer's Test.* The presence of sugar in the urine can usually be detected by Trommer's test, which depends upon the reduction of copper sulphate in the presence of strong alkali. Boil fresh Fehling's solution and add to it a few cubic centimeters of urine. When sugar is present a reddish-yellow precipitate of copper oxide comes out. The test should be set away for a few minutes when, if only traces of the reduction are present, a reddish-brown stain will appear on the bottom of the test tube. Uric acid, if present in excess, may produce a slight precipitation of the copper.

Fermentation Test. If sugars are present in the urine, they can be detected by adding yeast to a fermentation tube filled with urine, the liberation of carbon dioxide indicating the presence of sugar. Cane sugar does not support the growth of yeast, so it forms an exception by this test.

Phenyl-Hydrazin Crystals. Phenyl-hydrazin forms crystals of phenyl-glucosazone. To 10 c.c. of urine in a small beaker add 0.1 of a gram of phenyl-hydrazin hydrochloride and a double quantity of sodium acetate.

Heat in the water bath for 20 minutes. Upon cooling a deposit of yellow crystals of phenyl-glucosazone takes place, if glucose is present.

18. **Quantitative Determination of Sugar in the Urine.** Fill a 10-c.c. graduated pipet with freshly prepared Fehling's solution. Take 10 c.c. of urine, measured with a dropping-pipet into a small beaker, and boil. While continuing to boil, add Fehling's solution slowly and cautiously so long as the color is discharged. The amount of Fehling's required to reduce the sugar is a measure of the quantity of reducing sugar present—1 c.c. of Fehling's being equivalent to 5 milligrams of dextrose.

For the presence of blood pigments and other abnormal constituents of the urine, the student is referred to special handbooks on the subject.

CHAPTER XI

METABOLISM, NUTRITION, AND DIET

THE term *metabolism* means, literally, an exchange of material. In its broadest physiological sense it includes the study of the exchange of material between the living tissues of the body and their surrounding media. This includes the study of the income and outgo of material; the storing of energy-yielding materials in the body; the transfer of this potential energy into kinetic energy; and the nutritional processes within the various tissues. The building up of absorbed food material into the protoplasm of the cell or of simpler compounds into more complex ones, which may be stored in the cell, is known as *anabolism*, and the compounds themselves as *anabolites*. The breaking down of these substances into simpler forms, whereby the potential energy of the anabolites is transformed into kinetic energy, is known as *catabolism*, and its products as *catabolites*.

In order to form an estimate of these processes going on in the body, the amount and nature of the ingested material must be known, as well as the amount of refuse or unused material that passes out of the alimentary canal as feces, and the amount of excreted material from the various excretory organs. It is also necessary to know the potential energy of the ingested materials, and the possible potential energy must be checked against the actual energy liberated.

The food is intended to supply the place of the material which has been utilized by the body, and, in a simpler form, eliminated in the excretions. But in the choice of a diet this is not enough; the food should be sufficient to supply such need without waste and without unduly increasing the output of excreta, while at the same time the body should be maintained in health, without increase or loss of weight. The food must also supply the energy liberated without undue waste of the tissues themselves.

These requisites of a diet scale then allow for wide alterations in the amount of different kinds of foods under different circumstances. Numerous and most valuable experiments have been performed in recent years to determine just what each article of the common food materials contributes to the growth of the tissues and to the kinetic energy liberated by the tissues. The potential energy of the food can also be checked against the kinetic energy liberated. A single illustration of this class will serve. In an experiment with mixed food lasting through four days, on a man with body weight of 64 kilograms, and doing a minimum amount of work, Atwater made the following determinations:

WEIGHT, COMPOSITION, AND HEAT OF COMBUSTION OF FOODS AND EXCRETA PER DAY.

	Weight per day.	Water.	Protein.	Fats.	Carbohydrates.	Nitrogen.	Carbon.	Hydrogen.	Heat of combustion.
Food	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Calories.
Beef	100	61.2	35.1	3.1	....	5.62	20.05	2.90	227
Butter	25	2.6	.5	21.1	....	.08	15.77	2.50	194
Whole milk	850	726.8	32.3	45.1	39.9	5.10	67.74	9.94	768
Bread	300	123.9	22.2	12.0	139.2	3.90	82.53	12.24	835
Shredded wheat biscuit	50	4.1	4.8	.7	39.7	.84	20.46	2.87	204
Ginger snaps	50	3.3	2.8	3.6	39.2	.50	21.12	3.07	212
Sugar	20	.....	....	....	20.0	....	8.42	1.30	79
Total food per day	1,395	921.9	97.7	85.6	278.0	16.04	236.09	34.82	2,519
Average feces per day	98.8	77.7	7.7	4.0	6.3	1.23	9.98	1.42	110
Average urine per day	1420.8	1363.9	....	....	....	15.85	11.79	2.98	135
Excretions lungs and skins	....	881.0	....	....	....	....	221.5	.....	2397
Total excreta per day	....	2322.6	....	....	....	17.08	243.27	4.40	2642
Balance	....	.....	....	....	....	−1.04	−7.18	+30.42	−123

Careful analyses of the excreta, many of which we have already had occasion to call attention to, show that they are made up, besides water, chiefly of the chemical elements carbon, hydrogen, oxygen, and nitrogen, but that they also contain, to a less extent, sulphur, phosphorus, chlorine, potassium, sodium, calcium, magnesium, iron, and certain other of the elements. Since this is the case it must be evident that, to balance this waste, foods must be supplied containing all these elements to a certain degree, and some of them in large amount, viz., those which take a principal part in forming the excreta.

The waste products of the body are eliminated through the lungs, the skin, the alimentary canal, and the kidney. In the lungs the chief waste product is water, carbonic-acid gas, and traces of ammonia compounds which are composed of the elements carbon, oxygen, nitrogen, and hydrogen. Traces of carbonic-acid gas and small quantities of urea and salts are eliminated through the skin. From the alimentary canal there are lost, through the feces, the indigestible and unabsorbed substances from the food, together with products secreted into the canal by the liver, pancreas, and mucous membrane.

The secretion lost daily by the kidney, aside from a large quantity of water, consists of nitrogenous waste products, chiefly urea, and inorganic solids, as were mentioned in the chapter on Excretion.

The relations between the amounts of the chief elements contained in these various excreta in twenty-four hours may be thus summarized:

	Water.	C.	H.	N.	O.
By the lungs	330	248.8	....	....	651.15
By the skin	660	2.6	....	....	7.2
By the urine	1,708	9.8	3.3	15.8	11.1
By the feces	120	20.	3.0	3.0	12.0
Grams	2,818	281.2	6.3	18.8	681.45

From the water in this table should be subtracted the 296 grams of water which are produced by the union of hydrogen and oxygen in the body during the process of oxidation, and there should be added to the respective columns the corresponding amounts of the constituent elements, *i.e.*, 33 grams of hydrogen and 262 grams of oxygen. There are 26 grams of salts eliminated through the urine, and 6 by the feces; a total of 32 grams.

The quantity of carbon daily lost from the body amounts to about 281.2 grams and of nitrogen 18.8 grams, and if a man could be fed by these elements, as such, the problem would be a very simple one; a corresponding weight of charcoal and, allowing for the oxygen in it, of atmospheric air would be all that is necessary. But an animal can live upon these elements only when they are arranged in a particular manner with others, in the form of such food stuffs as we have already enumerated, page 297 *et seq.;* moreover, the relative proportion of carbon to nitrogen in either of these compounds alone is by no means the proportion required in the diet of man. Thus, in proteid, the proportion of carbon to nitrogen is only as 3.5 to 1. If, therefore, a man took into his body, as food, sufficient proteid to supply him with the needed amount of carbon, he would receive more than four times as much nitrogen as is needed; and if he took only sufficient to supply him with nitrogen, he would be starved for want of carbon. It is plain, therefore, that he should take with the albuminous part of his food, which contains so large an amount of nitrogen in proportion to the carbon he needs, substances in which the nitrogen exists in relatively much smaller quantities than the carbon.

It is, therefore, evident that the diet must consist of several compounds, not of one alone.

Many valuable observations have been made with a view of ascertaining the effect upon the metabolism of a variation in the amount and nature of food. These are of great assistance in the consideration of dietetics.

METABOLISM OF PROTEIDS.

Nitrogenous Equilibrium. Experiments have been made, to a considerable extent upon dogs, which demonstrate the necessity for proteid food. After a preliminary period without food, during which the output of nitrogen as shown by the urea has diminished to a comparatively constant amount, an animal is fed with a diet of lean meat which would suffice to produce the amount of urea, and so of flesh, which it has been losing during its starvation period. The effect of this, however, is at once to send up the amount of urea excreted to a point above that which had been lost previous to the commencement of the flesh diet. Thus the output of nitrogen still exceeds its income, and the weight of the animal continues slowly to diminish. It is only after a considerable increase of the flesh given in the food that a point is reached where the income and expenditure of nitrogen are equal, and at which the animal is not using up quickly or slowly the nitrogen of its own tissue, and is no longer losing flesh. This condition in which the nitrogen of the egesta equals the nitrogen of the ingesta is known as *nitrogenous equilibrium.*

EXPERIMENT IN NITROGENOUS EQUILIBRIUM.

DAYS OF EXPERIMENT.	N Intake. Grams.	N Output. Grams.	Per cent Difference.	S Intake. Grams.	S Output. Grams.
I. 1–5	90.00	89.81	—0.21	.....	.....
6–12	131.60	132.75	+0.88	.....	.....
II. 1–2	35.80	36.16	+1.00	.....	.....
3–11	144.50	143.13	—0.86	.....	.....
III. 1–7	154.81	153.02	—0.51	.....	.....
8–17	213.72	213.26	—0.21	12.77	12.79

In the dog, according to Waller, nitrogenous equilibrium does not occur until the amount of flesh of the food is over three times as great as would be necessary to supply the nitrogen of the urea during a period of starvation. Thus a dog excretes during a starvation period 0.5 gram of urea per kilo of body weight; in order to satisfy this waste it would be necessary to administer 1.5 grams per kilo of meat; this at once increases the urea excreted to about 0.75 gram per kilo of body weight, and nitrogenous equilibrium is not attained until over three times, viz., 3 grams per kilo of body weight, of meat is given. Foster gives even a larger figure. The effect, therefore, of proteid food is largely to increase the excretion of urea, which indicates an increase in the metabolism of the tissues.

Studies in nitrogenous equilibrium are based on the fact that when an

animal is given a diet with a constantly increasing amount of proteid food from day to day, after a few days the total nitrogen found in the excreta exactly balances that taken in the food. This condition of nitrogenous equilibrium is established at different levels, varying sometimes according to the individual and with the kind and quantity of other food principles taken at the same time as the nitrogenous foods.

Chittenden's latest metabolism experiments have shown that with free choice, but moderate use, of accessory articles of diet, the human body can maintain itself in nitrogenous equilibrium for at least several months on an average of 4 to 10 grams of nitrogen per day, the equivalent of 25 to 62.5 grams of proteid.

The Rôle of Proteids in Metabolism. The proteids of food are described by Voit as having two relations to the proteid metabolism and to outgoing urea; the first part going to maintain the ordinary and quiet metabolism of the tissues, for which purpose it is actually built up into the living protoplasmic molecule, and the second part causing a more rapid formation of urea, but never becoming a part of the actual protoplasmic molecule. The former proteids are called *morphotic* or *tissue* proteids, the latter *circulating* or *floating* proteids. Normally more proteid is eaten than is needed to supply proteid to the protoplasm for growth, as has just been stated. Pflüger takes the view, however, that the tissues must have an excess of proteid to destroy in order to perform their metabolic processes normally. This use of the proteids to form heat by their oxidation, and not to produce tissue, was looked upon by the older physiologists as a wasteful use of good material, and was called a *luxus consumption*.

Folin has recently announced a theory of proteid metabolism in which he calls special attention to the relation of the nitrogenous excretion products to the nitrogenous intake. He has shown that the urea contained in the urine varies almost directly with the quantity of proteid in the food; that the ammonia varies with the proteid in the food; that the uric acid decreases (and increases) with the proteid in the food, but not in direct ratio; while the creatinin excreted is "wholly independent of quantitative changes in the total amount of nitrogen eliminated."

TABLE SHOWING THE OUTPUT OF NITROGEN IN A NORMAL, HEALTHY INDIVIDUAL ON A FOOD RICH IN NITROGEN, JULY 13TH, AND POOR IN NITROGEN JULY 20TH (FOLIN).

	July 13th.		July 20th.	
Volume of urine.....	1,170 c.c.		385 c.c.	
Total nitrogen.....	16.08 grams		3.60 grams	
Urea-nitrogen	14.70 "	= 87.5 per cent	22.0 "	= 61.7 per cent
Ammonia-nitrogen	0.49 "	= 3.0 "	0.42 "	= 11.3 "
Uric-acid-nitrogen	0.18 "	= 1.1 "	0.09 "	= 2.5 "
Kreatinin-nitrogen.....	0.58 "	= 3.6 "	0.60 "	= 17.2 "
Undetermined nitrogen	0.85 "	= 4.9 "	0.27 "	= 7.3 "

Folin states this theory as follows: "It is clear that the metabolic processes resulting in the end products which tend to be constant in quantity appear to be indispensable for the continuation of life; or, to be more definite, those metabolic processes probably constitute an essential part of the activity which distinguishes living cells from dead ones. I would therefore call the protein metabolism which tends to be constant, *tissue* metabolism, or *endogenous* metabolism; the other, the variable protein metabolism, I would call the *exogenous* or intermediate metabolism.

"The endogenous metabolism sets a limit to the lowest level of nitrogen equilibrium attainable. Just where that level is fixed will depend on how much, if any, urea is derived from the same catabolic processes that produce the creatinin. If this can be determined, we shall have a formula expressing more or less definitely the point of lowest attainable protein catabolism, because at such a point the percentage composition of the urine should be practically constant. The total nitrogen eliminated when this constant composition of the urine has been reached will indicate the lowest attainable level of nitrogen equilibrium."

The condition of nitrogenous equilibrium, therefore, is one which may be maintained even if the amount of proteid taken as diet far exceeds the necessities of the economy, the urea being excreted in excessive amount; and the wasteful use of proteid food which is so common may not be attended with harmful consequences, so long as the excreting organs are able to eliminate nitrogen from the body.

It is only in cases of growth, by putting on of flesh, as in growing children, that nitrogen is retained in the body in health, except to a very small amount. According to calculations which have been made, it appears that the body puts on thirty grams of flesh for every gram of nitrogen so retained.

Proteids as Fat- and as Glycogen-Formers. Proteid food is undoubtedly a source of energy in the body; and one can say that such proteid as is, according to Voit's view, metabolized without becoming part of the tissue may be considered a source of energy. If this be true, one might expect that proteids could be metabolized into other forms, such as carbohydrates and fats. Bernard long ago stated that proteid was a glycogen-former; that abundant glycogen was stored in the liver when flesh diet was fed, and argued that proteid was the source of the glycogen. The careful work of a number of investigators has not obtained sufficient evidence to clear up this question absolutely, but the weight of evidence is in favor of the view that in the body sugar can be formed from proteids. Whether or not proteid can be metabolized into fat, and stored as such, seems at present an open question, notwithstanding the immense amount of work expended in trying to solve the problem.

Cramer fed 450 grams of lean meat per day to a cat in a respiration chamber for 8 days. The daily excretion of nitrogen was 13 grams, of carbon

34.3 grams; calculating the amount of carbon in the food as 41.6 grams daily, this would leave 7.3 grams retained. This carbon might be stored in the form of glycogen or as fat. Calculated as glycogen, it gives an amount greater than an animal of that size could retain. Therefore, the probabilities are that the carbon is deposited in the form of fat.

In the examination of the fat formed in the larvæ of blow-flies developing in a quantity of coagulated blood, Hoffmann found ten times more fat than existed in the blood. These experiments point in the direction of fat formation from proteid.

The Effect of an Albuminoid Diet. The albuminoid eaten in greatest quantity is gelatin. Though gelatin closely resembles the proteid molecule chemically, it cannot replace the proteid of the food. In other words, nitrogenous equilibrium cannot be maintained on a diet consisting of gelatin, carbohydrates, and fats. Proteid food is absolutely essential to the reconstruction of the proteid molecule. Gelatin is one of the proteid-like substances whose food value is comparable to that of carbohydrates and fats, as the following experiments will prove: On a diet of 500 grams of meat, without any gelatin, the subject lost nitrogen to the equivalent of 22 grams of proteid, but when 200 grams of gelatin were added the subject gained 54 grams. In another experiment, when the diet consisted of 2,000 grams of meat without gelatin, the gain was the equivalent of 30 grams of proteid, but when 200 grams of gelatin were added the gain became 376 grams. The lack of real proteid food value is proven by still a third experiment in which the diet consisted at first of 200 grams each of meat and of gelatin; here the gain was the equivalent of 25 grams of proteid, but, when the meat was omitted and the gelatin alone given, there was a loss of 118 grams. In these cases gelatin did not take the place of proteid in any sense, but rather saved it from oxidation as a source of energy. The proteid was so protected that, instead of being used up, it helped to form tissue and increased the body weight. Gelatin, therefore, saves proteid material for constructive processes.

Formation of Urea. The nitrogenous fraction of the proteid molecule is in the end converted largely into urea and is excreted from the body in that form, as described in the chapter on Excretion. The method of formation of urea, as well as the place where this occurs, has given rise to great controversy, while the intermediate products between proteids and urea have not as yet been fully determined. We can state with certainty that urea is not formed in the kidneys, since it is not only found in the blood of the renal artery, but it accumulates in the blood if the kidneys are diseased or removed and the separation of the urine is interfered with. Circulation of blood through the kidney does not result in the formation of more urea than is present in the blood to begin with.

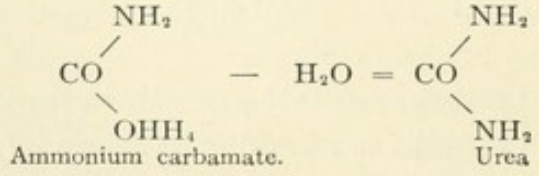
There are a number of experiments that prove that urea is formed in the liver. The power of the liver cells to form urea is shown by the increase of

urea in the blood leaving an isolated living liver through which an artificial circulation is kept up. When ammonium carbamate and other ammonium salts are added to the blood, the urea increases more rapidly and to a greater extent. This change occurs even when the living hepatic tissue is chopped up and simply mixed with the ammonium compounds in a beaker.

If blood from a well-fed animal be circulated through the isolated liver, there is a distinct increase in the amount of urea it contains. On the other hand, if the blood be from a fasting animal there is little or no increase of urea. Evidently, then, the blood from a well-fed animal contains something which the liver cells are capable of transforming into urea. And, finally, if the liver be removed and the animal kept alive, as has been done by Pawlow, there is a marked diminution in the quantity of urea in the urine. The power of the liver to form urea is thus demonstrated. The question which now presents itself is, what is this antecedent substance or substances?

It has already been indicated that urea follows closely the amount of proteid taken with the food, hence we must look directly to the nitrogenous fraction of proteid cleavage as the final source of urea. While the different steps in the process of cleavage, probably hydrolytic (Folin), are yet very obscure, still it is believed that proteids are first broken down to an ammonia stage and then again built up into urea by the liver. It is now believed that *ammonium carbamate* is at least one true antecedent of urea.

In these experiments the liver is first shut out of the general circulation by an Eck's fistula connecting the portal vein with the vena cava. This operation cuts off the chief blood supply of the liver, viz., the portal blood, but it leaves the small hepatic artery with its oxygen supply to the liver. When animals survive this operation it is found that they can live only when fed very carefully on a mixed diet from which proteids are almost entirely eliminated, and that, if the food contain an excess of proteids, convulsions ensue with fatal termination. Investigation of the composition of the urine and of the blood, with the Eck's fistula, shows that the end product of proteid metabolism is represented by ammonium carbamate and that there is a considerable decrease in urea. If ammonium carbamate is injected into the blood of normal animals in a larger quantity than the liver can dispose of, death ensues, following convulsions of the same nature as those produced by an excess of proteid food in the animals operated on. Ammonium carbamate is shown to be, in part at least, the direct antecedent of urea; it is also shown to be a toxic substance which may cause death by accumulating in excess. The reaction by which the liver changes it to the inert form of urea is as follows:



The steps by which absorbed proteids are changed to ammonium carbamate, etc., are as yet undecided. According to one view, while still in the circulating medium, they are metabolized by direct contact with the living bioplasm of the tissues; according to another, they must first be incorporated into the substance of the body tissues and then changed. The intermediate steps occur chiefly in the intestinal tract and in muscle tissue, and there is good reason to suppose that some of the steps are represented by various extractives which are formed in these regions. These substances probably break down into carbon dioxide, ammonia, and amido-acids, and are then built up by synthetic processes into ammonium carbamate. Another possible antecedent is ammonium lactate; this is derived from the lactic acid which is produced in large quantities in the muscles. The elimination of urea is increased very slightly by muscular activity. But there is no direct relationship between the amount of work done and the amount of nitrogen excreted as urea.

There is experimental evidence to show that while the liver produces the major part of the urea eliminated, other organs or tissues are capable of forming it to a limited degree.

Formation of Uric Acid. The relations which uric acid and urea bear to each other in different animals, as we have seen, is still obscure. The fact that they exist together in the same urine makes it seem probable that they have different origins. The entire replacement of one by the other, as of urea by uric acid in the urine of birds, serpents, and many insects, and of uric acid by urea, in the urine of the feline tribe of mammals, shows their close relationship. But although it is true that one molecule of uric acid is capable of splitting up into two molecules of urea and one of mes-oxalic acid, this is not evidence that uric acid is an antecedent of urea in the nitrogenous metabolism of the body. The chemical structure of the uric acid shows it has a nucleus of purin, and therefore is a close relative of adenin, guanin, hypoxanthin, xanthin, theobromin, caffein, etc. The nucleins on cleavage yield members of this group, hence may be looked to as the primary source of uric acid in man. Uric acid, according to Chittenden, has a double origin—endogenous from nuclear metabolism, and exogenous from metabolism of foods rich in nuclear and other purin compounds. In man, at least, the uric acid is to be ascribed to these two sources.

Operative experiments on birds tend to show that the final step in uric-acid formation takes place chiefly in the liver, for on the removal of this organ other nitrogenous compounds, *i.e.*, lactates, accumulate in the blood.

Hippuric Acid, Creatinin, etc. The hippuric acid found in the urine is derived in part from some constituents of vegetable diet, though man has no hippuric acid, as such, in his food, nor, commonly, any benzoic acid that might be converted into it. It is derived in part from the natural disintegration of tissues, independent of vegetable food. Weismann constantly found

an appreciable quantity, even when living on an exclusively animal diet. Hippuric acid is formed from the union of benzoic acid with glycin ($C_2H_5NO_2 + C_7H_6O_2 = C_9H_9NO_3 + H_2O$), which union takes place under experimental conditions in the kidneys themselves.

The source of the nitrogenous extractives of the urine is chiefly from the metabolism of the nitrogenous foods and tissues, but we are unable to say whether these nitrogenous bodies have merely resisted further decomposition into urea, or whether they are the representatives of the decomposition of special tissues, or of special forms of metabolism of the tissues. There is, however, one exception, and that is in the case of *creatinin*. This represents not only the creatinin which enters the body in ordinary flesh food, but is a nitrogenous waste which Folin regards as a measure of muscle metabolism. The creatinin eliminated is almost a constant quantity in a given individual, irrespective of the quantity of proteid in the diet. Koch has attempted to trace a quantitative relation of creatinin excretion to lecithin in the food.

THE METABOLISM OF FATS.

Fats, with carbohydrates, are the direct source of most of the energy manifested by the body, a fact demonstrated by numerous observations.

The Energy Value of Fats in Metabolism. Fats, in comparison with other food principles, are of especial value as sources of energy. They are completely oxidized in the body to carbon dioxide and water, and yield, therefore, as much energy to the body as they yield upon oxidation outside the body. The energy equivalent of one gram of fat is 9.3 large Calories, more than twice that of starch or of proteid, which in the body yield only 4.1 Calories each per gram.

A study of the elimination of nitrogen and of carbon during fasting shows that the fats contribute to energy formation for many days. This is illustrated by the following computation by Voit:

METABOLISM IN A DOG DURING FASTING. (VOIT.)

LOSS PER KILOGRAM OF LIVE WEIGHT.	Proteids in Grams.	Fats in Grams.	Total Weight.
Second day	2.21	2.62	32.87
Fifth day	1.13	3.25	31.67
Eighth day	0.96	3.25	30.54

The amount of fat metabolized is sharply influenced by the amount and kind of other food. For example, if the amount of fat metabolized per day in fasting is first determined, then a ration of proteid given for a few days, followed by a second fasting period, it will be found that the metabolism of

body fat is sharply increased in the second period, due to the stimulating influence of the proteid.

This is demonstrated by the following determination of Rubner:

Food of Dog. (Rubner.)	Nitrogen of Food.	Nitrogen Excreted.	Body Fat Metabolized.
0.....	0.	4.38	49.33
415 grams lean meat.....	14.11	13.72	25.44 average
0.....	0.	2.80	79.94
760 grams lean meat.....	25.16	20.63	30.73 first two days

The fat of the ordinary daily diet is absorbed into the blood and no doubt contributes directly to oxidation processes. Just the steps in this oxidation process cannot at present be given. If the fat food is insufficient, then the body store is drawn upon; if in excess, then it is stored in the body.

Source of the Body Fat. Excess of fat in the food can be stored as fat in the body. This fact is demonstrated by Voit, Hoffmann, Rubner, and others. Rubner states that 82 to 92 per cent of the fat excess can be stored. The fat stored is of the same kind given in the food, even though the usual fat of the animal is different. The melting point of dog's fat is about 20° C., but by feeding an excess of mutton fat the melting point has been raised to 40° C. The subcutaneous fat of pigs subjected to this experiment is more or less fluid according to the melting point of the fat fed.

The body fat can also be derived from carbohydrate food, a fact which the practices of the stock feeder and dairyman constantly verify. Two experiments will present the matter more vividly than pages of description.

Gain in Fat of a Pig Fed on Rice. (Meissl and Strohmer.)

Pig Weight.	Rice Fed Daily.	Fat in Food.	Proteid in Food.	Proteid Gain.	Carbon Gain.	Net Gain in Carbon.
140 kgm.	2 kgm.	5.3 gm.	104 gm.	38 gm.	289 gm.	269 gm.

It is obvious that the 5.3 grams of fat and the 66 grams of proteid cannot account for the carbon retained, and one must look to the carbohydrate as the source of the fat.

Jordan placed a Jersey cow on a feed of hay and grain from which the fat was extracted. The cow in 95 days assimilated 5.7 pounds of fat, increased 47 pounds in weight, and produced 62.9 pounds of fat in the milk. The nitrogen excreted was the equivalent of 33.3 pounds of proteid. The non-nitrogenous moiety of the proteid, if its carbon had all gone into fat, could not have produced over 17 pounds. Summarized, this experiment

shows conclusively that fat is synthesized from carbohydrate. It requires about 2.7 grams of dextrose to form 1 gram of fat, and this condensation takes place with the formation of carbon dioxide and water and the liberation of about 15 per cent of the available heat of oxidation.

Persistent excess of carbohydrate food produces an accumulation of fat, which may not only be an inconvenience causing obesity, but may interfere with the proper nutrition of muscles, produce a feebleness of the action of the heart, and other troubles.

The formation of fat from proteid is discussed on page 410.

Obesity is a condition of excessive storage of fats. In many of these cases there is persistent storing of fat in the presence of a diet of low energy value and with considerable physical labor. It seems that such persons must have a very economic protoplasmic metabolism, a biological factor that lacks sufficient explanation.

THE METABOLISM OF CARBOHYDRATES.

Energy Value. The nutritive function of carbohydrates in the body is to serve as a source of energy. They are oxidized, with the ultimate production of carbon dioxide and water, and must liberate the same amount of energy as when burned outside the body, *i.e.*, 4.1 Calories. A given weight of dextrose, therefore, furnishes much less energy than a corresponding weight of fat.

Carbohydrates are strictly energy-formers and may be regarded as the immediate source of the energy of oxidations, while fats are reserves drawn on only after the carbohydrates are used up. Dextrose is a constant constituent of the blood to the extent of about 1 to 1.5 per cent. When this percentage is increased above 2.5, the dextrose is either stored as glycogen, *i.e.*, in the case of the portal blood during the absorption of a carbohydrate meal, or eliminated by the kidney, *i.e.*, in diabetes.

The Formation of Glycogen—Glycogenesis. The important fact that the liver normally forms sugar, or a substance readily convertible into it, was discovered by Claude Bernard in the following way: He fed a dog for seven days with food containing a large quantity of sugar and starch; and, as might be expected, found sugar in both the portal and hepatic blood. But when the dog was fed with meat only, to his surprise, sugar was still found in the blood of the hepatic veins. Repeated experiments gave invariably the same result. No excess of sugar was found in the portal vein under a meat diet, if care was taken to prevent reflux of blood from the hepatic venous system. Bernard found sugar also in the substance of the liver. It thus seemed certain that the liver formed sugar even when, from the absence of saccharine and amyloid matters in the food, none could be brought directly to it from the stomach or intestines.

Bernard subsequently found that a liver removed from the body, and from which all sugar had been completely washed away by injecting a stream of water through its blood-vessels, contained sugar in abundance after the lapse of a few hours. This post-mortem production of sugar was a fact which could be explained only on the supposition that the liver contained a substance readily convertible into sugar. This theory was proved correct by the discovery of a substance in the liver allied to starch, termed *glycogen.*

Bernard's brilliant researches led him to announce the theory that the carbohydrate which is periodically absorbed in large amount is stored in the liver only to be reconverted to dextrose and discharged back into the blood stream whenever the percentage falls below a certain level. He regarded the liver as a storehouse which regulated the blood dextrose to a constant level. This is the glycogenic function of the liver.

Source of Glycogen. The greatest amount of glycogen is produced by the liver upon a diet of starch or sugar, but a certain quantity is, or at least may be, produced upon a proteid diet. The glycogen, when stored in the liver cells, may readily be demonstrated in sections of liver containing it by its reaction (red or port-wine color) with iodine, and, moreover, when the hardened sections are so treated that the glycogen is dissolved out, the protoplasm of the cell is so vacuolated as to appear little more than a framework. There is no doubt that in the liver of a hibernating frog the amount of glycogen stored up in the liver cells is very considerable.

AVERAGE AMOUNT OF GLYCOGEN IN THE LIVER OF DOGS UNDER VARIOUS DIETS. (PAVY.)

Diet.	Amount of Glycogen in the Liver.
Flesh food	7.19 per cent
Flesh food with sugar	14.5 "
Vegetable diet, *i.e.*, potatoes with bread or barley meal	17.23 "

The dependence of the formation of glycogen on the kind of food taken is also shown by the following results, obtained by the same experimenter:

AVERAGE QUANTITY OF GLYCOGEN FOUND IN THE LIVER OF RABBITS AFTER FASTING, AND AFTER A DIET OF STARCH AND SUGAR RESPECTIVELY.

After three days' fasting	Practically absent
" diet of starch and grape-sugar	15.4 per cent
" " cane-sugar	16.9 "

Glycogen is also formed from fats in diabetes, but there is no clear proof that fats increase the amount of glycogen in the cells. Glycerin injected into the alimentary canal may also increase the glycogen of the liver. The diet most favorable to the production of a large amount of glycogen is a mixed diet containing a large amount of carbohydrate, but with some proteid.

Glycogen is stored in other organs of the body. Of these the muscles are deserving of special mention. The amount of glycogen in the muscles

of young animals is often considerable. The placenta is also a storehouse of glycogen.

The Destination of Glycogen. The chief theories concerning the use of glycogen in the organism are advanced by Bernard and by Pavy. The former considers glycogen as a reserve supply of carbohydrate. Whenever the glycogen of the blood is reduced below the normal level, *i.e.*, about 0.1 to 0.15 per cent, there is a conversion of glycogen into sugar. The sugar enters the blood and passes to the tissues where its oxidation is a source of energy. Pavy considers glycogen to be a stage in the synthesis of carbohydrate to fat and proteid. Bernard's theory is more generally accepted. It explains more satisfactorily why the sugar content of the blood is so constant. The conversion of glycogen to sugar takes place by the action of an intracellular ferment in the glycogenic cells. Such an enzyme has been isolated for the liver. It is this enzyme that converts the liver glycogen to dextrose after death, and which is destroyed by boiling in the usual process of isolating glycogen.

Glycosuria. Sugar may be present to excess not only in the hepatic veins, but in the systemic blood. When such is the case, the sugar is excreted by the kidneys, and appears in variable quantities in the urine. This condition is known as glycosuria.

Glycosuria may be experimentally produced by puncture of the medulla oblongata in the region of the vaso-motor center, puncture diabetes. The better fed the animal, the larger is the amount of sugar found in the urine following this operation. In the case of a starving animal no sugar appears. It is, therefore, highly probable that the sugar comes from the hepatic glycogen, since in the one case glycogen is in excess, and in the other it is almost absent. The nature of the influence is uncertain. This influence may be exercised in dilating the hepatic vessels, or possibly may be exerted on the liver cells themselves.

Many other circumstances will cause glycosuria. It has been observed after the administration of various drugs, *e.g.*, strychnine; phloridzin, a glucoside, and its derivative phloretin, which is not a glucoside; morphine; adrenalin; nitrite of amyl, etc.; after the injection of curari, poisoning with carbonic-oxide gas, the inhalation of ether, chloroform, etc., the injection of oxygenated blood into the portal venous system. Glycosuria has been observed in man after injuries to the head and in the course of various diseases. In such cases the glycosuria appears to be due either to some abnormal activity of the liver cells themselves or to an interference with the normal metabolism of the carbohydrate group. In this latter case it is possible that the usual complete oxidation of carbohydrate is interfered with.

The well-known disease, diabetes mellitus, in which a large quantity of sugar is persistently excreted daily with the urine, has, doubtless, some close relation to the normal functions of the pancreas. The nature of the relation-

ship has not yet been determined, though some recent experiments seem to be pertinent, page 431.

Mineral Matters, Water, etc. The chief mineral constituents of the foods are sodium, potassium, calcium, magnesium, and iron, together with chlorine, sulphur, and phosphorus. The inorganic substances are not a source of heat. They may supply a certain amount of energy, as osmotic energy, but this is of no significance as compared with their influence on the metabolism of organic substances. An animal fed on a normal food deprived of the mineral constituents survives only a few weeks at most.

The amount of mineral matter in the tissues of the human body, exclusive of the skeletal parts, is about one per cent. It is safe to say that this is chiefly in complex organic combination in the body. The daily quantity excreted is about twenty to thirty grains. This quantity enters the body in the food, chiefly in combination with complex compounds. It is a question as to what per cent of inorganic salts, like the calcium, the phosphates, and the iron, is available when taken into the body in inorganic form.

We have discussed in previous chapters the rôle of certain salts in their influence on metabolism; for example, of sodium, potassium, calcium, iron, etc. Foods like milk and eggs are especially rich in calcium and phosphorus, and are particularly desirable for young children, the former for its influence on the growth of the skeleton, the latter for the same reason and as a stimulator of growth of protoplasm in general. Lack of mineral constituents, especially calcium compounds, in food shows its influence on metabolism in the disease known as rickets.

Investigations are in progress at the present time which may demonstrate more fully the specific influence of phosphorus on animal nutrition and on growth. Tunnicliff has just demonstrated that an increase of the phos-

NUTRITION EXPERIMENT IN FIVE-MONTHS-OLD PIGS. (E. B. FORBES.)

Rations.	Per cent Gain in Live Weight in 60 Days' Feeding.	Per cent Gain in Certain Tissues Corresponding to One per Cent Gain in Live Weight.		
		Psoas Muscle.	Ash of Humerus.	Thickness of Back Fat.
Hominy; blood flour; bran extract. (Phosphorus mostly as phytin)	69.1	.81	.59	.64
Hominy; blood flour; bone flour. (Phosphorus mostly as tricalcic phosphate)	61.0	.61	.72	.82
Hominy; blood flour. (Low phosphorus ration)	41.6	.72	.08	1.04

phorus content of the food of children, if given in complex organic form, increases the efficiency of the metabolism of nitrogen by as much as 10 per cent. If given to children as calcium phosphate it has no beneficial influence in this regard. Forbes, in his experiments on the nutrition of pigs, shows that the individuals fed with food to which phosphorus was added, as ground fresh bone, grew larger and stronger skeletons.

PERCENTAGE OF PHOSPHORIC ACID (P_2O_5) IN SOME FRESH FOODS. (QUOTED FROM GIRARD, BY HUTCHINSON, IN "FOOD AND DIETETICS.")

Vegetable.	Per cent.	Animal.	Per cent.
Carrot	0.036	Pork	0.160
Turnip	0.058	Milk	0.220
Cabbage	0.089	Beef	0.285
Potato	0.140	Eggs	0.337
Chestnuts	0.200	White cheese	0.374
Barley meal	0.230	Mutton	0.425

Salts in the body not only take part in the reactions themselves, but they stimulate in other substances reactions that are of incalculable benefit to the body.

The necessity for the taking of water in order to balance the daily excretion, is sufficiently obvious. Man will live only a few days if deprived of water.

Effects of Deprivation of Food. The animal body deprived of all food dies from starvation in the course of a variable time. The length of time that any given animal will live in such a condition depends upon many circumstances, the chief of which are the nature and activity of the metabolism of its tissues.

The effect of starvation on the lower animals is, first of all, as might be expected, a loss of weight. The loss is greatest at the beginning of the deprivation period, but afterward decreases to a level from which it does not vary much day by day until death ensues. Chossat found that the ultimate proportional loss in different animals experimented on was almost exactly the same, death occurring when the body had lost forty per cent of its original weight. Different parts of the body lose weight in very different proportions. The following most noteworthy losses are taken, in round numbers, from the table given by Chossat:

	Per Cent.		Per Cent.
Fat	93	Liver	52
Blood	75	Muscles	43
Spleen	71	Nervous tissues	2
Pancreas	64		

These figures are in practical agreement with those of later experimenters. They show that the chief losses are sustained by the adipose tissue, the muscles and glands.

The effect of starvation on the *temperature* of the various animals experimented on by Chossat was very distinct. For some time the variation in the daily temperature was more marked than its absolute and continuous diminution, the daily fluctuation amounting to 3° C. instead of 0.5° to 1° C., as in health. The temperature fell very rapidly a short time before death,

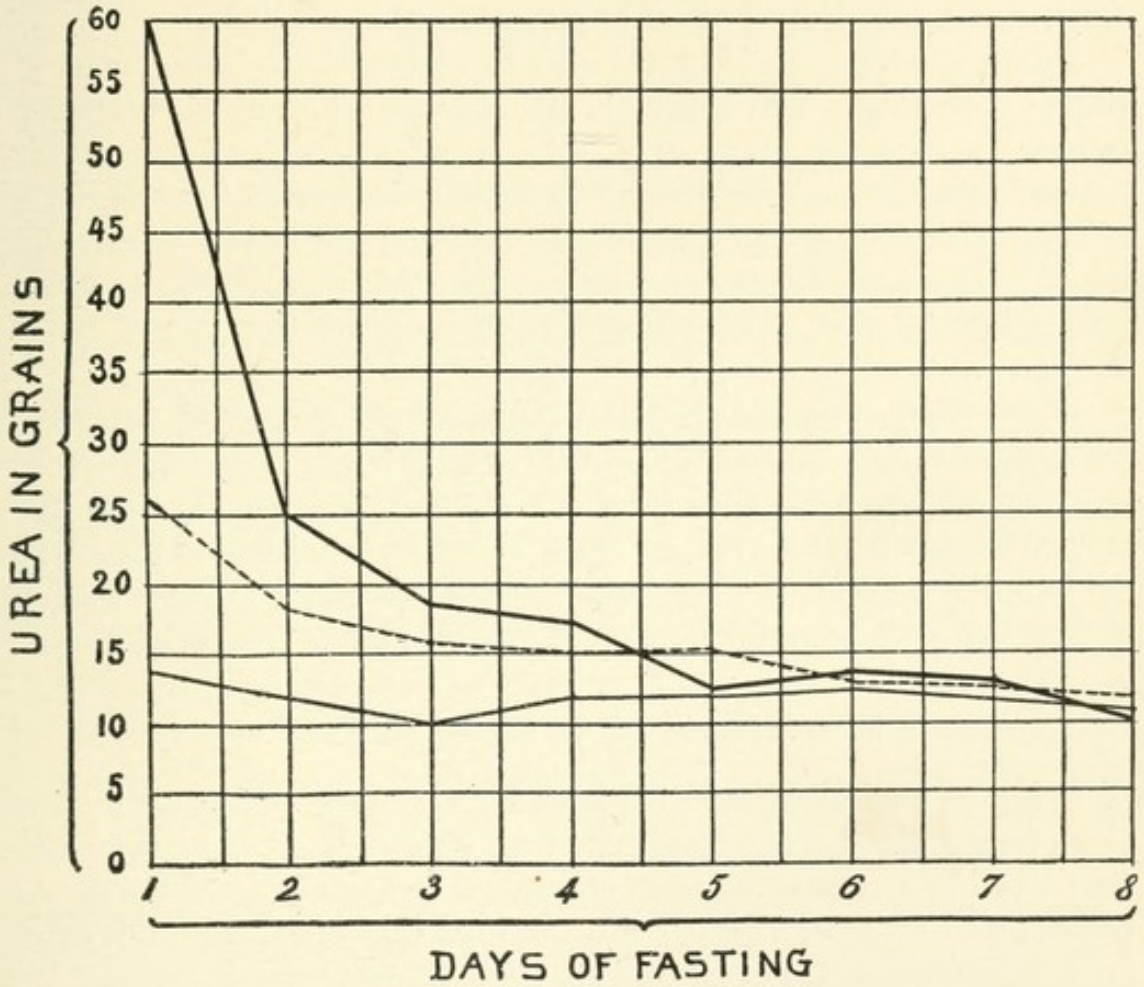


FIG. 310.—The Elimination of Urea by Dogs during Fasting. (Voit.)
Following 2,500 grams of meat in the food.
" 1,500 " " " " " "
" minimal amount of proteid in the food.

and death ensued when the loss had amounted to about 16.2° C. It has been often said, and with truth, that death by starvation is really death from want of heat. The effect of the application of external warmth to animals cold and dying from starvation is more effectual in reviving them than the administration of food.

The symptoms produced by starvation in the human subject are hunger, accompanied, or it may be replaced, by pain, referred to the region of the stomach; insatiable thirst; sleeplessness; general weakness, and emaciation. The exhalations both from the lungs and from the skin are fetid, indicating the tendency to decomposition which belongs to badly nourished tissues; and death

occurs often with symptoms of nervous disorder, delirium, or convulsions. Death commonly occurs within from six to ten days after total deprivation of food. This period may be considerably prolonged by taking a very small quantity of food, or even by water alone. The cases so frequently related of survival after many days or even some weeks of abstinence have been due either to the last-mentioned circumstances, or to other no less effectual conditions which prevented the loss of heat and moisture.

During the starvation period the excretions diminish. The urea, as representing the nitrogen, falls quickly in amount, reaches a minimum where it remains constant for several days, then finally falls rapidly immediately before death. The sulphates and phosphates undergo much the same type of reduction. The carbon dioxide given out and the oxygen taken in diminish. The feces diminish, as well as the bile. It is highly probable that the greater part of the nitrogen represents the loss of weight of the muscles.

In starvation, then, we see that the only income consists of water and the inspired oxygen. The whole of the energy of the body given out in the form of heat and mechanical labor is obtained at the expense of its own tissues, there being as a result a constant drain of the nitrogen and carbon, not to mention the other elements of which the tissues are composed. It is obvious that such a condition cannot be endured for any length of time.

REQUISITES OF A NORMAL DIET.

It will be understood from the preceding discussion that it is necessary that a normal diet should be made up of the various classes of foods in sufficient quantity to supply the same amounts of carbon and nitrogen that are gotten rid of by the excreta. No doubt these desiderata may be satisfied by many combinations of foods, and it would be unreasonable to expect the diet of every adult to be the same. The age, sex, strength, and circumstances surrounding each individual must ultimately determine what he takes as food. A dinner of bread and cheese with an onion contains all the requisites for a meal, but such diet would be suitable only for those possessing strong digestive powers. It is a well-known fact that the diet of the continental nations differs from that of our own country, and that of cold from that of hot climates, but the same principle underlies all, viz., the replacement of the losses of the body in the most convenient and economical way possible. Any one in active work requires more food than one at rest, and growing children require less food than, but a different variety, from adult men and women.

The chief diet-scales which have been drawn up with the object of supplying the proximate principles in the required proportions are given in the table below:

STANDARD DIETARIES.

AUTHOR.	Proteid.	Fat.	Carbohydrate.	Calories.
Voit	118 grams	56 grams	500 grams	3,055
Rubner	127 "	52 "	509 "	3,092
Moleschott	130 "	40 "	550 "	3,160
Munk	105 "	56 "	500 "	3,022
Wolff	125 "	35 "	540 "	3,030
Playfair	119 "	51 "	531 "	3,140
Atwater	125 "	125 "	450 "	3,520
Average	121 grams	59 grams	510 grams	3,135

The basis of these diets is to supply the necessary proteid nitrogen first of all, and, second, to supply enough potential energy to balance the energy expended per day.

The amount of the excreted carbon and nitrogen is not always the same. It has been proved possible, for example, to subsist on 9 or 10 grams of nitrogen and 200 grams of carbon per diem, the ordinary diet for needle-women in London, and the average of the cotton operatives in Lancashire during the famine, 1862. The amount of these elements excreted falls to figures corresponding to such an income. Of course, upon such a diet the metabolism is low, and persistent physical weakness must be the result, probably from insufficient carbon. The 9 or 10 grams of nitrogen in such a semi-starvation diet would be equivalent to 58.5 to 65 grams of proteid, whereas the amount of proteid in some diets may be as high as 150 and more grams per day. Chittenden's nutritional experiments, so often referred to in these pages, have proven that adult men can subsist in nitrogenous equilibrium, and do vigorous work and maintain good health, on a proteid diet below that given in the above example, *i.e.*, on 4 to 10 grams of nitrogen. In such diets a plentiful supply of carbohydrates is permitted.

Not only the proteids but also the fats may vary. The amount may be as low as 35 grams and as high as 125 grams. The carbohydrates may vary from 200 grams to 500 grams and upward. Sometimes, with a small proportion of fat, the carbohydrate may be correspondingly increased to make up the necessary carbon. A useful table, after Payen, will help to show in

TABLE OF PERCENTAGES OF N AND C IN THE FOLLOWING SUBSTANCES.

	N.	C.		N.	C.
Beef (without bone)	3.	11.	Oatmeal	1.95	44.
Roast beef	3.528	17.76	Bread	1.	28.
Eggs	1.9	13.5	Potatoes	0.33	11.
Cow's milk	0.66	8.	Eels	2.	30.
Cheese	2 to 7	35. to 71	Mackerel	3.74	19.26
Beans	4.5	42.	Sardines in oil	6.	29.
Lentils	4.1	48.	Butter	0.64	83.

what ways it is possible to obtain the requisite amount of nitrogen and carbon from the most common food stuffs.

In order to obtain the amount of proteid present from the proportion of nitrogen, multiply by 6.25.

From these data, or from the composition of foods on page 298, it is possible to form various diet-scales which shall supply the needs of different conditions of growth and decay of the body. Assuming that the average amount of carbon and nitrogen required is about 300 grams and 20 grams respectively, this may be obtained as follows:

	N.	C.
340 grams (12 oz. or ¾ lb. avoirdupois) lean uncooked meat*..	10 grams	37 grams
906 " (32 oz. or 2 lbs. avoirdupois) bread.....	9 "	252 "
	19 grams	289 grams

But this diet is not the usual one; a certain proportion of the carbon is usually supplied as butter, or bacon, and so if 90 grams of butter or bacon be used it would supply about 72 grams of carbon, and the carbohydrate would be diminished nearly one-third; but the nitrogen would also be diminished from 9 grams to 6 grams. It would be necessary to supply some extra nitrogenous principle, which might be done by the addition of eggs, milk, cheese, beans, or of any of the food-stuffs already enumerated at page 298 *et seq.*, as supplying nitrogenous food chiefly. For example, 56 grams (2 oz.) cheese contain, on an average, 3 grams of nitrogen and 20 grams of carbon; or 28 grams cheese, containing 1.5 grams of nitrogen and about 10 grams carbon, together with 225 grams potatoes and 225 grams carrots, supplying about 1 gram of nitrogen and 35 grams of carbon, may be added. The diet would then read as follows:

			N.	C.
340 grams	lean uncooked meat.....		10.0 grams	37 grams
600 "	bread		6.0 "	168 "
90 "	butter.....		0.5 "	72 "
28 "	cheese		1.5 "	10 "
225 "	potatoes.. }	.....	1.0 "	35 "
225 "	carrots... }			
			19.0 grams	322 grams

The 30 grams of salts necessary to replenish the daily loss by excretion in the urine are contained in the meat 16 grams, the bread 12 grams, and vegetables about 4 grams.

The fluids should consist of about 2,500 to 2,800 grams, and might be given as water, with or without tea, coffee, or cacao, which are chiefly stimulants.

The Energy Requirements of the Body. The food must not only make up for the substances eliminated from the body but must also supply the potential energy of heat and motion set free in the living body. The

*As meat loses 23 to 34 per cent in cooking, the weight of cooked meat would be proportionately less.

amount of heat is measured in terms of calories, or more often in large calories. The work energy may be expressed in gram-centimeters or in kilogrammeters. The heat-unit calories may be transferred into the work-unit gramcentimeters by multiplying by .042, and the converse.

The source of the heat and work energy which is produced in the body is from the metabolic changes of the tissues, the chief part of which is of the nature of oxidation, since it may be supposed that the oxygen of the atmosphere taken into the system is ultimately combined with carbon and hydrogen. Any change, indeed, which occurs in the protoplasm of the tissues, resulting in an exhibition of its function, is attended by the evolution of heat and the formation of carbon dioxide and water. The more active the changes the greater is the heat produced. But, in order that the protoplasm may perform its function, the waste of its own destructive metabolism must be repaired by the due supply of food material to be built up in some way into the protoplasmic molecule. Food is therefore necessary for the production of heat. In the tissues, as we have several times remarked, two processes are continually going on: the building up of the protoplasm from the food, anabolism, which is not accompanied by the evolution of heat, and the oxidation of the protoplastic materials, catabolism, resulting in the production of energy, by which heat is set free. It is not necessary to assume that the combustion processes, indeed, are as simple as the bare statement of the fact might seem to indicate. But complicated as the various stages may be, the ultimate result is as simple as in ordinary combustion outside the body, and the products are the same.

This theory, that the maintenance of the temperature of the living body depends on continual chemical change, chiefly by oxidation of combustible materials in the tissues or by the tissues, has long been established. The quantity of carbon and hydrogen supplied as food, which, in a given time, unites in the body with oxygen, is sufficient to account for the amount of heat generated in the animal within the same period, page 406; an amount capable of maintaining the temperature of the body at from 36.8° to 38.7° C., notwithstanding a large loss by radiation and evaporation. This estimation depends upon the chemical axiom that when a body undergoes a chemical change the amount of energy set free is the same, supposing the resulting products are the same, whether the change takes place suddenly or gradually. If a certain number of grams of different substances are introduced as food, and if they undergo complete oxidation, the amount of kinetic energy, as shown in the amount of heat and mechanical work, is the same as would be developed if the same bodies were completely oxidized outside the body. If one gram of fat be taken into the body and is completely oxidized, resulting in the production of a definite amount of carbon dioxide and water, it may be supposed to have produced the same amount of heat as it would have produced outside the body. In the case of proteid food it is a little different,

since it is never completely oxidized within the body, but may be supposed to give rise to a definite amount of urea, not a completely oxidized body. In this case the gram of proteid may be considered to perform the same amount of heat as the proteid would outside the body minus the amount which would be obtained from the complete oxidation of the resulting urea.

The actual amount of heat produced per diem has been experimentally ascertained in the case of man and animals by the aid of an apparatus, the calorimeter. An animal is enclosed in a metal cage completely contained in a second cage containing water. Air is led into and out of the inner box by means of metal tubes so arranged that the inlet tubes maintain a constant temperature and the outlet tubes pass through water between the two chambers. The heat given out by the animal warms the water in the outside box, and may be estimated by the rise of its temperature, the amount of which is known. At the same time the carbon dioxide output is measured.

The amount of heat evolved by the oxidation of various food stuffs has been carefully measured by numerous observers; the figures calculated by Rubner being perhaps most satisfactory, which are:

HEAT VALUE TO THE BODY.

1 gram carbohydrate	4.1	Calories
1 " fat	9.3	"
1 " proteid	4.1	"

One gram of dry proteid has a total heat value of 5.754 (Rubner), hence it is obvious that proteid is not completely oxidized by the body. Each gram of proteid yields at least one-third of a gram of urea, which has a heat value of 2.5 Calories per gram.

Atwater has checked the energy value of the foods actually consumed against the actual liberation of heat and work energy of the human body. He finds a wonderfully close agreement both for periods of rest and for periods of work. Atwater's estimate for the energy needs of man are summarized as follows:

Man without muscular work	2,700	Calories
" with light muscular work	3,000	"
" " moderate muscular work	3,500	"
" " severe " "	4,500	"

The daily output of energy for the adult man is, according to McKendrick, as follows:

	Kilogrammeters.	Calories.
Work of heart per day	88,000	
Work of respiratory muscle	14,000	
Eight hours' active work	213,344	
	315,334 or	743
Amount of heat produced in 24 hours	1,582,700 or	3,724
	1,898,034 or	4,467

This estimate is relatively high for ordinary activity as determined by Atwater and others. It is indeed more energy than the standard diets in the table given on page 423 will yield to the body. For example, Voit's diet yields 3,055 Calories, and the average of the table is only 3,125 Calories.

THE INFLUENCE OF THE DUCTLESS GLANDS ON METABOLISM.

A further question to be considered is the relationship between the metabolism of one tissue and the products of the metabolism of other tissues. The metabolism of one tissue may produce products, proteid or otherwise, which when taken up by the blood and carried to other tissues supply exactly what is necessary for their complete anabolism.

The physiology of the internal secretions has revealed a number of such influences that are best explained on the assumption of the presence of special products.

The Thyroid. The thyroid gland is situated in the neck. It consists of two lobes, one on each side of the trachea, extending upward to the

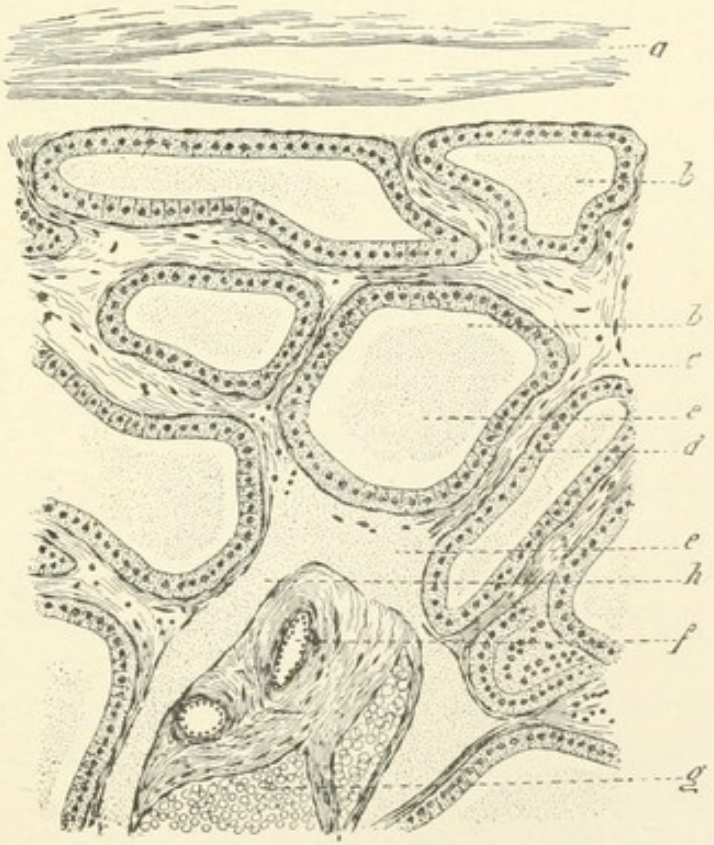


FIG. 311.—Part of a Section of the Human Thyroid. *a*, Fibrous capsule; *b*, thyroid vesicles filled with, *e*, colloid substances; *c*, supporting fibrous tissue; *d*, short columnar cells lining vesicles; *f*, arteries; *g*, veins filled with blood; *h*, lymphatic vessel filled with colloid substance. (S. K. Alcock.)

thyroid cartilage, covering its inferior cornu and part of its body; these lobes are connected across the middle line by a middle lobe or isthmus. The

thyroid is covered by the muscles of the neck. It is highly vascular, and varies in size in different individuals.

The gland is encased in a thin transparent layer of dense areolar tissue, free from fat, containing elastic fibers.

These gland vesicles are each lined with a single layer of cubical cells and are filled with transparent nucleo-albuminous colloid material.

Accessory Thyroids. The accessory and the parathyroids possess the structure of the thyroid and apparently perform the same function. The accessory thyroids undergo hypertrophy when the thyroid has been removed.

The colloid material which is formed within the thyroid vesicles, and is believed to be their secretion, finally ruptures through their walls into the lymph channels and thus gains entrance to the circulation. The secretion of the thyroid falls into the class known as internal secretions, and exerts a profound influence upon the metabolic processes of the body, probably through its influence on the central nervous system. Complete extirpation of the thyroid, at least in some animals, produces death, preceded by a group of characteristic symptoms. In man and the monkey the symptoms after removal come on slowly and resemble the disease known in man as *myxedema*.

This disease is known definitely to be due to disease of the thyroid, whereby its function is interfered with. Moreover, if a piece of thyroid of sufficient size be grafted into an animal from which the glands have been removed, and the graft takes, the symptoms of thyroid removal are lessened in intensity or disappear altogether. Thyroid feeding or the administration of thyroid extracts relieves the symptoms of the disease myxedema.

The above facts show that the thyroid gland must perform some important function in the animal economy, and it is believed that this is accomplished by virtue of its internal secretion. The colloid material of the gland has been submitted to much chemical study, and a substance called *iodothyrin* has been isolated as its active principle. Baumann and Roos state that iodothyrin exists in the gland in combination with proteid bodies. Iodothyrin relieves the symptoms of thyroid removal much to the same extent as thyroid feeding. It is a very resistant substance, and is not injured by the action of the gastric juice or by boiling with 10 per cent sulphuric acid for a long time.

The Suprarenal Capsules or Adrenals. These are two flattened, more or less triangular or cocked-hat shaped bodies, resting by their lower border upon the upper border of the kidneys.

The gland tissue proper consists of an outside firmer cortical portion, and an inside soft dark medullary portion, figure 312.

The adrenals are very abundantly supplied with nerves, chiefly composed of medullated fibers. These fibers are derived from the solar and renal plexuses and the vagi, but the method of their termination is unknown.

A vast amount of information has been given concerning the function of

the suprarenal capsules within the last few years by the researches of Schäfer and Oliver, Zyboulski, Abel, and others. Brown-Séquard, it is true, showed by experiment as early as 1856 that removal of the suprarenals is followed by the death of the animal, but his experiments were repeated by others who

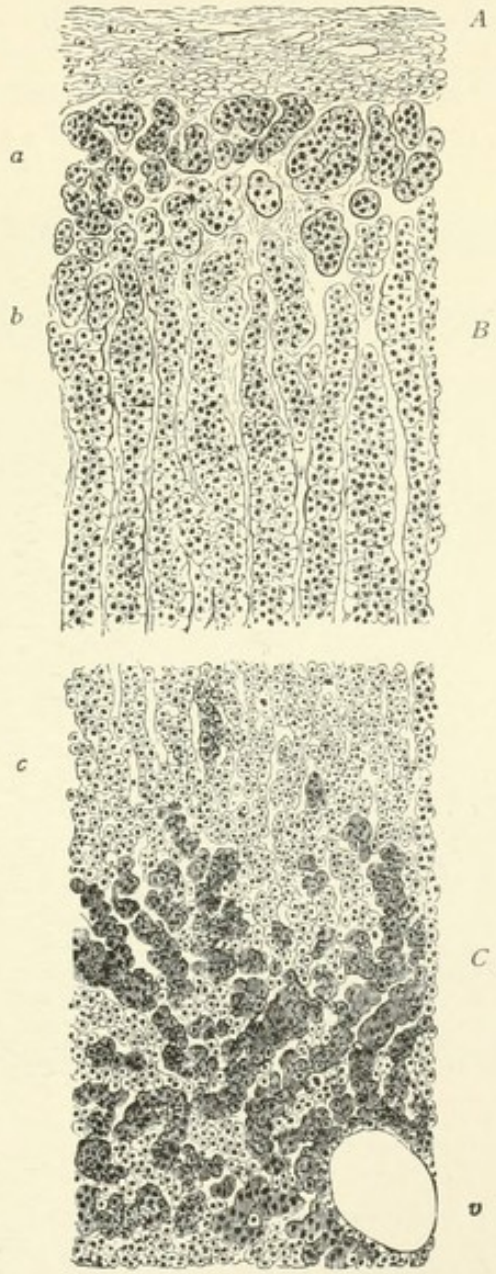


FIG. 312.—Vertical Section of Adrenal. *A*, Capsule; *B*, cortex; *C*, medulla; *a*, glomerular zone; *b*, fascicular zone; *c*, reticular zone; *v*, vein in medulla. (Merkel-Henle.)

did not obtain the same results; and it was concluded that the suprarenal capsules had no function, or at least that their function was not known. Death was preceded in the case of Brown-Séquard's animals by symptoms somewhat analogous to those of the disease of man known as Addison's disease. The failures to produce symptoms after attempted removal of the glands have probably resulted from incomplete removal or the presence of

accessory bodies. Accessory suprarenal capsules are commonly present in some animals and are sometimes found in man. Further, if one gland is removed, the other hypertrophies. The experiments of all recent observers confirm the original experiments of Brown-Séquard. The presence of the suprarenal capsules is essential to life.

Schäffer and Oliver found that injections of suprarenal extract produced marked effects upon the muscular layer of the arteries, the muscular tissue of the heart, and the skeletal muscles. The muscular layer of the arteries is markedly contracted, causing vaso-constriction and a rise of blood pressure.

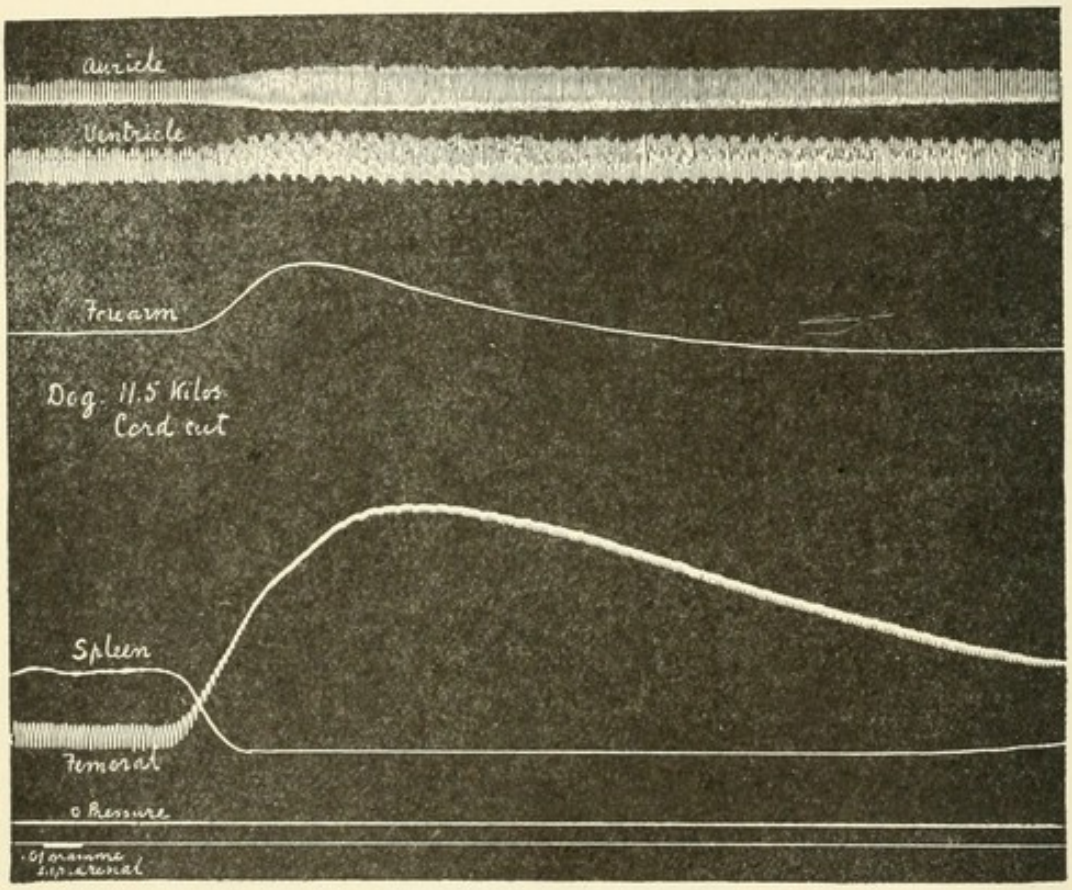


FIG. 313.—Injection of Suprarenal Extract. Effect upon the heart, limb, spleen, and blood pressure, after section of cord and vagi. (Reduced to one-half.) (Schäffer.)

When the heart is freed from nervous control its contractions are increased both in force and frequency, still further raising blood pressure. If the vagi are undisturbed the heart beats more slowly, showing an increase of vagus tone due to stimulation of the vagus center in the medulla. The contraction of the skeletal muscles in response to a single stimulus is increased.

Very small doses of suprarenal extract are sufficient to produce marked effects. Thus Schäffer states that less than $\frac{1}{13000}$ gram ($\frac{1}{800}$ grain) of the desiccated gland is sufficient to produce an effect upon the heart and arteries of an adult man.

It is a curious fact that only extracts of the *medullary portion* of the gland

are active. It has been further shown, by Christiani and others, that if only small portions of the medulla remain, the animal operated upon survives; while if all the medullary substance be removed, even though large portions of the cortex remain, the animal invariably dies.

Abel has succeeded in separating the blood-pressure-raising constituent of the extract, and calls it *epinephrin*, $C_{10}H_{13}NO_3$ $\frac{1}{2}H_2O$. Adrenalin was isolated by Takamine and assigned the formula $C_9H_{13}NO_3$. The hydrochloride salt is prepared commercially and produces all the vascular effects assigned to the gland.

Destruction of the suprarenal capsules through disease in man results in the production of a group of symptoms known as Addison's disease. The administration of suprarenal extract to these cases sometimes results beneficially, but not so uniformly as thyroid feeding does in myxedema.

Dreyer has given evidence that the products of this gland are discharged into the blood of the adrenal vein in increased quantity on splanchnic stimulation.

This gland furnishes, on the whole, very conclusive evidence of the presence of an internal secretion that is absolutely necessary to the normal metabolism of other organs.

The Pituitary Body. This body is a small reddish-gray mass, occupying the sella turcica of the sphenoid bone.

It consists of two lobes, a small posterior one of nervous tissue, and an anterior one resembling the thyroid in structure. The gland spaces are oval, nearly round at the periphery, spherical toward the center of the organ, and are filled with nucleated cells of various sizes and shapes not unlike ganglion cells.

The function of the pituitary body has not yet been fully established. It has been supposed that the pituitary body has a function associated with that of the thyroid. On the other hand, tumors or other disease of the pituitary body have been found after death in association with a disease known as acromegaly, in which the bones and soft parts undergo great hypertrophy. Howell has found that extracts of the glandular lobe are inactive, but that extracts of the infundibular lobe, when injected into the circulation, produce marked rise of blood pressure, increase of vagus tonic inhibition, and an augmentation of the heart's force.

The Internal Secretion of the Pancreas. Minkowski and von Mering have shown that total extirpation of the pancreas is followed in all cases by the appearance of sugar in the urine in the course of a few hours. The amount of sugar which appears is considerable, from 5 to 10 per cent. This experimental disease is accompanied by an increase in the quantity of urine and by abnormal thirst and appetite, and proves fatal in fifteen days or less. These results are obtained only when the entire gland or more than nine-tenths of it have been removed. If one-tenth or more of the gland be left

behind, sugar appears in the urine when carbohydrates are eaten, but not otherwise. Nor is it necessary that the remaining portion of the gland be in its normal situation. Successful grafts of pancreas under the skin of the abdomen or elsewhere will prevent the appearance of sugar in the urine and the other symptoms. If, however, the graft be subsequently removed, the sugar in the urine and the other symptoms reappear, and the experimental disease proceeds to a rapidly fatal issue.

The symptoms produced by total extirpation of the pancreas do not depend upon the loss of the pancreatic juice proper to the organism. This secretion may be diverted from the intestine through a pancreatic fistula without the production of diabetes. Moreover, Hédon and Thiroloix have rendered the acini of the gland functionally inactive, and ultimately destroyed them, by the injection of paraffin or other substances into the duct of Wirsung, without the supervention of diabetes.

These experiments have shown that the ordinary secreting cells degenerate and the islands of Langerhans increase in size, leading to the conclusion that these are the structures that produce a special internal secretion which influences or controls carbohydrate metabolism in the body. Whether this hypothetical substance is necessary to the dehydration and synthesis of dextrose in the body or whether it is necessary to the complete oxidation of carbohydrate is at present a matter of inference.

The Reproductive Glands. The ovary and the testes are undoubtedly concerned with metabolism in the body. It has been shown repeatedly that extracts of the testes when injected into the system lead to increased vigor, both of the muscular and of the nervous systems. Ergograms show an increase in muscular power. Spermin isolated from the testes is claimed by its discoverer to produce the beneficial effects described. The removal of the testes in domestic animals is followed by an entire change in the character of the development of the animal, especially in the so-called secondary sexual characters. Such animals show less vigor and muscular power.

The removal of the ovaries in women, through surgical operation, has resulted in very marked nervous symptoms. These symptoms are reduced or entirely disappear on grafting a portion of the gland, and the disturbed menstruation following ovariotomy becomes regular again. Experiments by Loewy and Richter indicate that oxidations in the body are greatly increased on feeding ovarian extract to ovariotomized animals.

There are other organs whose function is still obscure but in which the indirect evidence points to an influence on metabolism at one stage or another of the existence of the animal body. Enough has been given here to show that the interrelation of the organs is extremely complex in so far as the metabolism is concerned. It is not enough simply to know the foods and their composition. The whole complex of intermediary metabolism and their influence must constantly be taken into consideration.

CHAPTER XII

ANIMAL HEAT

HEAT is produced by the metabolism of the tissues of the body. In man and in such animals as are called warm-blooded, *i.e.*, only mammals and birds, there is an average body temperature which is maintained with only slight variations in spite of changes in their environment. The possible variations above and below this average are comparatively slight. The average temperature in all mammals and birds is not the same, for, as we shall see, the average temperature of man is 37° C. (98.6° F.), in some birds it is as high as 44° C., while in the wolf it is said to be under 36° C.

The average temperature of the human body in those internal parts which are most easily accessible, as the mouth and rectum, is from 36.9° to 37.4° C. (98.5° to 99.5° F.). In different parts of the external surface of the human body the temperature varies only to the extent of one or two degrees centigrade, when all are alike protected from cooling influences; and the difference which under these circumstances exists depends chiefly upon the different degrees of blood supply. In the axilla and in the groin, the most convenient situations, under ordinary circumstances, for examination by the thermometer, the average temperature is 37° C. (98.6° F.). In different internal parts, the variation is one or two degrees; those parts and organs being warmest which contain most blood, and in which there occurs the greatest amount of chemical change, *e.g.*, the muscles and the glands. The temperature is highest when they are in a condition of activity. Those tissues which subserve only a mechanical function and are the seat of least active circulation and chemical change are the coolest. These differences of temperature, however, are actually but slight, on account of the provisions which exist for maintaining uniformity of temperature in different parts.

The average temperature of a healthy body varies somewhat according to age, sex, time of day, climate, etc. The mean temperature is said to be slightly higher, 0.5° C., in young children and in old persons than in adults. It is perhaps very slightly higher in women than in men, in warm climates than in cold, in winter than in summer. It varies slightly at different times in the day, especially during sleep when metabolism is at a low ebb.

Heat-producing Organs. Heat is liberated in the body wherever oxidative metabolism takes place. Of all the tissues of the body *muscular tissue* is conspicuous for its mass and for its activity. It is evidently the great

heat-producing tissue. The manifestation of muscular energy is always accompanied by the evolution of heat and the production of carbon dioxide. This production of carbon dioxide goes on while the muscles are in mechanical rest, only in a less degree than that which is noticed during muscular activity, and so it is certain that an active catabolism is going on in resting as well as in contracting muscles. This catabolism is a source of much heat, and so the total amount of heat produced in the muscular tissues per day must be very great. It has been calculated that, even neglecting the heat produced by the quiet catabolism of muscular tissue, the amount of heat generated by muscular activity would supply the principal part of the total heat produced within the body. The *heart*, as a special muscle, deserves particular mention since it is in constant vigorous activity. All its energy is ultimately converted into heat, accounting for about 5 per cent of the total heat of the body. The *secreting glands*, and principally the liver as being the largest and most active, come next to the muscles and heart as heat-producing tissues. It has been found by experiment that the blood leaving the glands is considerably warmer than that entering them. The metabolism in the glands is very active; and the more active the catabolism, the greater the heat produced.

It must be remembered, however, that although the organs mentioned are the chief heat-producing parts of the body, all living tissues contribute their quota, and this in direct proportion to their activity. The blood itself is also the seat of catabolism, and, therefore, of the production of heat; but the share which it takes in this respect, apart from the tissues in which it circulates, is very inconsiderable.

Regulation of the Temperature of the Human Body. The average temperature of the body is maintained under different conditions of external circumstance by mechanisms which permit of (1) variation in the loss of heat, and (2) variations in the production of heat. In healthy warm-blooded animals the loss and gain of heat are so nearly balanced one by the other that, under all ordinary circumstances, a uniform temperature, within a degree or two, is preserved.

Variation in the Loss of Heat. The loss of heat from the human body is principally regulated by the amount given off by radiation and conduction from its surface, by means of the constant evaporation of water from the same part, heat being thus rendered latent, and to a much less degree by loss from the air-passages. In each act of respiration, heat is lost to a greater or less extent according to the temperature of the atmosphere; unless indeed the temperature of the surrounding air exceeds that of the blood. We must remember, too, that all food and drink which enter the body at a lower temperature abstract a small measure of heat; while the urine and feces which leave the body at about its own temperature are also means by which a certain small amount of heat is lost.

Heat Lost from the Surface of the Body. By far the most impor-

tant loss of heat from the body, probably 90 per cent and upward of the whole amount, is that which takes place by radiation, conduction, and the evaporation of moisture from the skin. The actual figures are as follows: For every 100 calories of heat produced, 2.6 are lost in heating the food and drink; 2.6 in heating the air inspired; 14.7 in evaporation; and 80.1 by radiation and conduction. The means by which the skin is able to act as one of the most important organs for regulating the temperature of the blood, are, 1, that it offers a large surface for radiation, conduction, and evaporation; 2, that it contains a large but adjustable amount of blood, and the quantity of blood is greater under those circumstances which demand a loss of heat from the body, and *vice versa ;* 3, that it contains the sweat glands, which discharge a quantity of moisture to be evaporated from its surface.

The circumstance which directly determines the quantity of blood in the skin is that which governs the supply of blood to all the tissues and organs of the body, namely, the power of the vaso-motor nerves to cause a greater or less tension of the muscular element in the walls of the arteries, and, in correspondence with this, a lessening or increase of the caliber of the vessel, accompanied by a less or greater current of blood. A warm or hot atmosphere so acts on the sensory nerves of the skin as to lead them reflexly to cause a relaxation of the muscular fiber of the blood-vessels; as a result, the skin becomes full-blooded, relatively hot, and moist from sweating; and much heat is lost. With a low temperature, on the other hand, the blood-vessels shrink, and with the consequently diminished blood supply, the skin becomes pale, cold, and dry, an effect produced through the vascular centers in the medulla and spinal cord.

The activity of the sweat glands of the skin is also regulated reflexly through the sweat centers. The increased blood supply just described is favorable to increased production of sweat by the sweat glands. Thus, by means of the self-regulation the skin becomes the most important of the means by which the temperature of the body is regulated.

The relative loss of heat by the means given, *i.e.*, radiation, conduction, and evaporation, will depend on two factors: first, the relative temperature of the body to the surrounding air; and, second, the humidity of the air. If the atmospheric temperature is the same as that of the body, of course there will be no loss of heat by radiation and convection; if the air temperature is higher, there will be an actual gain. When the humidity of the air is great, there will be reduced evaporation of perspiration and consequent diminished heat loss by this means. If we assume a moisture-saturated air at the body temperature, then heat loss becomes impossible and the temperature of the body will rise. This is why a hot moist climate is so oppressive, while a hot but dry atmosphere is readily borne by the human body. The increased evaporation of perspiration compensates for the decreased loss by radiation and convection.

Many examples may be given of *the power which the body possesses of resisting the effects of a high temperature*, in virtue of evaporation from the skin. Blagden and others supported a temperature varying between 92° to 100° C. (198°–212° F.) in dry air for several minutes; and in a subsequent experiment he remained eight minutes in a temperature of 126.5° C. (260° F.). "The workmen of Sir F. Chantrey were accustomed to enter a furnace, in which his molds were dried, while the floor was red-hot, and a thermometer in the air stood at 177.8° C. (350° F.), and Chabert, the fire-king, was in the habit of entering an oven the temperature of which was from 205°–315° C. (400°–600° F.)." (Carpenter.)

But such heats are not tolerable when the air is moist as well as hot, so as to prevent evaporation from the body. C. James states that in the vapor baths of Nero he was almost suffocated in a temperature of 44.5° C. (112° F.), while in the caves of Testaccio, in which the air is dry, he was but little incommoded by a temperature of 80° C. (176° F.). In the former, evaporation from the skin was impossible; in the latter it was abundant, and the layer of vapor which would rise from all the surface of the body would, by its very slowly conducting power, defend it for a time from the full action of the external heat.

Man is able by suitable clothing to increase or to diminish the amount of heat lost by the skin. There are baths and other means which man and animals instinctively adopt for lowering the temperature when necessary.

Although under any ordinary circumstances the external application of cold only temporarily depresses the temperature to a slight extent, it is otherwise in cases of high temperature in fever. In these cases a cool bath may reduce the temperature several degrees, and the effect so produced lasts in some cases for many hours.

Extreme heat and cold produces effects too powerful, either in raising or lowering the heat of the body, to be controlled by the proper regulating apparatus. Walther found that rabbits and dogs kept exposed to a hot sun, reached a temperature of 46° C. (114.8° F.), and then died. Cases of sunstroke furnish us with several examples in the case of man; for it would seem that here death ensues chiefly or solely from elevation of the temperature.

The effect of mere loss of bodily temperature in man is less well known than the effect of heat. From experiments by Walther it appears that rabbits can be cooled down to 8.9° C. (48° F.) before they die, if artificial respiration be kept up. Cooled down to 17.8° C. (64° F.), they cannot recover unless external warmth be applied together with the employment of artificial respiration. Rabbits not cooled below 25° C. (77° F.) recover by external warmth alone.

Loss of Heat from the Lungs. The lungs and air-passages are very inferior to the skin as a means for lowering the temperature. In giving heat to the air breathed, the lungs stand next to the skin in importance. As a regulating power, the inferiority is very marked. The air which is expelled from the lungs leaves the body at about the temperature of the blood, and is always saturated with moisture. No inverse proportion, therefore, exists, as in the case of the skin, between the loss of heat by radiation and conduction, on the one hand, and by evaporation, on the other. The colder the air and the drier, for example, the greater will be the loss in all ways. Neither is the quantity of blood which is exposed to the cooling influence of

the air diminished or increased in the lungs, so far as is known, in accordance with any need in relation to temperature. It is true that by varying the number and depth of the respirations, the quantity of heat given off by the lungs may be made to vary also for a few minutes. But the respiratory passages, while they must be considered important means by which heat is lost, are altogether subordinate, in the power of actively regulating the temperature.

The loss of heat used to warm foods is an obvious method of expenditure of heat which may be resorted to, especially in certain fevers. The loss of heat by the excreta discharged from the body at a high temperature must be of little use as a means of regulating the temperature, since the amount so lost must be capable of little variation.

Variation in the Production of Heat. It may seem to have been assumed, in the foregoing pages, that the only regulating apparatus for temperature required by the human body is one that shall, more or less, produce a cooling effect; as if the amount of heat produced were always, therefore, in excess of that which is required. Such an assumption would be incorrect. The body has the power of regulating the production of heat, as well as its loss.

The production of heat in the body is apparently different for each animal; *i.e.*, the absolute amount of heat set free by different animals in a given period varies. Each individual has his own coefficient of heat production. From all that has been said on the subject it will be seen that the amount of heat for all practical purposes depends upon the metabolism of the tissues of the body; everything, therefore, which increases that metabolism will increase the heat production; so, therefore, the absolute amount of heat produced by a large animal, having a larger amount of tissues in which metabolism may go on, will be, *cæteris paribus*, greater than that of a small animal. But the activity of the tissue change in a small animal may be greater than in a large one, as measured per kilo of body-weight, and naturally no strict line can be drawn between the two.

HEAT PRODUCED PER KILO PER HOUR. (MUNK.)

Man	1.5	calories
Dog (large)	1.7	"
Dog (small)	3.8	"
Guinea-pig	7.5	"
Rat	11.3	"
Mouse	19.0	"
Sparrow	35.5	"

The ingestion of foods increases the metabolism of the tissues. As one would expect, the rate of heat production is found by experiment upon the dog to be increased after a meal, reaching its height about six hours after a meal.

It has also been experimentally ascertained that the rate of heat production varies with the kind of food taken: for example, if sugar be added to the meal of meat given to the dog, the height of maximum production is reached. It is often said that the various nations have found by experience what food is most suitable for the climate in which they live, and that such experience can be trusted to regulate the quantity consumed. Although there have been no very conclusive experiments to prove the view, yet it is a matter of general observation that in northern climates and in colder seasons the quantity of food taken is greater than in warmer climates or in warmer seasons. Moreover, the kind of food is different. For example, persons living in the colder climates require much fat in order to produce the requisite amount of heat.

Influence of the Nervous System on Heat Production. The influence of the nervous system in modifying the production of heat must be very important, as upon the nervous influence depends the amount of the metabolism of the tissues. The experiments and observations which best illustrate it are those showing, first, that, when the supply of nerves to a part is cut off, the temperature of that part falls below its ordinary degree after a time; and, second, that when there is severe injury to or removal of the nervous centers the temperature of the body rapidly falls, even though artificial respiration be performed, the circulation maintained, and to all appearance the ordinary conditions for chemical changes in the body be completely maintained.

There is a heat-regulating nervous apparatus closely comparable to that which regulates the secretion of saliva or of sweat, by means of which the production of heat in the warm-blooded animals is increased or diminished, as occasion requires. This apparatus probably consists of a center or centers in the brain which may be reflexly stimulated, as, for example, by impulses from the skin, and which act through special nerves supplied to the various tissues. The evidence upon which the existence of this regulating apparatus depends is the marked effect in the increase of the oxygen consumed by a warm-blooded animal when exposed to cold, and the corresponding increase in the output of carbon dioxide, indicating that there is an increase of the metabolism and so an increased production of heat under such circumstances, and not a mere diminution of the amount of heat lost by the skin, etc. A cold-blooded animal reacts very differently to exposure to cold; instead of increasing the metabolism as in the case of the warm-blooded animal, cold diminishes the metabolism of its tissues. It is clear, therefore, that in warm-blooded animals there is some apparatus not possessed by cold-blooded animals, which counteracts the effects of cold. In warm-blooded animals poisoned by curara, or in which section of the medulla has been done, it has been found that this regulating apparatus is no longer in action, and under such circumstances no difference appears to exist between such animals and those

which are naturally cold-blooded. Warmth increases their temperature, and cold lowers it, and with this there is, of course, evidence of diminished metabolism.

The explanation of these experiments is that in such animals the connection between the skin and the muscles through the nervous chain, such as a thermotaxic nervous apparatus might be supposed to afford, is broken either at the termination of the nerves in the muscles (curara) or at the sectioned point of the bulb.

The position of these hypothetical centers is a matter of some difference of opinion. It has been demonstrated that stimulation of certain parts of the brain may, among other symptoms, produce increased metabolism of the tissues with increased output of carbon dioxide and a raised temperature: the parts of which this may be asserted are parts of the corpus striatum and of the optic thalamus. The general thermogenic centers are probably closely associated with the motor centers of the cord and brain stem. The thermoregulative centers are the nuclei in the corpus striatum and optic thalamus. Assuming a constant or tonic activity of the thermogenic regulative centers, it is easy to understand the fall of temperature on their destruction or on the destruction of the nerve path to the active tissues.

Experimental observations, such as have been made upon animals, receive confirmation from the observations on patients who suffer from fever or pyrexia; in them the temperature of the body may be raised several degrees, as we have already pointed out. This increase of temperature might, of course, be due to diminished loss of heat from the skin, but this, although a factor, is not the only cause. The amount of oxygen taken in and the amount of carbon dioxide given out are both increased, and with this there must be increased metabolism of the tissues, and particularly of the muscular tissues, since at the same time the amount of urea in the urine is increased. Every one is familiar with the rapid wasting which is such a characteristic of high fever; it must indicate not only too rapid metabolism of the body, but also insufficient time for the tissues to build themselves up. In fever, then, there may be supposed to be some interference with the ordinary reflex channel by which the skin is able to communicate to the nervous system the necessity of an increased or diminished production of heat in the muscles and other tissues. In consequence of this, and in spite of the condition of increased heat of the body, both at the surface and in the deeper tissues, the production of heat goes on at an abnormal rate. It is not certain whether the pathological condition is one which stimulates the thermogenic center by means of which the metabolism of the tissues is increased, or whether the normal reflexes which ordinarily inhibit the activity of the center when the temperature rises fail to bring about their usual reaction. The first is the probable explanation of the high fevers of certain toxemias.

CHAPTER XIII

MUSCLE-NERVE PHYSIOLOGY

CHEMICAL COMPOSITION OF MUSCLE

Muscle Plasma. The principal substance which can be extracted from muscle, when examined after death, is the proteid body, *myosin*, some of the reactions of which have been already discussed. This body appears to bear somewhat the same relation to the living muscle that fibrin does to the living blood, since the coagulation of muscle after death is due to the formation of myosin. Thus, if coagulation be delayed by removing the muscles immediately that an animal is killed, and rapidly cooling them to a temperature below 0° C. before the muscles themselves lose their irritability, it is possible to express from them a viscid fluid of slightly alkaline reaction, called *muscle plasma* (Kühne, Halliburton). Muscle plasma, if exposed to the ordinary temperature of the air (or more quickly at 37° to 40° C.), undergoes coagulation much in the same way as does blood plasma under similar circumstances when separated from the blood-corpuscles at a low temperature. The appearances presented by the fluid during the process are also very similar to the phenomena of blood-clotting, viz., first of all an increased viscidity appears on the surface of the fluid, and at the sides of the containing vessel, which gradually extends throughout the entire mass, until a fine transparent clot is obtained. In the course of some hours the clot begins to contract, and to squeeze out of its meshes a fluid corresponding to blood serum. In the course of coagulation, therefore, muscle plasma separates into *muscle clot* and *muscle serum*. The muscle clot contains the substance myosin. It differs from fibrin in being easily soluble in a 2 per cent solution of hydrochloric acid, and in a 10 per cent solution of sodium chloride. It is insoluble in distilled water, and its solutions coagulate on application of heat; in short, it is a *globulin*. During the process of clotting the reaction of the fluid becomes distinctly acid.

The coagulation of muscle plasma can be prevented not only by cold, but also, as Halliburton has shown, by the presence of neutral salts in certain proportions; for example, of sodium chloride, magnesium sulphate, or sodium sulphate. It will be remembered that this is also the case with blood plasma. Dilution of the salted muscle plasma will produce its slow coagulation, which is prevented by the presence of the neutral salts in strong solution.

It is highly probable that the formation of muscle clot is due to the presence of a ferment, *myosin ferment*. The antecedent myosin in living muscle has received the name of *myosinogen*, in the same way that the fibrin-forming element in the blood is called fibrinogen. Myosinogen is, however, a mixture of two globulins which coagulate at the temperatures 47° C. and 56° C. respectively.

Myosin may also be obtained from dead muscle after all the blood, fat, and fibrous tissue, and substances soluble in water have been removed by subjecting it to a 10 per cent solution of sodium chloride, or a 5 per cent solution of magnesium sulphate, or a 10 to 15 per cent solution of ammonium chloride, filtering and allowing the filtrate to drop into a large quantity of water. The myosin separates out as a white flocculent precipitate. The precipitate gives all the globulin reactions.

Muscle Serum. Muscle serum is acid in reaction, and almost colorless. It contains three proteid bodies, viz.: A *globulin* (*myoglobulin*), which can be precipitated by saturation with sodium chloride, or magnesium sulphate, and which can be coagulated at 63° C.; *serum albumin* (*myo-albumin*), which coagulates at 73° C., but is not precipitated by saturation with either of those salts; and *myo-albumose*, which is neither precipitated by heat nor by saturation with sodium chloride or magnesium sulphate, but may be precipitated by saturation with ammonium sulphate. It is closely connected with, even if it is not itself, myosin ferment. Neither casein nor peptone has been found by Halliburton in muscle extracts. In extracts of muscles, especially of red muscles, there is a certain amount of *hemoglobin*, and also of a pigment special to muscle, called by McMunn *myo-hematin*, which has a spectrum quite distinct from hemoglobin, viz., a narrow band just before D, two very narrow bands between D and E, and two other faint bands, near E b, and between E and F close to F.

Other Constituents of Muscle. In addition to muscle *ferments*, already mentioned, muscle extracts contain certain small amounts of *pepsin* and *fibrin ferment* and an *amylolytic ferment*.

Certain *acids* are also present, particularly sarco-lactic, as well as traces of acetic and formic.

Of carbohydrates, *glycogen* and *glucose* (or maltose) and *inosite* are present. Glycogen is present in considerable amount, especially in the muscles of well-nourished young animals. The glycogen is converted to maltose in the muscles on standing some hours after death.

Nitrogenous crystalline bodies, such as *creatin*, *creatinin*, *xanthin*, *hypoxanthin*, or carnin, *taurin*, *urea* in very small amount, *uric acid*, and *inosinic acid*, are all found on extracting dead muscle.

Salts of potassium and calcium are present in muscle, the chief of which is *potassium phosphate*.

THE PROPERTIES OF LIVING MUSCLE.

Elasticity. Muscle has a certain amount of elasticity during rest. It admits of being considerably stretched, but returns readily and completely to its normal condition. In the living body the muscles are always stretched somewhat beyond their natural length, they are always in a condition of slight tension; an arrangement which enables the whole force of the contraction to be utilized in approximating the points of attachment. If the extensibility of a given muscle be measured by adding to it equal increments of weight, it will be found that the extension or stretching is considerable at first, but that the amount decreases with each additional weight. If the figures obtained be plotted on coordinate paper, a curve approaching a parabola is obtained, whereas a steel spring is perfectly elastic and gives a straight line. When the weights are removed from a stretched muscle, one by one, the muscle regains its original length, though slowly. Extreme fatigue greatly decreases the elasticity, while an increase of temperature increases it.

Cardiac muscle and smooth muscle both manifest elasticity in the same manner as skeletal muscle. In fact the elasticity of the arterioles is chiefly due to the smooth muscle in their walls, a fact that is of great importance in the adaptability of the circulatory apparatus. The flexibility of the stomach, the urinary bladder, etc., is traceable to the same property of their muscular walls.

Contractility and Irritability of Muscle. The property of muscular tissue by which its peculiar functions are exercised is its *contractility*, which is excited by all kinds of stimuli applied either directly to the muscles or indirectly to them through the medium of their motor nerves. The property of the muscle which enables it to respond to a stimulus is called its *irritability*. This property, although commonly brought into action through the nervous system, is inherent in the muscular tissue. This is proven: 1, By the fact that contractility is manifested in a muscle which is isolated from the influence of the nervous system by division of the nerves supplying it so long as the natural tissue of the muscle is duly nourished. 2, It is manifested in a portion of muscular fiber in which, under the microscope, no nerve fiber can be traced. 3, Substances such as *curara*, which paralyze the nerve endings in muscles, do not at all diminish the irritability of the muscle itself. 4, When a muscle is fatigued, a local stimulation is followed by a contraction of a small part of the fiber in the immediate vicinity, without any regard to the distribution of nerve fibers.

Forms of Stimuli for Muscle or Nerve. The power of contraction in voluntary muscles is normally called forth in the body by nerve impulses which reach the muscles over the motor nerves. But a muscle will respond to stimuli of various kinds, and these stimuli may be applied directly to the muscle or indirectly to the nerve supplying it. There are distinct advantages,

however, in applying the stimulus to the nerve, as it is more convenient, as well as more potent. The stimuli which will produce contraction in a muscle are:

1. *Mechanical Stimuli.* A blow, pinch, prick of the muscle or its nerve will produce a contraction, repeated on the repetition of the stimulus. If applied to the same point for a number of times such stimuli will soon destroy the irritability of the preparation.

2. *Thermal Stimuli.* If a needle or glass rod be heated and applied to a muscle or its nerve, the muscle will contract. A temperature of over 45° C. will cause the muscles of a frog to pass into a condition known as *heat rigor.* The sudden change of temperature acts as a stimulus.

3. *Chemical Stimuli.* A great variety of chemical substances will excite the contraction of muscles, some substances being more potent in irritating the muscle itself, and other substances having more effect upon the nerve. Of the former may be mentioned dilute acids, salts of certain metals, *e.g.*, zinc, copper, and iron; to the latter belong strong glycerin, strong acids, ammonia, bile salts in strong solution, etc.

4. *Electrical Stimuli.* Any form of electrical current may be employed to stimulate a muscle to contract, but either galvanism or the induced current is usually chosen. For experimental purposes electrical stimuli are most frequently used, as the strength of the stimulus may be conveniently regulated. In order that a stimulus shall be effective, it must have a certain amount of energy and the application to the muscle must have a certain abruptness. For example, a comparatively weak galvanic current suffices to stimulate a muscle to action when suddenly applied in full force. But if the electric current be applied very gradually, a current many times stronger will fail to arouse contraction of a muscle.

Necessary Apparatus used to Produce and Record a Muscle Contraction. Galvanic currents are usually obtained by the employment of a continuous-current cell such as that of Daniell, by which an electrical current which varies but little in intensity is obtained. The cell (figure 314 A) consists of a positive plate of well-amalgamated zinc im-

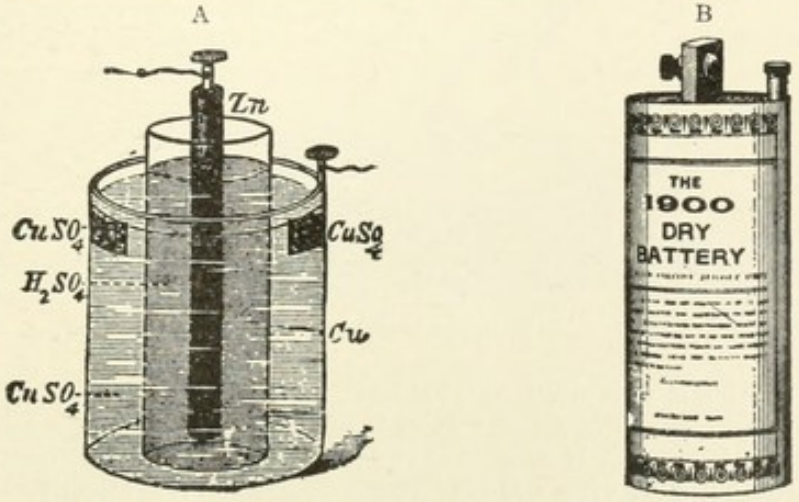


FIG. 314.—Diagram of a Daniell's Cell *A*, Dry Cell *B*.

mersed in a porous cell containing dilute sulphuric acid; and this cell is again contained within a large copper vessel (forming the negative plate) containing a saturated solution of copper sulphate. The electrical current is made continuous by the use of the two fluids in the following manner. The action of the dilute sulphuric acid upon the zinc plate partly dissolves it, and liberates hydrogen, and this gas passes through the porous vessel, and decomposes the copper sulphate into copper and sulphuric acid. The former is deposited upon the copper plate, and the latter passes through the porous vessel to renew the sulphuric

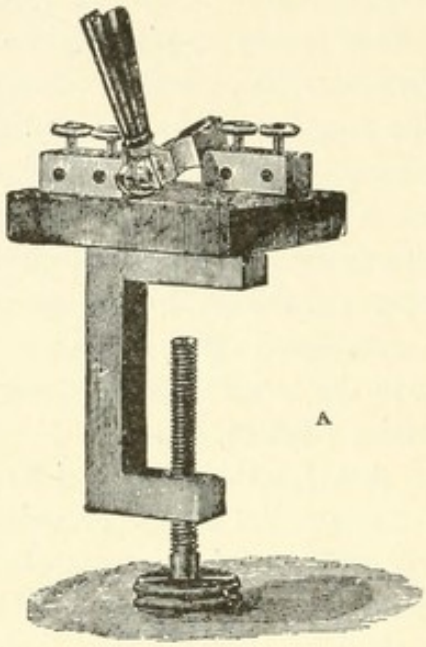


FIG. 315.—Du Bois Reymond's Key.

acid which is being used up. The copper-sulphate solution is renewed by crystals of the salt, which are kept on a little shelf attached to the copper plate and slightly below the level of the solution in the vessel. The current of electricity supplied by this cell will continue without variation for a considerable time. Other cells, such as the dry cell (which, however, is adapted to open-circuit work) may be used in place of Daniell's. The

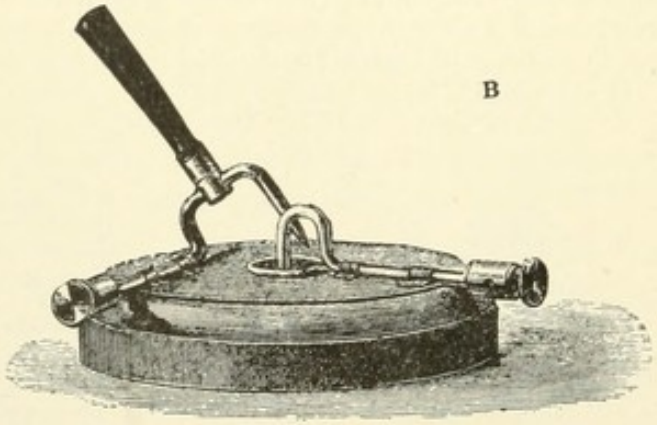


FIG. 316.—Mercury Key.

way in which the apparatus is arranged is to attach wires to the copper and zinc plates, and to bring them to a *key*, connecting the wires of the battery. One often employed is Du Bois Reymond's, figure 315. It consists of two pieces of brass about an inch long, in each of which are two holes for wires and binding-screws, to hold them tightly. These pieces of brass are fixed upon a vulcanite plate to the under surface of which is attached a screw

clamp by which it can be secured to the table. The interval between the pieces of brass can be bridged over by means of a third thinner piece of similar metal fixed by a screw to one of the brass pieces, and capable of movement by a handle at right angles, so as to touch the other piece of brass. If the wires from the battery are brought to the inner binding-screws, and the bridge connects them, the current passes across it and back to the battery. Wires are connected with the outer binding-screws, and the other ends are joined together for about two inches, but, being covered except at their points, are insulated; the uncovered points are about an eighth of an inch apart. These wires are the *electrodes*, and the electrical stimulus is applied to the muscle through them, if they are placed behind its nerve. When the connection between the two brass plates of the key is broken by depressing the handle of the bridge, the key is then said to be opened.

An **induced current** is developed by means of an apparatus called an *induction coil*, and the one most employed for physiological purposes is Du Bois Reymond's, the one seen in figure 317.

Wires from a battery are brought to the two binding-screws, d' and d, a key intervening. These binding-screws are the ends of a coil of coarse covered wire, c, called the primary coil.

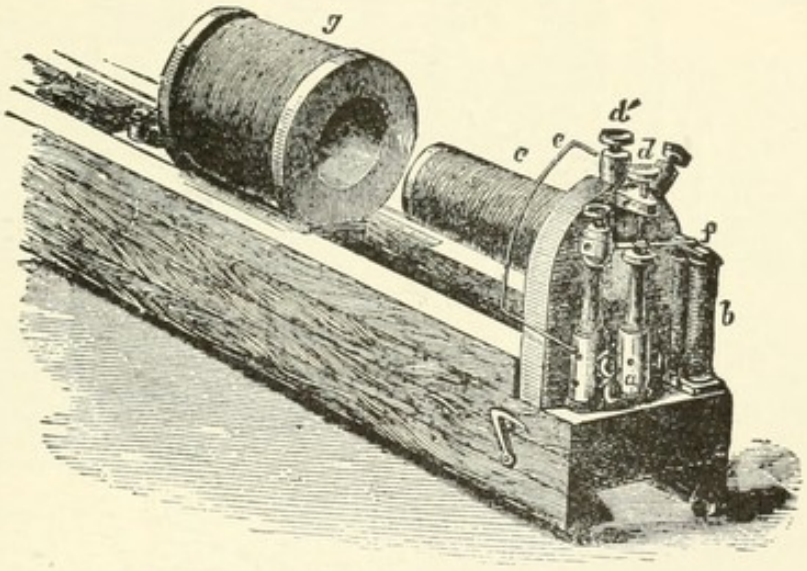


FIG. 317.—Du Bois Reymond's Induction Coil.

The ends of a coil of finer covered wire, g, are attached to two binding-screws to the left of the figure, one only of which is visible. This is the secondary coil, and is capable of being moved nearer to c along a groove and graduated scale. To the binding-screws to the left of g, the wires or electrodes used to stimulate the muscle are attached. If the key in the circuit of wires from the battery to the primary coil (primary circuit) be closed, the current from the battery passes through the primary coil, and across the key to the battery, and continues to pass as long as the key continues closed. At the moment of closure of the key, at the exact instant of the completion of the primary circuit, an instantaneous current of electricity is induced in the secondary coil, g, if it be sufficiently near and in line with the primary coil; and the nearer it is to c, the stronger is the current induced. The current is *only momentary in duration* and does not continue during the whole of the period while the primary circuit is complete. When, however, the primary current is broken by opening the key, a second current, also momentary, is induced in g. The former induced current is called the *making* and the latter the *breaking* shock; the former is in the opposite direction to, and the latter in the same direction as, the primary current.

The induction coil may be used to produce a rapid series of shocks by means of the accessory apparatus at the right of the figure, called the *magnetic interrupter*. If the wires from a battery are connected with the two pillars by the binding-screws, one below c, and the other at a, the course of the current is indicated by the arrows in figure 318. The current passes up the pillar from e, and along the springs if the end of d' is close to the spring,

then to the primary coil *c*, and to wires covering two upright pillars of soft iron, *b*, to the pillar *a*, and out by the wires to the battery. In passing along the wire *b* the soft iron is converted into a magnet, and so attracts the hammer, *f*, of the spring, breaks the connection of the spring with *d'*, and so cuts off the current from the primary coil, and also from the electro-magnet. As the pillars, *b*, are no longer magnetized the spring is released, and the current passes in the first direction, and is in like manner interrupted. At each make and break of the primary current, currents corresponding are induced in the secondary coil. These currents are opposite in direction, but are not equal in intensity, the break shock being greater. In order that the shocks should be nearly equal at the make and break, a wire, figure 318, *e*, connects *e* and *d'*, and the screw *d'* is raised out of reach of the spring, and *d* is raised as in figure 318, so that part of the current always passes through the primary coil and electro-magnet. When the spring touches *d* the current in *b* is diminished,

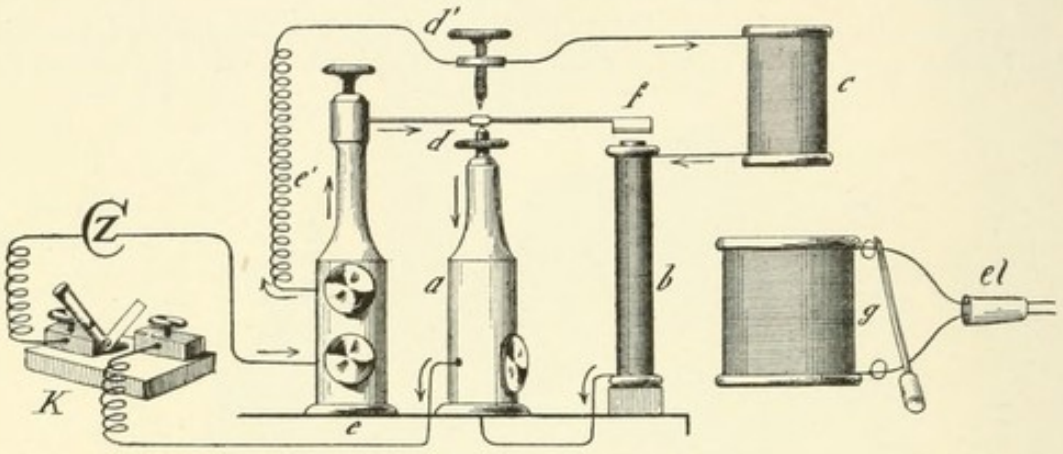


FIG. 318.—Diagram of the Course of the Current in the Magnetic Interrupter of Du Bois Reymond's Induction Coil. (Helmholz's modification.)

but never entirely withdrawn, and the primary current is altered in intensity at each contact of the spring with *d*, but never entirely broken.

Preparation of a Muscle for Contraction under Stimuli. The muscles of the frog are most convenient for the purpose of recording contractions. The frog is pithed, that is to say, its central nervous system is entirely destroyed by the insertion of a stout needle into the spinal cord, and the parts above it. One of its lower extremities is used in the following manner. The large trunk of the sciatic nerve is dissected out at the back of the thigh, and a pair of electrodes is inserted behind it. The tendo Achillis is divided from its attachment to the os calcis, and a ligature tightly tied round it. This is the tendon of the gastrocnemius, which arises from above the condyles of the femur. The femur is now fixed to a board covered with cork, and the ligature attached to the tendon is tied to the upright of the muscle lever, figure 319, *B*. When the muscle contracts the lever is raised. It is necessary to attach a small weight to the lever. In this arrangement the muscle is *in situ*, and the nerve disturbed from its relations as little as possible.

The muscle may, however, be detached from the body with the lower end of the femur from which it arises, and the nerve going to it may be taken away with it. The femur should be divided at about the lower third, and the bone fixed in a firm clamp; the nerve is placed upon two electrodes connected with an induction apparatus, and the lower end of the muscle is connected by its tendon with a lever which can write on a recording apparatus.

To prevent evaporation this so-called *muscle-nerve preparation* is placed under a glass cover (*moist chamber*, figure 350). The air in the moist chamber is kept moist by means of water adherent to its sides.

Recording the Effects of a Single Induction Shock. With a muscle-nerve preparation arranged in either of the above ways, on closing or opening the key in the primary circuit we obtain and can record a contraction, and if we use the clock-work apparatus revolving rapidly, a curve is traced such as is shown in figure 320.

Another way of recording the contraction is by use of the pendulum myograph, figure 352. Here the swing of the pendulum along a certain arc is substituted for the clock-driven movement of the other apparatus. The pendulum carries a smoked-glass plate upon which the writing lever of a myograph is made to mark. The opening or breaking shock

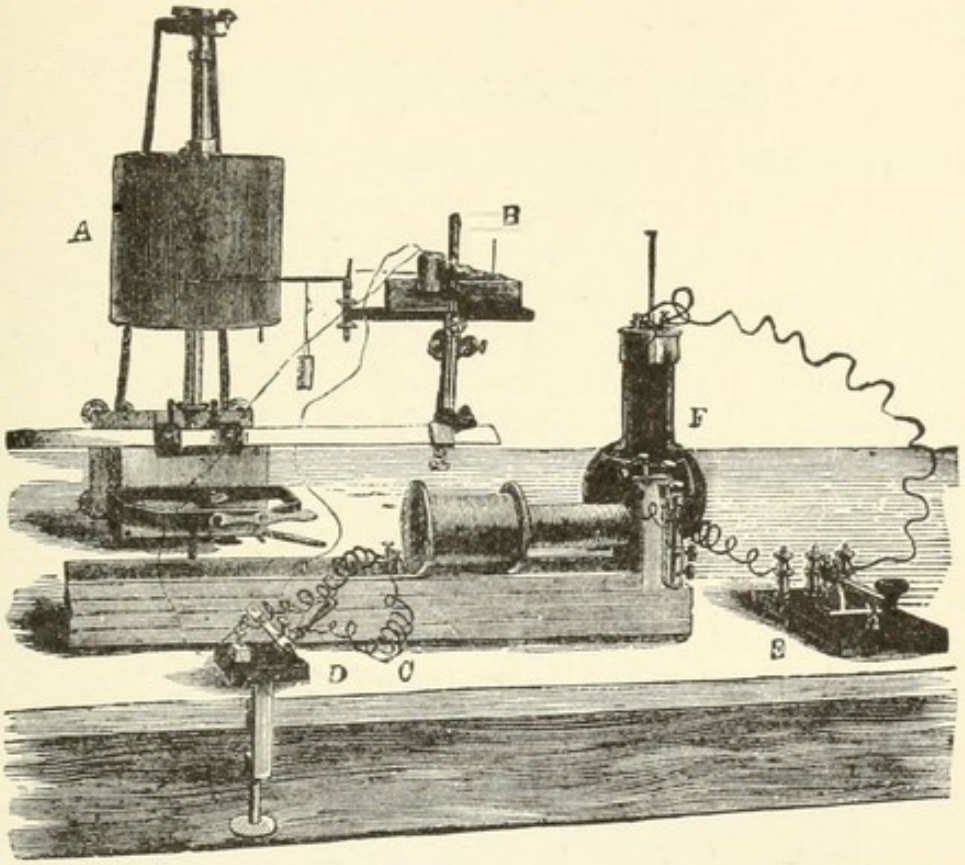


FIG. 319.—Arrangement of the Apparatus Necessary for Recording Muscle Contractions with a Revolving Cylinder Carrying Smoked Paper. A, Revolving cylinder; B, the frog arranged upon a cork-covered board which is capable of being raised or lowered on the upright, which also can be moved along a solid triangular bar of metal attached to the base of the recording apparatus—the tendon of the gastrocnemius is attached to the writing lever, properly weighted, by a ligature. The electrodes from the secondary coil pass to the apparatus—being, for the sake of convenience, first of all brought to a key, *D* (Du Bois Reymond's); *C*, the induction coil; *F*, the battery (in this figure a bichromate one); *E*, the key (Morse's) in the primary circuit.

is sent into the nerve-muscle preparation by the pendulum in its swing opening a key, figure 352, *C*, in the primary circuit. A muscle or its nerve is more irritable to an opening shock than it is to a closing shock of the same strength, because the duration of the former is shorter than that of the latter.

Conductivity in Muscle. In an ameba or other simple undifferentiated contractile protoplasmic unit a stimulus applied at any point is quickly transmitted throughout the entire mass. Just so is it with differentiated muscle. A stimulus applied at any point of a muscle will quickly be propagated through the mass as far as there is protoplasmic continuity. In cardiac muscle and in smooth muscle there is uninterrupted conduction from cell to cell. But in voluntary muscle each fiber is physiologically isolated from its neighbors. When a voluntary muscle fiber is stimulated either at the extremities or at its middle, the effect of the stimulus quickly passes through the entire fiber, whether it arouses a distinct act of contraction or not.

The rate at which conduction takes place when a contraction accompanies it has been carefully measured by numerous observers. It varies greatly in the different kinds of muscle, from two-tenths of a meter per second in the rabbits' ureter (Engelmann) to ten meters per second in the voluntary muscles of man.

SINGLE MUSCLE CONTRACTIONS.

Characteristics of a Single Contraction. The Myogram. The contraction of a muscle in response to a single effective stimulus of short duration is called a simple muscle contraction. A record of such a contraction is called a myogram. The character of the myogram, and therefore the facts revealed by it, are dependent on whether or not the record is made on a rapidly moving recording surface. If the myogram is made on a recording surface that is standing still, then it shows merely the extent of shortening of the muscle. The amount of shortening for a given muscle will depend on a series of conditions, such as nutrition, load, temperature, etc., all of which will be discussed presently.

When the record is made on a rapidly moving drum or on the pendulum myograph, it is revealed that the simple contraction occupies a definite period of time with well-marked periods or phases. Although the stimulus may be

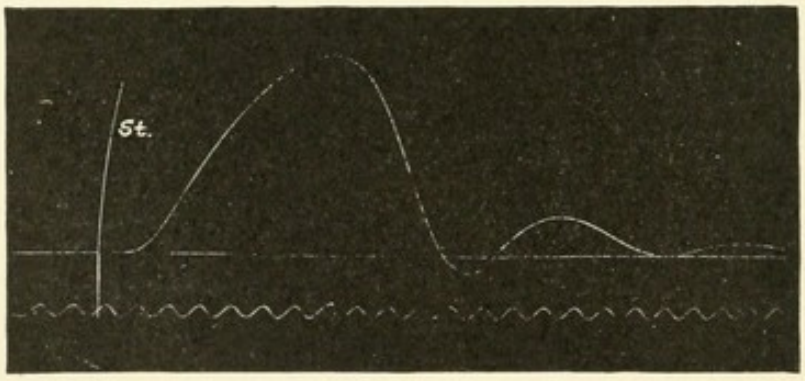


FIG. 320.—Record of a Simple Contraction of the Gastrocnemius of the Frog. Time in .01 seconds. *St*, Moment of stimulation. Record taken on a rapid drum that was provided with an automatic key.

practically instantaneous, the contraction lasts a considerable fraction of a second, in the frog's gastrocnemius about 0.1 of a second.

It will be observed that after the stimulus has been applied, as indicated by the vertical line *St*, there is an interval before contraction commences. This interval, termed the *latent period*, when measured by the number of vibrations of the tuning-fork directly beneath, is found to be about 0.01 of a second. The latent period is longer in some muscles than in others, and differs also according to the condition of the muscle and the kind of stimulus employed. During the latent period there is no apparent change in the

muscle. The second part of the record shows the *contraction phase* proper. The lever is raised by the sudden shortening of the muscle. The contraction is at first very rapid, but then progresses more slowly to its maximum. It occupies on an average 0.04 of a second in the frog's gastrocnemius. The third stage is the *relaxation phase*. After reaching its highest point, the lever begins to descend, in consequence of the elongation of the muscle. At first the fall is rapid, but it then becomes more gradual until the lever reaches the abscissa or base line, when the muscle has attained its precontraction length. The stage occupies 0.05 of a second. Usually after the contraction proper is over the lever oscillates below and above the base line in a series of diminishing waves, the elastic rebound following movement of the simple contraction. These are, of course, wholly passive and would occur equally well if we should lift the weight to the height of the contraction, then simply let it fall while taking a record.

Change in Shape during Muscular Contraction. There is a considerable difference of opinion as to the mode in which the transversely striated muscular fibers contract. The most probable account is that the contraction is

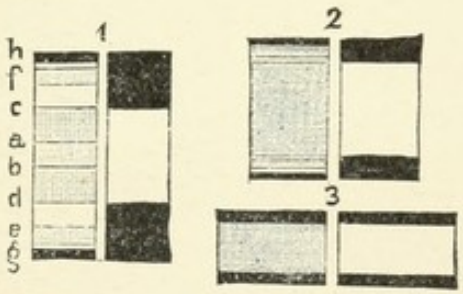


FIG. 321.—The Microscopic Appearances During a Muscular Contraction in the Individual Fibrillæ, after Engelmann. 1. A passive muscle-fiber; *c* to *d* = doubly refractive discs, with median disc *a b* in it; *h* and *g* are lateral discs; *f* and *e* are secondary discs, only slightly doubly refractive; figure on right same fiber in polarized light. The bright part is doubly refracted, black ends not so. 2. Transition stage. 3. Stage of entire contraction. In each case the right-hand figure represents the effect of polarized light. (Landois, after Engelmann.)

effected by an approximation of the constituent parts of the fibrils, which, at the instant of contraction, without any alteration in their general direction, become closer, flatter, and wider, a condition which is rendered evident by the approximation of the transverse striæ seen on the surface of the fasciculus, and by its increased breadth and thickness. The appearance of the zigzag lines into which it was supposed the fibers are thrown in contraction is due to the relaxation of a fiber which has been recently contracted and is not at once stretched again by some antagonist fiber, or whose extremities are kept close together by the contractions of other fibers. The contraction is therefore a simple and, according to Edward Weber, a uniform, simultaneous, and steady shortening of each fiber and its contents. What each fibril or fiber loses in length, it gains in thickness. The contraction is a change of form, not of size; it is, therefore, not attended with any diminution in bulk from condensation of the tissue.

This has been proved for entire muscles, by making a mass of muscles, or many fibers together, contract in a vessel full of water, with which a fine, perpendicular, graduated tube communicates. Any diminution of the bulk of the contracting muscle would be attended by a fall of fluid in the tube; but when

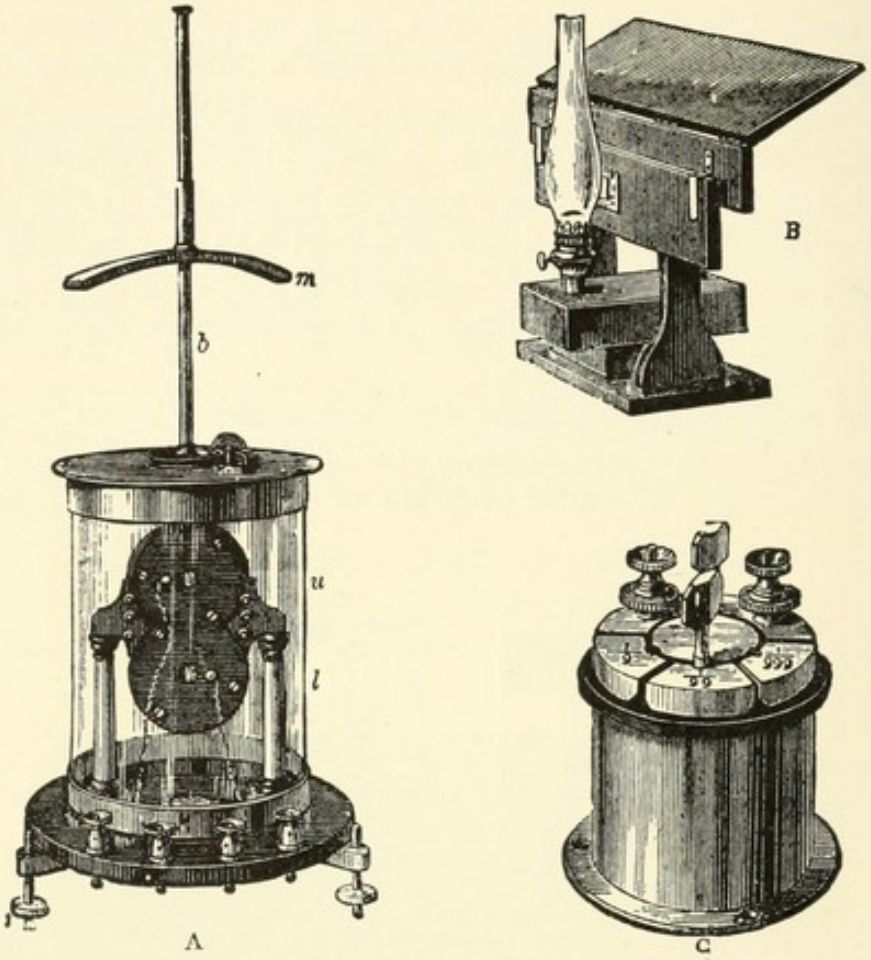


FIG. 322.—Reflecting Galvanometer. (Thomson.) *A*, The galvanometer, which consists of two systems of small astatic needles suspended by a fine hair from a support, so that each set of needles is within a coil of fine insulated copper wire; that forming the lower coil is wound in an opposite direction to the upper. Attached to the upper set of needles is a small mirror about ¼ inch in diameter; the light from the lamp at *B* is thrown upon this little mirror, and is reflected upon the scale on the other side of *B*, not shown in figure. The coils *u* are arranged upon brass uprights, and their ends are carried to the binding-screws. The whole apparatus is placed upon a vulcanite plate capable of being leveled by the screw supports, and is covered by a brass-bound glass shade, *l*, the cover of which is also of brass, and supports a brass rod, *b*, on which moves a weak curved magnet, *m*. *C* is the shunt by means of which the amount of current sent into the galvanometer may be regulated. When in use, the scale is placed about three feet from the galvanometer, which is arranged east and west, the lamp is lighted, the mirror is made to swing, and the light from the lamp is adjusted to fall upon it, and it is then regulated until the reflected spot of light from it falls upon the zero of the scale. The wires from the non-polarizable electrodes touching the muscle are attached to the outer binding-screws of the galvanometer, a key intervening for short-circuiting; or if a portion only of the current is to pass into the galvanometer the shunt should intervene as well with the appropriate plug in. When a current passes into the galvanometer the needles and, with them, the mirror are turned to the right or left according to the direction of the current. The amount of the deflection of the needle is marked on the scale by the spot of light traveling along it.

the experiment is carefully performed, the level of the water in the tube remains the same, whether the muscle be contracted or not.

In thus shortening, muscles *appear to swell up, becoming rounder, more prominent, harder, and apparently tougher.* But this hardness of muscle in the state of contraction is not due to increased firmness or condensation of the

muscular tissue, but to the increased tension to which the fibers, as well as their tendons and other tissues, are subjected from the resistance ordinarily opposed to their contraction. When no resistance is offered, as when a muscle is cut off from its tendon, not only is no hardness perceived during contraction, but the muscular tissue is even softer and more extensible than in its ordinary uncontracted state. During contraction in each fiber it is said that the anisotropous or doubly refractive elements become less refractive and the singly refractive more so, figure 321.

Chemical Changes in Contracting Muscle. 1. The reaction of the muscle, which is normally alkaline or neutral, becomes decidedly *acid* during contraction, from the development of sarcolactic acid. 2. The muscle gives out carbon dioxide gas and takes up oxygen. The amount of the carbon dioxide given out does not appear to be entirely dependent upon the oxygen taken in, and so doubtless in part arises from some other source. Muscle contracts in

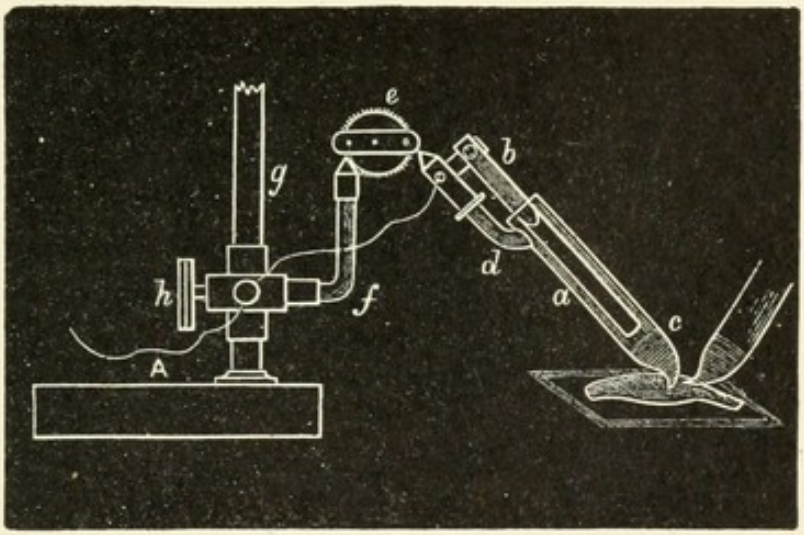


FIG. 323.—Diagram of Du Bois Reymond's Non-polarizable Electrodes. *a*, Glass tube filled with a saturated solution of zinc sulphate, in the end, *c*, of which is china clay drawn out to a point; in the solution a well-amalgamated zinc rod is immersed and connected, by means of the wire which passes through *a*, with the galvanometer. The remainder of the apparatus is simply for convenience of application. The muscle and the end of the second electrode are to the right of the figure.

an atmosphere of hydrogen, showing that oxygen is present in fixed combination. A muscle, however, contracts for a longer time in an atmosphere of oxygen. 3. Certain imperfectly understood chemical changes occur, in all probability connected with 1 and 2, in which glycogen is diminished, and glucose and muscle sugar, inosite, appear. The nitrogenous extractives are also increased.

Electrical Changes in Contracting Muscle. Resting muscles uninjured in the body have a uniform potential, are isoelectric. But when removed from the body they are more or less injured and, therefore, show differences of electrical potential between different points on the muscle, called *currents of injury* or *demarcation currents*.

The Demonstration of Muscle Currents. The demonstration of electrical currents in muscle requires a galvanometer and non-polarizing electrodes. A muscle prism is insulated, and a pair of non-polarizable electrodes connected with a very delicate galvanometer, figure 322, are applied to various points of the prism; and by a deflection of the needle to a greater or less extent in one direction or another, the strength and direction of the currents in the piece of muscle can be determined. It is necessary to use non-polarizable and not metallic electrodes in this experiment, as otherwise there is no certainty that the whole of the current observed is communicated from the muscle itself and not derived from the metallic electrodes and arising in consequence of the action of the saline juices of the tissues upon them. The form of the non-polarizable electrodes is a modification of Du Bois Reymond's apparatus, figure 323, which consists of a somewhat flattened glass cylinder, *a*, drawn abruptly to a point, and fitted to a socket capable of movement, and attached to a stand, *A*, so that it can be raised or lowered as required. The lower portion of the cylinder is filled with china clay moistened with saline solution, part of which projects through its drawn-out point; the rest of the cylinder is filled with a saturated solution of zinc sulphate into which dips a well-amalgamated piece of zinc connected by means of a wire with the galvanometer. In this way the zinc sulphate forms a homogeneous and non-polarizable conductor between the zinc and the china clay. A second electrode of the same kind is, of course, necessary. Recently Porter has devised a boot-shaped clay electrode that is burned and hence has the immense advantage of permanency.

Currents of Injury, or Demarcation Currents. If a segment is cut out of a living gastrocnemius, its cut ends present regions of maximal injury. Such a preparation is called a muscle prism.

If the points on the surface of a muscle prism be connected with the galvanometer by non-polarizable electrodes, it will be found that the currents pass from point to point, as shown in the diagram, figure 324.

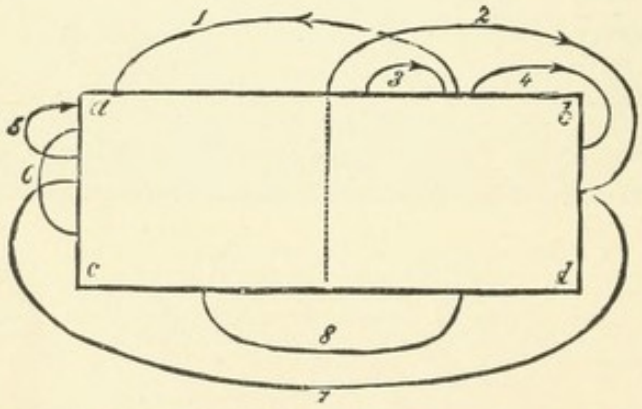


FIG. 324.—Diagram of the Currents in a Muscle Prism. (Du Bois Reymond.)

The strongest currents pass from the equator to a point representing the middle of the cut ends; currents also pass from points nearer the equator to those more remote, but not from points equally distant, which are isoelectric points. The cut ends are always negative to the equator. The currents are in all probability due to chemical changes going on in the muscles at the injured ends.

Action Currents. When a muscle is made to contract the demarcation current undergoes a sharp decrease as shown by the deflection of the galvanometer needle, which swings back in the direction of equilibrium.

This deflection, originally called the current of *negative variation*, has been shown to be due to the processes going on in the muscle during contraction and is therefore called the *action current*. It occurs where no previous demarcation current exists.

For the study of the action current the capillary electrometer is very convenient. The hearts of cold-blooded animals, because of their slow contraction, serve well for demonstration. The muscle contraction passes over the ventricle in the form of a wave, the electric potential of the muscle changing as it becomes active or passive. For any two points on the heart muscle, therefore, there will be two changes of potential, the active part first becoming negative to the inactive, and then, as the wave passes down and the in-

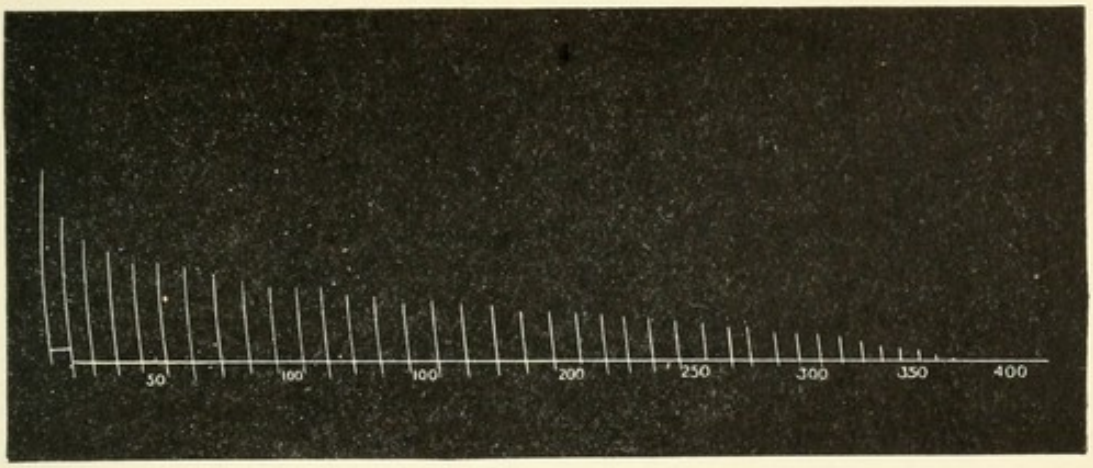


FIG. 325.—Figure for Work Energy, Showing Height of the Contraction of the Gastrocnemius of the Frog with Loads Increased by Ten Grams at a Time.

active part becomes active, the current is reversed. This is known as a *diphasic current*.

In certain fishes definite electrical organs exist, organs which are derived from muscle-like tissues and which may be regarded morphologically as muscles highly specialized for the production of energy in the form of electricity.

Heat Produced in a Simple Contraction. Becquerel and Breschet found, with the thermo-multiplier, about 0.5° C. of heat produced by each forcible contraction of a man's biceps; and when the actions were long continued, the temperature of the muscle increased 1° C. In the frog's muscle a considerable number of contractions have been found to produce an elevation of temperature equal on an average to less than 0.2° C., while a single contraction produces, according to R. Heidenhain, from 0.001° to 0.005° C. One gram of frog's muscle will produce in a single maximal contraction about 0.003 calorie or the equivalent of 126 gramcentimeters of work energy (since 1 calorie = 0.425 kilogrammeter of work). The cause of the rise of temperature is the increased chemical activity at the time of contraction. As we have already seen, in the chapter on Animal Heat, muscles have the power of producing heat even when not contracted.

The amount of heat energy developed during a single contraction will vary sharply according to the tension under which the muscle contracts. The heat production follows closely the energy of work produced, and apparently obeys the same laws.

The Work Energy Liberated by a Simple Muscle Contraction. When a muscle contracts against a resistance and a load is moved, work energy is liberated. In fact the liberation of *work energy* and *heat energy* are the specific functions of the muscles among the warm-blooded animals. A frog's gastrocnemius weighing 1 gram and loaded with 50 grams will contract from 0.5 to 0.6 cm, *i.e.*, will do 25 to 30 gramcentimeters of work for each simple contraction. The amount of work done is intimately associ-

TABLE SHOWING THE RELATION BETWEEN LOAD AND WORK.

Load or Tension. Grams.	Height Lifted. Centimeters.	Work Done. Gramcentimeters.
0	1.2	0
40	0.8	32
80	0.5	40
120	0.4	48
160	0.2	32
200	0.1	20
240	0.0	0

ated with the tension under which the muscle contracts. As the tension increases from no load up to 100 or 150 grams (for a 1-gram muscle), the work increases. But as the tension continues to increase, the work falls off until a point is reached at which the load is not lifted at all.

CONDITIONS WHICH AFFECT THE IRRITABILITY OF THE MUSCLE AND THE CHARACTER OF THE CONTRACTION.

There are a number of conditions which influence both the irritability of a muscle and the power and character of its contractions. Irritability and contractility may vary independently, but as a rule any condition which decreases the one also decreases the other. The most important of these conditions are: relation of the muscle to the central nervous system, condition of nutrition, stimulus, temperature, fatigue, drugs, disease, etc.

Effect of the Strength of Stimulus. A strength of current that is just sufficient to give the contraction of a muscle is called a *minimal* stimulus. This is a comparatively weak induction current, one which can scarcely be detected by the tip of the tongue. As the strength of the current is very gradually increased, the height of the contraction curve increases until the *maximal* stimulus is reached, which produces a contraction of an amplitude beyond which no increase occurs even though the strength of the stimulus be

multiplied many fold. The range between the strengths of the minimal and maximal stimuli is very restricted indeed. The absolute strength of a minimal stimulus varies exceedingly for a given muscle, depending on its degree of irritability. This narrow range between minimal and maximal stimuli serves as a convenient means for detecting the variations in irritability. One should count on a continued decrease in irritability in isolated muscles, hence

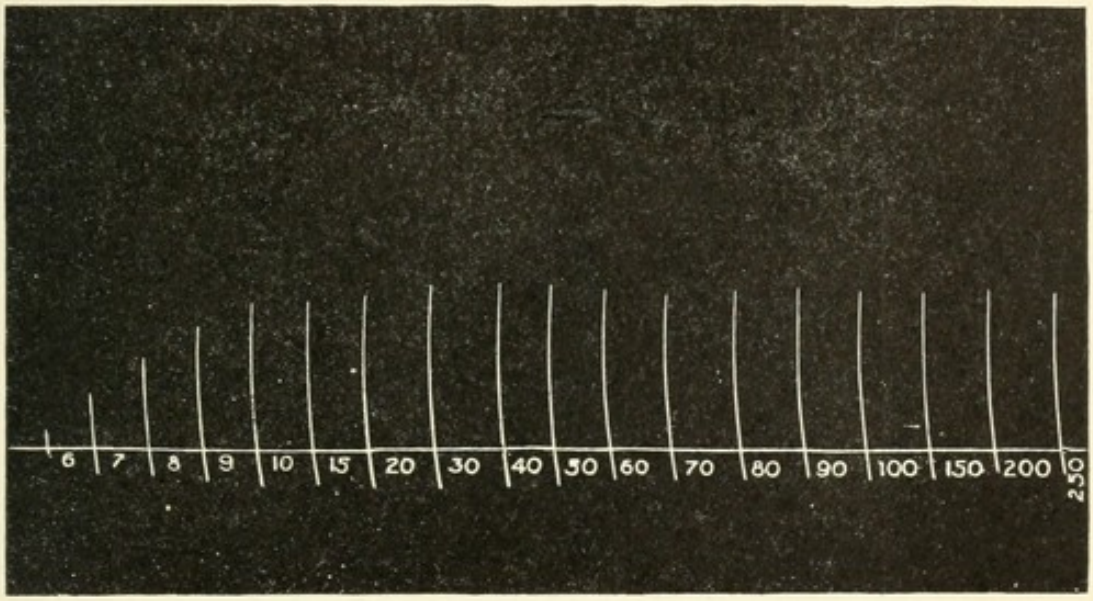


FIG. 326.—Contraction of the Gastrocnemius Under the Influence of Variation of Strength of Stimulus. The muscle was stimulated by Petzold's inductorium, graduated to show units of current. The figures 6, 7, 8, 9, 10, etc., indicate relative strength of stimulus.

should choose a supramaximal stimulus for all such preparations when other conditions surrounding the muscle are under investigation.

The Influence of Repeated Activity. The irritability of muscle is decreased by undue functional activity. The cause of the diminished irritability is twofold: when a muscle contracts, part of its substance is expended, part of its store of nutriment is exhausted, and it cannot contract so vigorously again until the loss is made up. To this extent fatigue has much the same effect as cutting off or diminishing the blood supply. The other cause for the diminution of irritability is the accumulation of poisonous products in the muscle, substances generated during contraction, probably sarcolactic acid chiefly. In a living animal these poisonous products exert their influence not only upon the muscle or muscles immediately concerned in contraction, but upon the musculature of the body generally, and the effect remains until they are eliminated from the body. Massage of the muscles increases the passage of waste products into the general blood stream and the rapidity of their elimination.

In the first few simple contractions, repeated in series, there is an increase in the amplitude of the contractions resulting in the phenomenon known as staircase contractions or "Treppe." This stage is followed by a period

of sustained contractions, and this finally by a diminishing series of amplitudes until the muscle fails to respond. After a few minutes' rest a muscle will again give strong contractions, but only for a brief series.

If the time of the simple contractions is measured, it will be found, figure 327, that not only is the amplitude decreased but the duration is greatly increased as the contractions are repeated. The latent period changes very little. The contraction phase is considerably prolonged, but the relaxation phase is very greatly increased. As fatigue progresses, the total time of the simple contraction may be two or three times longer than the normal. The

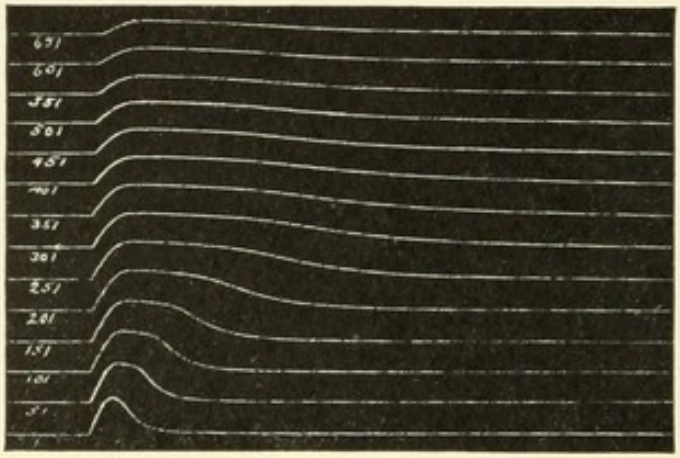


FIG. 327.—Contractions of the Gastrocnemius Muscle to Show Fatigue. The numbers printed on the figure indicate the contractions in the series which is recorded. (Lee.)

ability of the muscle to do work falls off rapidly, of course; and the greater the load during the time fatigue is coming on, the more quickly complete fatigue approaches.

The Influence of Temperature. The irritability of muscle is increased by raising its temperature slightly above that of the animal from which it has been taken, while it is decreased by cooling. If, however, the

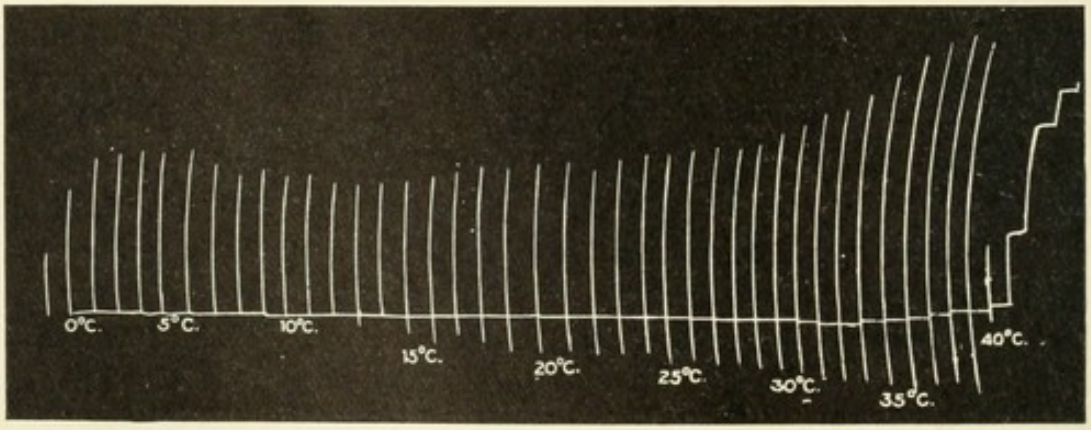


FIG. 328.—Contractions of the Gastrocnemius Muscle to Show the Influence of Temperature on the Amplitude of the Contractions. At 40° C. the muscle has begun to pass into rigor mortis, yet is able to give short contractions. The steps on the curve of rigor at the right occur at temperatures of 41°, 42°, and 43° C.

temperature be raised too high (40° C. for frog, 50° C. for mammal), the muscle enters into a condition of heat rigor and its irritability is forever lost. After cooling, unless the cold be too severe and prolonged, the irritability returns as the temperature is raised. A series of vertical records of simple contractions beginning at room temperature and decreasing with a contraction at each fall of one degree reveals the fact that the amplitude falls off slowly until a temperature of 12° to 10° C. is reached, then as gradually increases until 4° to 2° C., after which the amplitude drops off sharply to about — 1° C. However, this phenomenon is partly one of irritability, since a very strong stimulus will produce a vigorous contraction until the muscle begins to freeze. If at the freezing temperature the muscle be slowly and carefully increased in temperature it will recover from the effects of the cooling without apparent injury, and will give a reverse series to the one obtained by decreasing the temperature.

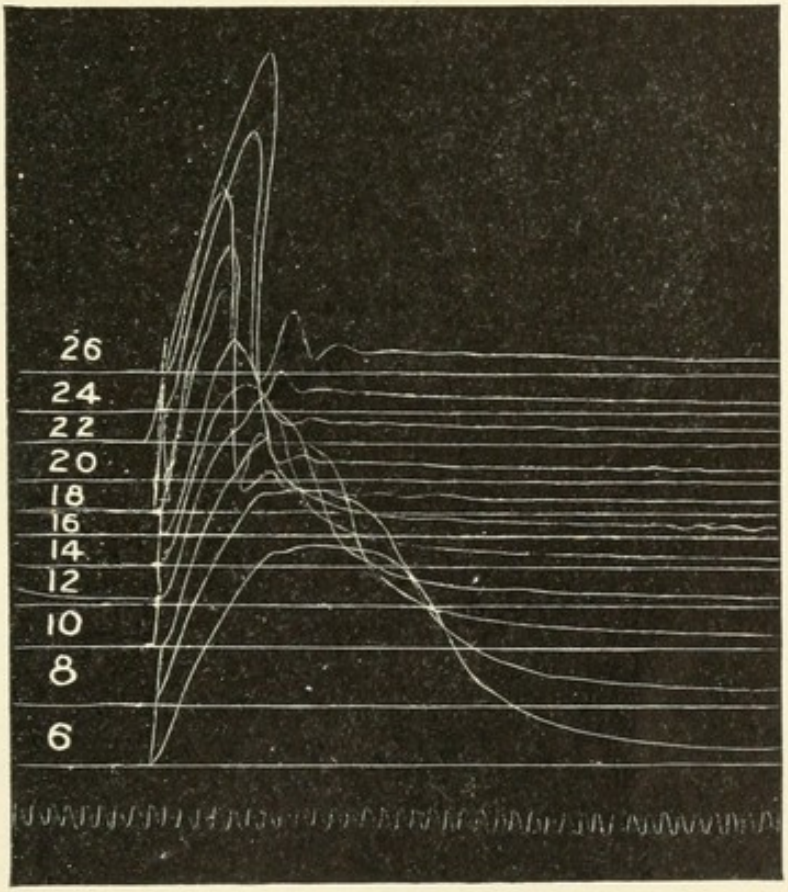


FIG. 329.—Influence of Temperature on the Duration of the Contraction of the Frog's Gastrocnemius.

As the increase of temperature is continued above room temperature the amplitude of the contractions very greatly increases (also the elasticity), reaching a maximum in the frog's gastrocnemius at about 35° to 36° C. The amplitude sharply decreases above 35° C. up to 37° to 38° C., where heat rigor begins and the muscle permanently shortens. Heat rigor is usually

complete at 40° to 41° C. A muscle cannot recover its irritability after heat rigor has set in strongly.

If the time of the contraction is measured at different temperatures it will be found to be greatly delayed at 2° to 4° C., and very much quicker than normal at 33° to 35° C. As in fatigue, the effect falls chiefly on the contraction and relaxation phases and only slightly on the latent period. The latent period is more sharply influenced by temperature than by fatigue.

Influence of Blood Supply. In the normal human muscle there is a delicately balanced vaso-motor mechanism by which the amount of blood flowing through a muscle is immediately increased when the muscle is in contraction. This blood stream is of course carrying nutritive materials to the muscle and taking away wastes. If the blood supply to a muscle is cut off, then the muscle can only draw on its stored supply of potential energy, which in active contraction is sooner or later exhausted. Under such conditions the muscle increases in irritability for a few minutes and then gradually loses both its irritability and its power to contract. Even mammalian muscles have been kept alive and normal in their activity for several hours by irrigating them with defibrinated and aerated blood (von Frey). Mammalian muscles will remain irritable for 30 minutes, or longer if cooled, after being shut off from their blood supply and isolated from the body, but both irritability and contractility soon disappear entirely.

Effect of Nerve Supply. The voluntary or skeletal muscle normally contracts in the body only when stimulated through its motor nerve. If the motor nerve is severed, the muscle is cut off from its normal source of activity, hence will undergo the changes resulting from disuse, which will be presently discussed. Aside from this, it is held by most observers that there are distinct nutritive or trophic nerves which exercise a controlling influence over the growth, development, and general nutritive processes going on in muscle.

When a motor nerve is cut, the muscle at first exhibits heightened irritability to all forms of stimuli. In a couple of weeks it decreases in its power to respond to rapidly changing stimuli like induced currents. It responds more readily to mechanical shocks and to galvanic currents for six or seven weeks, then gradually loses the power of contracting through as many months. The changes are due to protoplasmic degeneration. It is not clear in what degree these changes are due to loss of trophic nerve influence, to inactivity, and to changes in nutritive conditions. Since degeneration occurs when the vascular supply is maintained, it would seem that the nutritive condition must be chargeable to one or the other of the first two factors, probably to both.

Use of muscle increases its power and also its irritability. A properly regulated exercise is well known to contribute to the health and development of muscles. In cases of paralysis, mechanical or electrical stimulation is applied directly to the muscle in an effort to supply artificial exercise until the

nerves are regenerated and motor connections reestablished. If such stimulation is not applied, the muscle degenerates from disuse and loses its irritability often before the nerves regenerate.

The Effect of Drugs. Drugs affect the irritability of muscle, some augmenting, others depressing it. Voluntary muscle, which does not ordinarily contract except when stimulated, can be made so irritable by certain salts that it contracts automatically like heart muscle, and the converse. Ether, chloroform, etc., anesthetize muscle just as they do nerve, suppressing both irritability and contractility. Suprarenal extract increases the amplitude of contraction, as do also caffeine, digitalis, nicotine, and others. Veratrine is well known greatly to prolong the relaxation phase of the simple contraction without materially affecting the contraction phase, or the latent period.

TETANIC AND VOLUNTARY MUSCULAR CONTRACTIONS.

Effect of Rate of Stimulation. If we stimulate the muscle-nerve preparation with two induction shocks, one immediately after the other, when the point of stimulation of the second one corresponds to the crest of the contraction of the first, a second curve, figure 330, will occur, which will commence near the highest point of the first and will rise nearly as much higher, so that the sum of the height of the two curves almost exactly equals twice the height of the first. This phenomenon is called *summation.* If a third

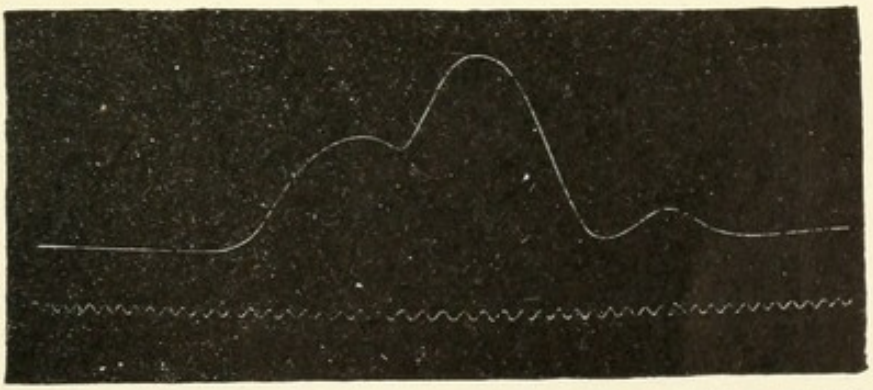


FIG. 330.—Tracing of a Double Muscle-Curve. To be read from left to right. While the muscle was engaged in the first contraction (whose complete course, had nothing intervened, is indicated by the dotted line), a second induction shock was thrown in, at such a time that the second contraction began just as the first was beginning to decline. The second curve is seen to start from the first, as does the first from the base line. (M. Foster.)

and fourth shock be passed, a similar effect will ensue, and curves one above the other will be traced, the third being slightly lower than the second, and the fourth than the third. If a continuous series of shocks occur, however, the lever after a time ceases to rise any further, and the contraction, which has reached its maximum, is maintained. The condition which ensues is called *Tetanus.* A tetanus is really a summation of contrac-

tions, but unless the stimuli become very rapid indeed, the muscle will still be in a condition of vibratory contraction and not of unvarying contraction.

If the shocks, however, be repeated at very short intervals, varying, in the frog, from eighteen to thirty per second, the muscle contracts to its utmost at once and continues at its maximum contraction for some time. The lever rises almost perpendicularly and then describes a straight line, figure 331, *c*. The rate of stimulation required increases with the rapidity of the simple contraction. If the stimuli are not so rapid, the line of maximum contraction becomes wavy, indicating a tendency of the muscle to relax during

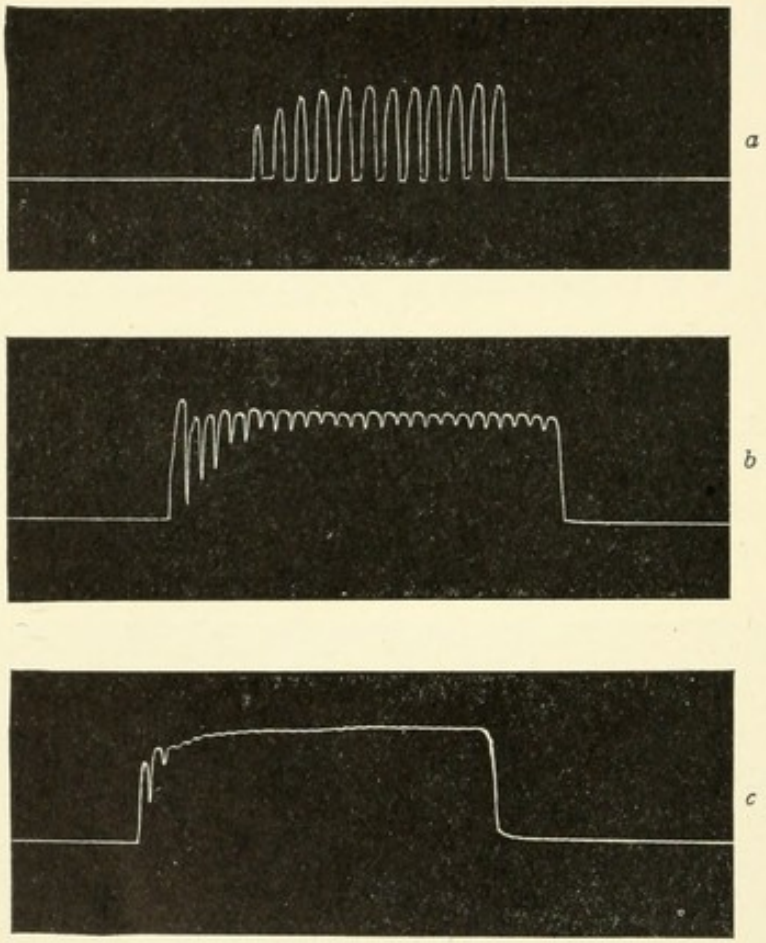


FIG. 331.—*a*, Frog's gastrocnemius muscle stimulated with four induction shocks per second, showing complete relaxation between stimuli; *b*, same muscle stimulated eight times per second, showing partial relaxation between stimuli (incomplete tetanus); *c*, same muscle stimulated twelve times per second, showing development of an almost complete tetanus.

the intervals between the stimuli, figure 331, *b*. As the muscle becomes fatigued, a less rapid rate of stimulation is required to produce a complete tetanus, owing to the prolongation of the relaxation period in such a muscle. The height of the contraction, however, is lessened. This condition of prolonged relaxation is known as *contracture*.

Coordinated Muscular Contractions. In the human body the skeletal muscles contract only on stimulation through their motor nerves, *i.e.*, under the influence of nerve impulses that have their origin in the central

nervous system. Such motor impulses may arise through reflexes, through automatic activity of the nerve center, or by higher cerebral origin associated with conscious psychic effort. In either case the apparatus consists of one or more central neurones, an anterior-horn motor cell, and the muscle itself. Conscious or voluntary effort may be taken as a type.

Simple contractions are possible to human muscles, but undoubtedly tetanic contractions are the rule. If one holds the arm out at right angles to the trunk, the movement requires the continuous or tetantic contraction of the deltoid and the series of extensor muscles. If the arm is retained in the extended position long enough, extreme fatigue is felt and presently one can no longer maintain the position. Yet, if the muscles involved are immediately stimulated directly with an electric current, they contract, showing that such exhaustion as exists is not wholly due to the muscle.

Mosso's ergograph was devised for the specific purpose of studying the character of fatigue of voluntary effort. This apparatus is adapted to the study of the fatigue of the flexors of the middle finger, or, in the newer instrument devised by Storey, to the abductor of the index finger. Numerous studies have shown, apparently, that the fatigue of voluntary effort involves, first, the nervous apparatus and, later, the muscle; that the muscle still retains a considerable reserve of energy when the apparatus as a whole is exhausted.

Muscle in Rigor Mortis. After the muscles of the dead body have lost their irritability or capability of being excited to contraction by the application of a stimulus, they spontaneously pass into a state of contraction apparently identical in effect with that which ensues during life. It affects all the muscles of the body, and, when external circumstances do not prevent it, commonly fixes the limbs in that which is their natural posture of equilibrium or rest. From the simultaneous contraction of all the muscles of the trunk, a general stiffening of the body is produced, which constitutes the *rigor mortis* or *post-mortem rigidity*.

When this condition has set in, the muscle *becomes acid in reaction* (due to development of sarcolactic acid), *gives off carbonic acid* in great excess, *diminishes in volume slightly, becomes shortened and opaque*, its substance sets in a firm coagulatio. Rigor comes on much more rapidly after muscular activity, and is hastened by warmth.

The immediate cause of rigor seems to be a chemical one, namely, the coagulation of the muscle plasma. We may distinguish three main stages: 1. Gradual coagulation. 2. Contraction of coagulated muscle clot (myosin), and 3, squeezing out of muscle serum. During the first stage, restoration is possible, by the circulation of arterial blood through the muscles; and even when the second stage has set in, vitality may be restored by dissolving the coagulum of the muscle in salt solution, and passing arterial blood through the vessels. After the second stage is advanced, recovery is impossible.

It has been noticed that the relaxation in muscles after rigor sometimes occurs too quickly to be caused by putrefaction. The suggestion that in such cases the relaxation is due to a ferment-action is very plausible. It is known that pepsin is present in muscles, and that this ferment will act in an acid medium. The conditions for the solution of the coagulated myosin are therefore present since the reaction of muscle in rigor is acid. Subjecting fresh muscle to the action of heat (50° to 60° C.) or immersing it in distilled water causes a similar coagulation to that of rigor mortis. The former is known as *heat rigor*, and the latter as *water rigor*.

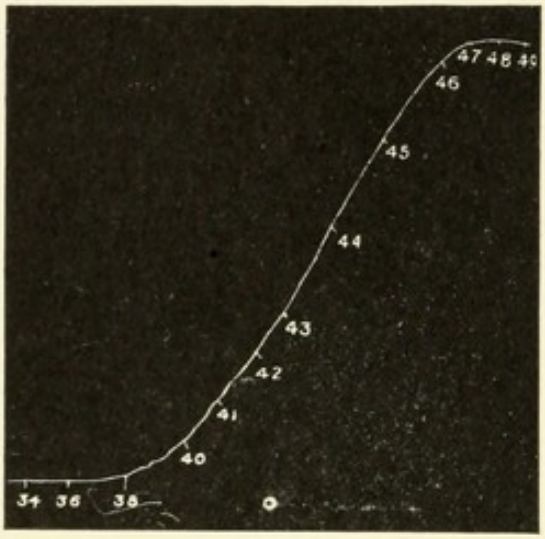


FIG. 332.—Curve of Shortening of the Gastrocnemius Muscle of the Frog, During Heat Rigor. The numbers indicate degrees centigrade.

The muscles are not affected simultaneously by rigor mortis. It affects the neck and lower jaw first; next, the upper extremities, extending from above downward; and, lastly, reaches the lower limbs. In some rare instances only, it affects the lower extremities before or simultaneously with the upper extremities. It usually ceases in the order in which it begins: first at the head, then in the upper extremities, and lastly in the lower extremities. It never ordinarily commences earlier than ten minutes, and never later than seven hours after death; and its duration is greater in proportion to the lateness of its accession. Heat is developed during the passage of a muscular fiber into the condition of rigor mortis.

Since rigidity does not ensue until muscles have lost the capacity of being excited by external stimuli, it follows that all circumstances which cause a speedy exhaustion of muscular irritability induce an early occurrence of the rigidity, while conditions by which the disappearance of the irritability is delayed are succeeded by a tardy onset of the rigidity of rigor. This is the explanation of its speedy occurrence, and equally speedy departure, in the bodies of persons exhausted by chronic diseases; and its tardy onset and long

continuance after sudden death from acute diseases. In some cases of sudden death from lightning, violent injuries, or paroxysms of passion, rigor mortis has been said not to occur at all; but this is not always the case. It may, indeed, be doubted whether there is really a complete absence of the post-mortem rigidity in any such cases; for the experiments of Brown-Séquard make it probable that the rigidity may supervene immediately after death, and then pass away with such rapidity as to be scarcely observable.

The occurrence of rigor mortis is not prevented by the previous existence of paralysis in a part, provided the paralysis has not been attended with very imperfect nutrition of the muscular tissue.

The rigidity affects the involuntary as well as the voluntary muscles, whether they be constructed of striped or unstriped fibers. The rigidity of involuntary muscles with striped fibers is shown in the contraction of the heart after death. The contraction of the muscles with unstriped fibers is shown by an experiment of Valentin, who found that if a graduated tube be connected with a portion of intestine taken from a recently killed animal, and the intestine be tied at the opposite end, and filled with water, the water will in a few hours rise to a considerable height in the tube, owing to the contraction of the intestinal walls. It is still better shown in the arteries, of which all that have muscular coats contract after death, and thus present the roundness and cord-like feel of the arteries of a limb lately removed, or those of a body recently dead. Subsequently they relax, as do all the other muscles, and feel lax and flabby and lie as if flattened, and with their walls nearly in contact.

Muscular Metabolism During Contraction. The question of the metabolism of muscle both in a resting and in an active condition has for many years occupied the attention of physiologists. It cannot be said even now to be thoroughly understood. Most of the facts with reference to the subject have been already mentioned. We may shortly recapitulate them here: First, muscle during rest absorbs oxygen and gives out carbon dioxide. This has been shown by an analysis of the gases of the blood going to and leaving muscles. During activity, *e.g.*, during tetanus, the same interchange of gases takes place, but the quantities of the oxygen absorbed and of the carbon dioxide given up are increased, and the proportion between them is altered thus:

Venous Blood.	O_2, less than in Arterial Blood.	CO_2, more than in Arterial Blood.
Of resting muscle.....	9 per cent	6.71 per cent
Of active muscle.....	12.26 per cent	10.79 per cent

There is then a greater proportion of carbon dioxide produced in muscle during activity than during rest.

During rigor mortis there is also an increased production of carbon dioxide.

Second, muscle during rest produces nitrogenous crystallizable substances, such as creatin, from the metabolism which is constantly going on in it during life; in addition there are formed, in all probability, sarcolactic acid and other non-nitrogenous matters.

During activity the nitrogenous substances, such as creatin, undergo very slight, if any, increase—about the amount produced during rest—but the sarcolactic acid is distinctly increased; sugar (glucose) is also increased, whereas the glycogen is diminished.

During rigor mortis the sarcolactic acid is increased, and in addition myosin is formed.

From these data it is assumed that the processes which take place in resting and active muscles are somewhat different, at any rate in degree. From actively contracting muscle, also, there are obtained an increased amount of heat and mechanical work; potential energy is converted into kinetic energy.

Many theories have been proposed to explain the facts of muscular energy. It has been suggested by Herman that muscular activity depends upon the splitting up and subsequent re-formation of a complex nitrogenous body, called by him *Inogen*. When this body so splits up there result from its decomposition carbon dioxide, sarcolactic acid, and a gelatino-albuminous body. Of these the carbon dioxide is carried away by the blood stream; the albuminous substance and possibly the acid, at any rate in part, go to re-form the inogen. The other materials of which the inogen is formed are supplied by the blood; of these materials we know that some carbohydrate substance and oxygen form a part. The decomposition, although taking place in resting muscle, reaches a climax in active muscle, but in that condition the destruction of inogen largely exceeds restoration, and so there must be a limit to muscular activity. But this is not the only change going on in muscle, there are others which affect the nitrogenous elements of the tissue, and from them result the nitrogenous bodies of which creatin is the chief; these changes may be unusually large during severe exercise.

It has been further suggested as myosin is undoubtedly formed in rigor mortis when the muscle becomes acid and gives off carbon dioxide, and since myosin is formed also when muscle contracts, that the phenomenon of contraction is a condition akin to partial death. The electrical reactions appear to justify this; both contracted and dead muscle are negative to living muscle when at rest. What happens to the myosin which is formed when muscle contracts, if this view be the correct one, is unknown. Halliburton suggests that the myosin, which can be made to clot and unclot easily enough outside the body, is able to do the same thing in the body. It is pos-

sible that the clotting of myosinogen which is supposed to occur during contraction is not of the same intensity or extent as that which occurs post mortem. The relation of the hypothetical inogen to the rest of the muscle fiber is undetermined. It may be that the inogen is formed by the activity of the muscle-protoplasm and stored up within itself, and that during rest of muscle it is gradually used up, whereas in activity it is suddenly and explosively decomposed. In the rest of the fiber the nitrogenous metabolism continues much the same during activity.

THE TYPE OF CONTRACTION IN INVOLUNTARY MUSCLE AND IN CILIA.

Cardiac Muscle. Some detail concerning the action of cardiac muscle has already been given in connection with the chapter on Circulation. As compared with the activity of skeletal muscle, cardiac muscle differs most strikingly in that it is automatic. A strip of heart muscle taken from any part of the heart, under proper conditions, gives off a series of contractions, whether it receives any special stimulus or not, whereas we have just found that skeletal muscle under similar conditions remains quiet unless stimulated in some special way. The fibers of skeletal muscle are more or less physiologically isolated from each other, and one fiber may contract without involving contractions of the others. Cardiac muscle, on the other hand, when stimulated at any point conducts the change produced throughout the continuity of the mass. Cardiac muscle contractions are influenced by tension, temperature, fatigue, etc., apparently, in the same way as skeletal muscle.

When the contraction occurs it is always maximal. The actual amplitude of the contraction is dependent on the condition of nutrition of the cardiac muscle. If the contractions are at a rapid rate they will be relatively of less amplitude. If an extra contraction is induced in an automatic series, so that the interval between two contractions is similar, then the amplitude will be correspondingly reduced. Such an extra contraction is followed by a delayed automatic contraction, the phenomenon of compensatory pause. The contractions in cardiac muscle are simple contractions. In fact, it is said to be impossible to produce a tetanus except in certain invertebrate hearts. This possibility depends upon the fact that during the time of a single contraction there is a certain interval between the beginning and the crest of the contraction, figure 174, in which the heart muscle is not irritable. This is known as the *refractory phase.*

The duration of the contraction of heart muscle is much greater than the contraction of skeletal muscle. The total time of a contraction in a frog's gastrocnemius is 0.1 of a second, while the time of a contraction of the ventricle in the same animal is at least 0.7 to 0.8 of a second. In the terrapin's

cardiac muscle the time of a contraction is over a second, but in the warm-blooded cardiac muscle the time is shorter, perhaps from 0.4 to 0.5 of a second for the human ventricular muscle.

Smooth Muscle. The physiology of smooth muscle has been given to some extent in previous chapters, particularly in connection with the movements of the stomach and intestines. As compared with skeletal and cardiac muscle it is a much more slowly acting contractile tissue. Isolated strips of smooth muscle, as a rule, contract only when stimulated, though preparations of certain tissues, like the stomach muscle of the frog, give off rhythmic contractions occasionally. In this regard smooth muscle stands intermediate between skeletal and cardiac muscle; the former is normally never automatic, the latter always.

Smooth muscle requires a different type of stimulus to produce contraction; the stimulus must be more prolonged and more intense. For example,

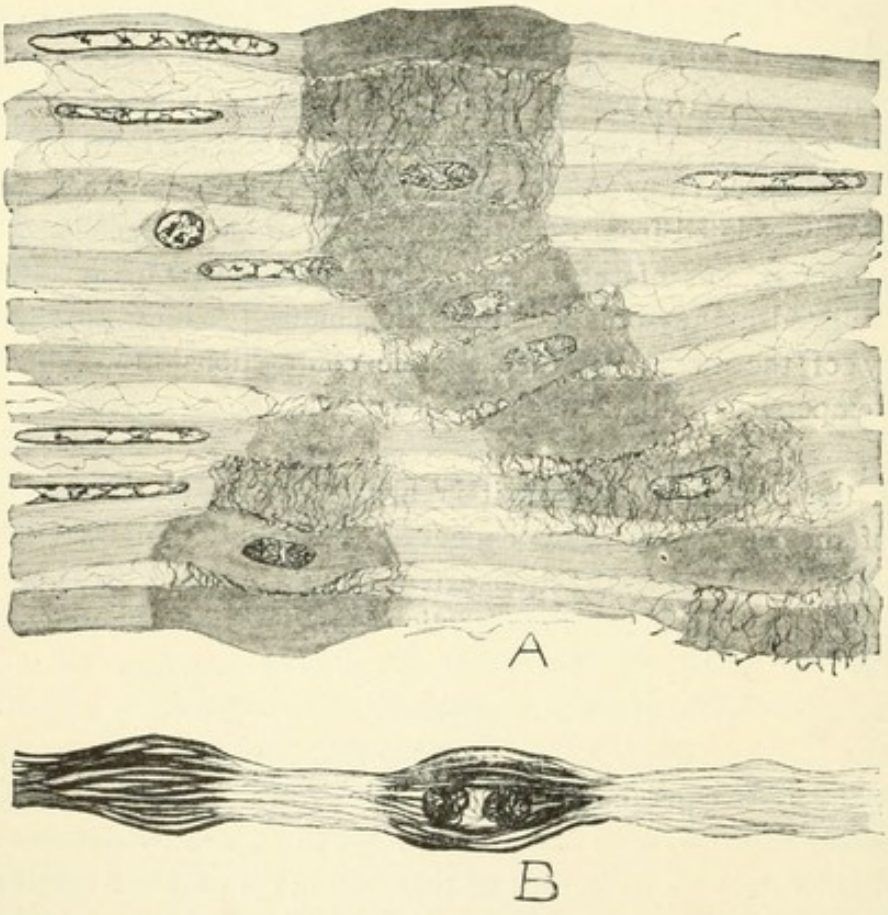


FIG. 333.—Contraction Area in Smooth Muscle. *A*, Showing the contraction nodes of the fibers, the deep staining of the nodes, the condensation of surrounding connective tissue; *B*, diagrammatic, showing the thickening of the longitudinal fibrillæ. Intestine of dog. (Unpublished figure by Caroline McGill.)

smooth muscle is not readily responsive to induction currents of short duration, but is readily stimulated by galvanic currents or induction currents of longer duration. The stimulus must be applied through a longer interval of time.

Preparations of the stomach muscle can scarcely be made to contract by a single induction current, no matter how intense. Such muscle in the body is always associated with the local nervous apparatus which plays an indeterminate part in its activity.

The ureters and gall-bladder are the parts most difficult to excite by stimuli; they do not act at all till the stimulus has been long applied, and then contract feebly and to a small extent. The contractions of the cecum and stomach are quicker, and still quicker those of the iris and of the urinary bladder. The contractions of the small and large intestines, of the vas deferens, and of the pregnant uterus, are yet more regular and more sustained.

Changes During the Contraction of Smooth Muscle. The duration as well as type of contraction in smooth muscle is very markedly different from that of voluntary muscle. A contraction in smooth muscle is

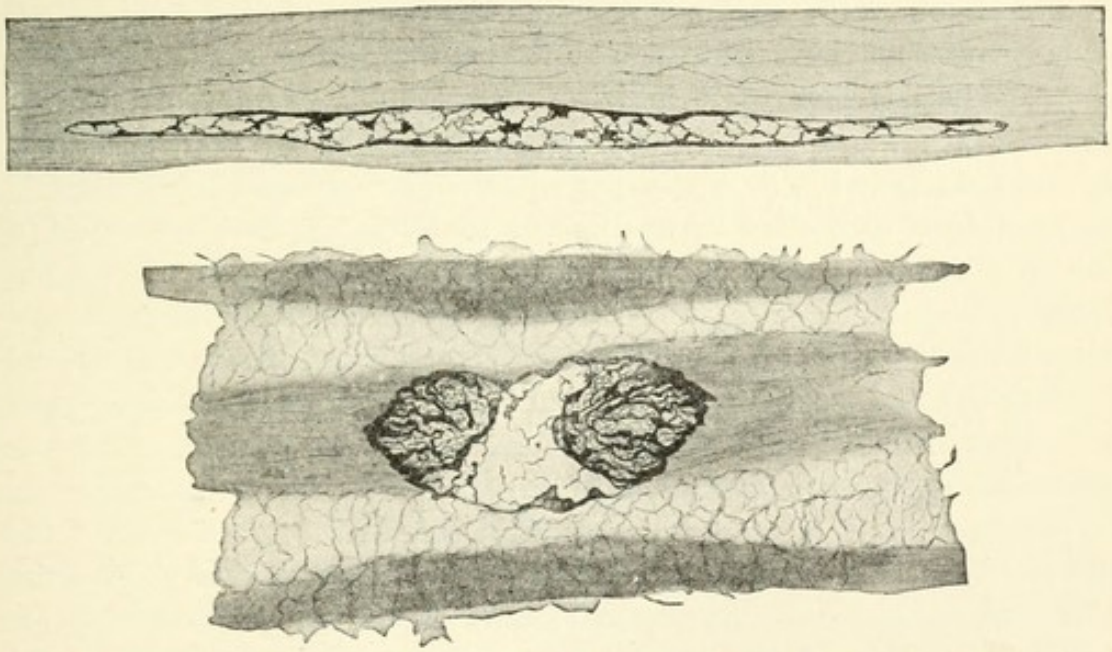


FIG. 334.—Enlarged Detailed Drawing of the Nucleus of Smooth Muscle in the Relaxed and in the Contracted State. Intestine of Necturus. Zeiss obj. 2, oc. 8. (Unpublished figure by Caroline McGill.)

characterized by a very long latent period, a slowly developed contraction phase, and an extremely delayed relaxation, figure 355. The amount and duration of the contractions are dependent upon the strength and duration of the stimulus, though the curve of contraction itself does not in other respects differ sharply from the type of curve of the simple muscle contraction.

Owing to the apparently different structural type of smooth muscle, especial interest attaches to the changes which occur during its contraction. Caroline McGill has recently re-examined the histological structure and investigated the function of this type of muscle, and we are able to present a figure showing the changes. The longitudinal fibrillæ, which are readily stained with iron hematoxylin, show distinct shortening and thickening at the

nodes of contraction of the muscle, figure 333, *B*. The whole fiber is thickened at the contraction nodes and stains very readily and usually uniformly. However, by certain stains the fibrillæ can be traced through the node. The node is an apparent area of chemical differentiation. There is a marked condensation of the intermuscular fibrous tissue, which is doubtless purely a passive phenomenon. The most striking change during contractions is observed in the nucleus, figure 333, *A*, and figure 334. The nucleus during rest is a long slender oval or spindle with a general chromatic network. "During contraction, the smooth muscle nuclei shorten and thicken by an active process. The chromatin collects, chiefly at the two ends of the nucleus, leaving a relatively clear area in the center."

Ciliary Motion. Ciliary motion, which is closely allied to ameboid and muscular motion, is alike independent of the will, of the direct influence of the nervous system, and of muscular contraction. It may continue for several hours after death, or removal of the ciliated tissue, provided the portion of tissue under examination be kept moist. Its independence of the nervous system is shown also in its occurrence in the lowest invertebrate animals which are apparently unprovided with anything analogous to a nervous system, and in its persistence when the ciliated cells are completely separated from each other by teasing out in serum or other physiological solution. The vapor of chloroform arrests the motion; but it is renewed on the discontinuance of the application of the anesthetic. The movement ceases when the cilia are deprived of oxygen (although it may continue for a time in the absence of *free* oxygen) but is revived on the admission of this gas. Carbon dioxide also stops the movement. The contact of various substances, *e.g.*, bile, strong acids, and alkalies, will stop the motion altogether; but this depends chiefly on destruction of the delicate substance of which the cilia are composed. Temperatures above 45° C. and below 0° C. stop the movement, whereas moderate heat and faintly alkaline solutions are favorable to the action and revive the movement after temporary cessation. The exact explanation of ciliary movement is not known. Whatever may be the exact explanation, the movement must depend upon some changes going on in the cells of which the cilia are a part and not on changes limited to the cilia themselves, since, when the latter are cut off from the cell the movement ceases, and when severed so that portions of the cilia are left attached to the cell, the attached and not the severed portions continue the movement. Ciliary contraction is to be regarded as a type of motor activity carried out in a specialized form of motor apparatus. The changes going on in the cell must be classed with similar changes in heart or skeletal muscle. Ciliary tissue is like cardiac in at least two characteristics: the cells are capable of conducting a stimulus from cell to cell, and ciliary activity is automatic. As a special illustration of cilia-like action may be mentioned the motion of spermatozoa, which are cells with a single cilium.

THE FUNCTION OF NERVE FIBER.

The Nerve Impulse. The motor nerve fibers of the muscle-nerve preparation are of the medullated type described on page 64. But the essential structure, possessed by all fibers, is the axis cylinder. The peculiar function of the nerve fiber, *i.e.*, of the axis cylinder, is its power to conduct a physiological change along its extent, a phenomenon known as a *nerve impulse*. A normal nerve impulse in a motor nerve has its origin in the motor cell of the central nervous system of which the fiber is an outgrowth. The manner in which such discharge from the cell takes place will be discussed later. But nerve impulses may be aroused by various artificial means, they are influenced by certain conditions in the environment, and possess certain other properties that may be discussed at this point.

Nerve Stimuli. Nerve fibers like skeletal muscle require stimulation before they can manifest any of their properties, since they have no power of themselves of originating nerve impulses. The stimuli which are capable of exciting nerves to action are, as in the case of muscle, very diverse. The mechanical, chemical, thermal, and electrical stimuli which may be used in the case of muscles are also, with certain differences in the methods employed, efficacious in stimulating the nerve. The chemical stimuli are chiefly these: withdrawal of water as by drying; strong solutions of neutral salts of potassium, sodium, etc.; free inorganic acids, except phosphoric; and some organic acids. The electrical stimuli employed are the induction and continuous currents concerning which the observations in reference to muscular irritability should be consulted. Galvanic currents stimulate nerves only at the moment of turning on the current and of turning it off. Weaker electrical stimuli will excite nerves than will excite muscles; the nerve impulse appears to gain strength as it descends, and a weaker stimulus applied far from the muscle will have the same effect as a slightly stronger one applied to the nerve near the muscle.

Characteristics of the Nerve Impulse. When a nerve impulse is aroused in a motor nerve, as by stimulating a nerve in its course by an induced current of medium strength, it is propagated along the axis cylinder to the muscle where it arouses a contraction of the muscle fiber. In the contraction of the muscle we have indirect but conclusive evidence of the passage of the nerve impulse, for it can be readily proven that the electrical current does not escape to the muscle. In this instance it can be shown that there is a nerve impulse passing from the point of stimulation in the direction away from the muscle; *i.e.*, the artificially aroused nerve impulse passes over the entire extent of the fiber stimulated. In fact, a nerve impulse is known to travel from its point of origin over the entire neurone affected. This antidromal nerve impulse, of course, does not exist in the normal case, since the nor-

mal nerve impulse arises in the nerve-cell body and passes out over the fiber from its origin to its extremity.

The nerve impulse travels over the nerve fiber with a velocity that was first determined by Helmholtz. He found that in the sciatic of the frog the nerve impulse travels at the rate of twenty-seven meters per second. The rate has been measured in a number of animals and varies between wide limits. In human nerves the rate is variously given, but thirty meters per second may be taken as a fair average.

The presence of the nerve impulse can be detected by the action current, which exists in nerve as in muscle (see page 451 for methods of detecting the action current).

Rheoscopic Frog. The action current may be demonstrated by means of the following experiment:

The muscle current produced by stimulating the nerve of one muscle-nerve preparation may be used to stimulate the nerve of a second muscle-nerve preparation. The hindleg of a frog with the nerve going to the gastrocnemius cut long is placed upon a glass plate and arranged in such way that its nerve touches in two places the gastrocnemius muscle, exposed but preserved *in situ* in the opposite thigh of the frog. The electrodes from an induction coil are placed behind the sciatic nerve of the second preparation, high up. On stimulating it with a single induction shock, the muscles not only of the same leg are found to undergo a twitch, but also those of the first preparation, although this is not near the electrodes. The stimulation cannot be due to an escape of the stimulating current into the first nerve, but is due to the action current of the second muscle. This experiment is known under the name of the *rheoscopic frog*.

When the nerve impulse is studied by means of the action current it is found that a nerve impulse can be aroused by a weaker stimulus than is required to produce a minimal contraction of a muscle. The response of the nerve to graduated strengths of the stimulus is increased very rapidly with slight increase of strength of the stimulus, the augmentation extending through a somewhat greater range than for muscle. If the stimulus is still further increased there is only slight increase of the resulting nerve impulse.

Fatigue of Nerve Fiber. Many efforts have been made to discover evidences of fatigue of nerve fiber, with practically complete negative results. A difficulty has been to secure means of measuring change in intensity of the nerve impulse. The muscle quickly fatigues so that the character of the muscle response cannot be taken when measured in the ordinary way. An effective method used by Howell, Budgett, and Leonard consists in cooling a segment of nerve to suspend its conductivity, during stimulation of the free end; and periodically warming up the cooled segment of nerve to test the strength of nerve impulse passing through it to the unfatigued muscle beyond. By this and other methods it has been found that a motor nerve is not fatigued by at least ten hours' continuous stimulation with induction currents.

One must hesitate to draw the conclusion, however, that the nerve fiber conducts the nerve impulse without loss of energy. The fiber can be anesthetized, it responds to temperature changes, and gives other evidences of sus-

ceptibility to conditions which influence metabolism in other forms of protoplasm. Perhaps the nerve fiber is capable of repairing its wastes as rapidly as they occur.

The Effects of Battery Currents on Nerve Fiber. Galvanic currents influence nerves in ways that call for special discussion. A constant current, say from a Daniell battery, can be introduced into the nerve of a muscle-nerve preparation by means of a pair of non-polarizable electrodes, figure 323, and a convenient key arranged for turning the current on or off the nerve. It will be found that with a current of moderate strength there will be a contraction of the muscle, both at the closing and the opening of the key (called respectively *making* and *breaking* contractions), but that during the interval between these two events the muscle remains flaccid, provided the battery current continues of constant intensity. If the current be a very weak or a very strong one, the effect is not quite the same; one or the other of the contractions may be absent. Which of these contractions is absent depends upon another circumstance, viz., the *direction of the current*. The direction of the current may be *ascending* or *descending:* If ascending, the anode or positive pole is nearer the muscle than the cathode or negative pole, and the current to return to the battery has to pass up the nerve; if descending, the position of the electrodes is reversed. It will be necessary before considering this question further to return to the apparent want of effect of the constant current during the interval between the make and the break contraction. To all appearances no change is produced, but in reality a very important alteration of the irritability and conductivity is brought about in the nerve by the passage of this constant or polarizing current.

A second way of showing the effect of the polarizing current is by stimulating the nerve by a pair of electrodes from an induction coil, while the polarizing current from the battery is flowing through the nerve. If the strength of stimulus required in order that a minimum contraction be obtained by the induction shock before the polarizing current is applied, and the secondary coil be removed slightly further from the primary, the induction current cannot now produce a contraction. If now the polarizing current be sent in a descending direction, that is to say, with the cathode nearest the muscle, and the induction current which was before insufficient be applied between the cathode and the muscle, it will now prove sufficient to cause a contraction. This indicates that with a descending current the irritability of the nerve is increased at the cathode. If instead of applying the induction electrodes below the polarizing electrodes, they are applied above them, the irritability of the nerve is found to be decreased. If the polarizing current is reversed, *i.e.*, made ascending, then the condition of irritability of the nerve is reversed. Both methods show that the polarization consists in an increase in irritability at the cathode, called *catelectrotonus*, and a decrease at the anode called *anelectrotonus*. The total change is called by the term *electrotonus*. As there

is between the electrodes both an increase and a decrease of irritability on the passage of a polarizing current, it is evident that there must be a *neutral point* where there is neither increase nor decrease of irritability. The position of this neutral point is found to vary with the intensity of the polarizing current; when the current is weak the point is nearer the anode, when strong nearer the

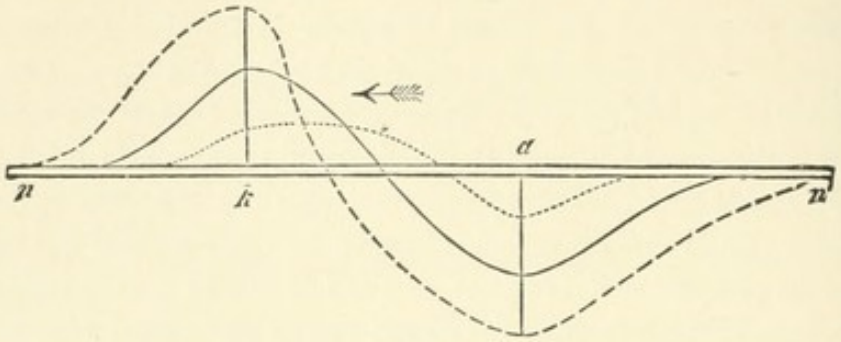


FIG. 335.—Diagram Illustrating the Effects of Various Intensities of the Polarizing Currents. *n*, *n'*, Nerve; *a*, anode; *k*, cathode; the curves above indicate increase, and those below decrease of irritability, and when the current is small the increase and decrease are both small, with the neutral point near *a*, and so on as the current is increased in strength.

cathode, figure 335. When a constant current passes into a nerve, therefore, if a contraction result, it may be assumed that it is due to the increased irritability produced in the neighborhood of the cathode, but the breaking contraction must be produced by a rise in irritability from a lowered state to the normal in the neighborhood of the anode.

The contractions produced in the muscle of a muscle-nerve preparation by a constant current have been arranged in a table which is known as **Pfluger's Law of Contractions.** It is really only a statement as to when a contraction may be expected:

Strength of Current Used.	Descending Current.		Ascending Current.	
	Make.	Break.	Make.	Break.
Very weak	Yes	No	No	No
Weak	Yes	No	Yes	No
Moderate	Yes	Yes	Yes	Yes
Strong	Yes	No	No	Yes

During the passage of a constant current through a nerve and immediately after its cessation, there is a change in the conductivity as well as of the irritability of the nerve at the anode and cathode, respectively. During the passage of the current, the conductivity is increased at the cathode and decreased at the anode. After the passage of the current, the effect is reversed. With strong currents the area of decreased conductivity may be sufficient to act as a block, preventing the passage of impulses over it.

The foregoing statements concerning the changes produced in a nerve by the passage of a constant current may be briefly summarized as follows:

I. A nerve is more irritable to the closing of a constant current than it is to the opening of a constant current.

II. During the passage of the current through the nerve, both its irritability and conductivity are increased at the cathode and decreased at the anode.

III. After the passage of the current, the irritability and conductivity are both decreased at the cathode and increased at the anode.

The Effect of Battery Currents on Deep-Seated Nerves. The following account is condensed from Lombard in "An American Text-book of Physiology."

As an electric current cannot be applied to living human nerves directly, it is applied to the skin along the course of the nerve. The current passes from the anode or positive pole through the skin, and spreads out in the tissues much as the bristles of a brush; it then gradually concentrates and leaves the skin at the cathode or negative pole.

In addition to the physical anode and cathode of the battery, there are what are called physiological anodes and cathodes. There is a physiological anode *at every point* where the current *enters* a nerve, and a physiological cathode at *every point* where it *leaves* it.

Generally when the current is applied to nerves through the skin, only part of it flows longitudinally along the nerves; most of it passes diagonally through

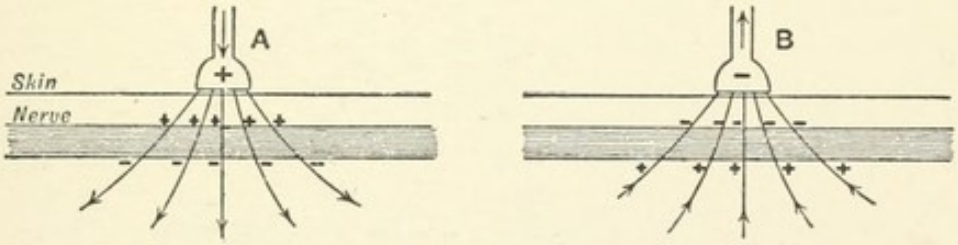


FIG. 335 A.—Diagram of Skin and Subjacent Nerve. *A*, the positive electrode or physical anode; *B*, the negative electrode or physical cathode. Signs, + physiological anodes; signs − physiological cathodes. (After Waller.)

them to the tissues below. Thus it happens that in that part of the nerve beneath either the physical anode or cathode, groups of physiological anodes and cathodes are found.

The contraction which occurs when the current is closed (*closing contraction*) represents irritation at the physiological *cathode*, while the *opening contraction* represents irritation at the physiological *anode*. Since there are physiological anodes and cathodes beneath each electrode, one or more of four conditions may arise:

1. *Anodic closing contraction, i.e.*, the effect of the change developed at the physiological cathode, beneath the physical anode (positive pole).

2. *Anodic opening contraction, i.e.*, the effect of the change developed at the physiological anode, beneath the physical anode (positive pole).

3. *Cathodic closing contraction, i.e.*, the effect of the change developed at the physiological cathode, beneath the physical cathode (negative pole).

4. *Cathodic opening contraction, i.e.*, the effect of the change developed at the physiological anode, beneath the physical cathode (negative pole).

The following abbreviations of these contractions are used: ACC, AOC, KCC, KOC.

The closing contractions, KCC and ACC, are stronger than the opening contractions, KOC and AOC. Of the closing contractions, KCC is stronger than ACC. Of the opening contractions, AOC is stronger than KOC. These facts are also shown in a table of the effects of gradually increasing the strength of the current.

Weak Currents.	Medium Currents.	Strong Currents.
KCC	KCC	KCC
——	ACC	ACC
——	AOC	AOC
——	——	KOC

Sometimes AOC is stronger than ACC.

In diseases which cause degeneration of the nerves going to a muscle, stimulation causes results different from the above, and we get what is known as the *reaction of degeneration.*

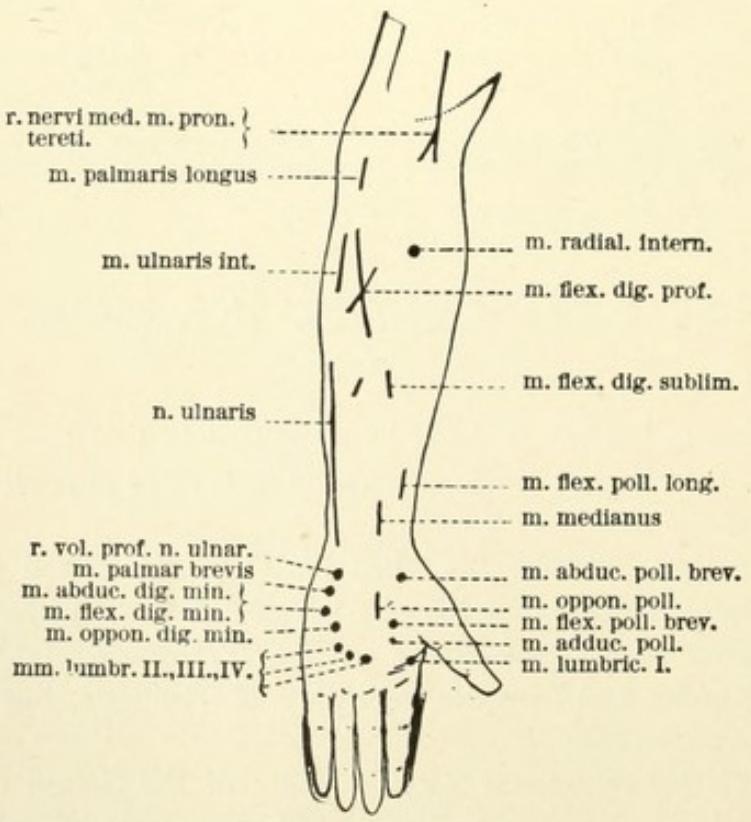


FIG. 336.—Figure Showing Motor Points in the Forearm.

The intensity of the anodic or cathodic effects is increased by using small electrodes, and decreased by electrodes of large surface. In fact in practice it is usual to apply the indifferent electrode to an extended surface, thus reducing its effect below the stimulating intensity. This gives only one active stimulating electrode and is known as the method of unipolar stimulation.

SOME SPECIAL COORDINATED MOTOR ACTIVITIES.

I. LOCOMOTION.

The greater number of the more important muscular actions of the human body, those, namely, which are arranged harmoniously so as to subserve some definite purpose in the animal economy, are described in various parts of this work in the sections which treat of the physiology of the processes by which these muscular actions are resisted or carried out. There are, however, some very important and somewhat complicated muscular acts which may be best described in this place.

Walking. The coordinated movements of the body are carried out by the skeletal muscles acting on the skeletal elements as a system of levers. Even the bones of the skull are levers in so far as their relations to muscles are concerned.

Examples of the three orders of levers in the Human Body. All levers have been divided into three kinds, according to the relative position of the *power*, the *weight* to be moved, and the *axis of motion* or *fulcrum*. In a lever of the *first* kind the *power* is at one extremity of the lever, the *weight* at the other, and the *fulcrum* between the two. If the initial letters only of the *power*, *weight*, and *fulcrum* be used, the arrangement will stand thus: P. F. W. A poker as ordinarily used, or the bar in figure 337, may be cited as an example of this variety of lever; while, as an instance in which the bones of the human

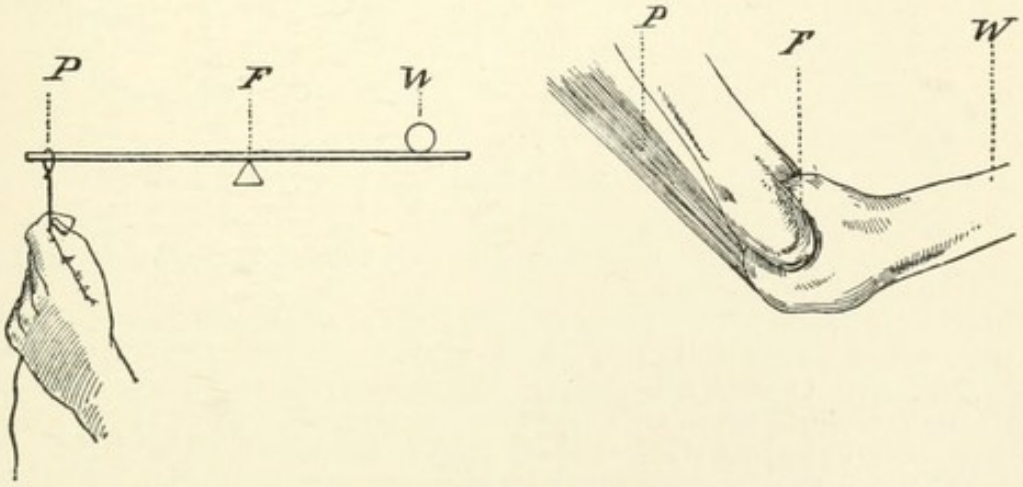


FIG. 337.

skeleton are used as a lever of the same kind, may be mentioned the act of raising the body from the stooping posture by means of the hamstring muscles attached to the tuberosity of the ischium or of the triceps which extends the forearm by action at the elbow, figure 337.

In a lever of the second kind, the arrangement is thus: P. W. F.; and this leverage is employed in the act of raising the handles of a wheelbarrow, or in stretching an elastic band, as in figure 338. In the human body the act of opening the mouth by depressing the lower jaw is an example of the same kind—the tension of the muscles which close the jaw representing the weight, figure 338.

In a lever of the third kind the arrangement is, F. P. W., and the act of raising a pole, as in figure 339, is an example. In the human body there are numerous examples of the

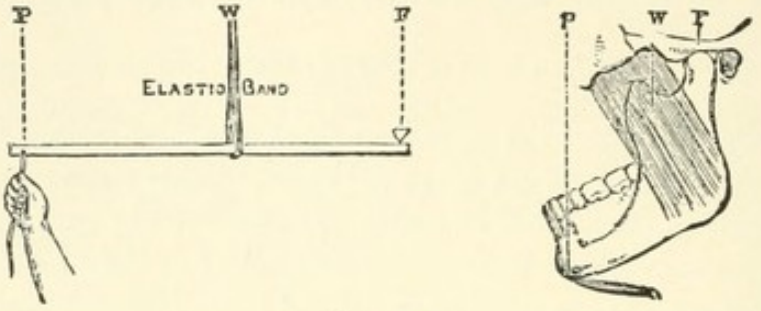


FIG. 338.

employment of this kind of leverage. The act of bending the forearm may be mentioned as an instance, figure 339. The act of biting is another example.

At the ankle we have examples of all three kinds of lever. 1st kind—Extending the foot. 3d kind—Flexing the foot. In both these cases the foot represents the weight: the ankle joint the fulcrum, the power being the calf muscles in the first case and the tibialis anticus in the second case. 2d kind—When the body is raised on tiptoe. Here

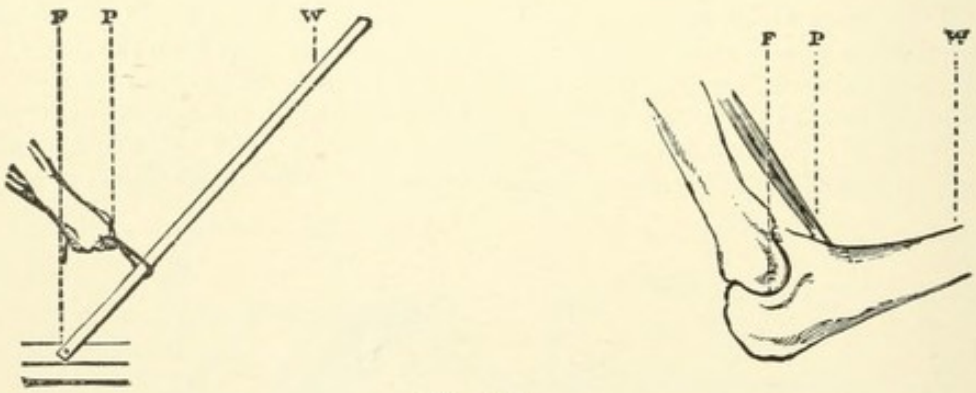


FIG. 339.

the tip of the toe is the fulcrum, the weight of the body acting at the ankle joint the weight, and the calf muscles the power.

In the human body, levers are most frequently used at a disadvantage as regards power, the latter being sacrificed for the sake of a greater range of motion. Thus in the diagrams of the first and third kinds it is evident that the power is so close to the fulcrum that great force must be exercised in order to produce motion. It is also evident, however, from the same diagrams, that by the closeness of the power to the fulcrum a great range of movement can be obtained by means of a comparatively slight shortening of the muscular fibers.

In the act of walking, almost every voluntary muscle in the body is brought into play, either directly for purposes of progression, or indirectly for the proper balancing of the head and trunk. The muscles of the arms are

least concerned; but even these are for the most part instinctively in action to some extent.

Among the chief muscles engaged directly in the act of walking are those of the calf, which, by pulling up the heel, pull up also the astragalus, and with it, of course, the whole body, the weight of which is transmitted through the tibia to this bone, figure 340. When starting to walk, say with the left leg, this raising of the body is not entirely dependent on the muscles of the left calf, but the trunk is thrown forward in such a way that it would fall prostrate were it not that the right foot is brought forward and planted on the ground to support it. Thus the muscles of the left calf are assisted in their action by those muscles on the front of the trunk and legs which, by their contraction, pull the body forward; and, of course, if the trunk form a slanting line, with the inclination forward, it is plain that when the heel is raised by the calf muscles, the whole body will be raised, and pushed obliquely forward and

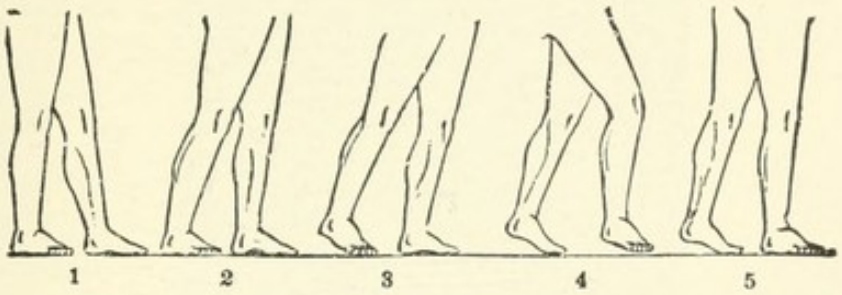


FIG. 340.

upward. The successive acts in taking the first step in walking are represented in figure 340, 1, 2, 3, etc.

Now it is evident that by the time the body has assumed the position No. 3, it is time that the right leg should be brought forward to support it and prevent it from falling prostrate. This advance of the right leg is effected partly by its mechanically swinging forward, pendulum-wise, and partly by muscular action; the muscles used being—1, those on the front of the thigh, which bend the thigh forward on the pelvis, especially the rectus femoris, with the psoas and the iliacus; 2, the hamstring muscles, which slightly bend the leg on the thigh; and, 3, the muscles on the front of the leg, which raise the front of the foot and toes, and so prevent the latter in swinging forward from striking the ground.

The second part of the act of walking, which has been just described, is shown in the diagram, 4, figure 340.

When the right foot has reached the ground the action of the left leg has not ceased. The calf muscles of the latter continue to act, and, by pulling up the heel, throw the body still more forward over the right leg, now bearing nearly the whole weight, until the time when the left leg should again swing forward, and the left foot be planted on the ground to prevent the body from falling

prostrate. As at first, while the calf muscles of one leg and foot are preparing, so to speak, to *push* the body forward and upward from behind by raising the heel, the muscles on the front of the trunk and the same leg (and of the other leg, except when it is swinging forward (are helping the act by pulling the legs and trunk, so as to made them incline forward, the rotation in the inclining occurring mainly at the ankle joint. Two main kinds of leverage, are, therefore, employed in the act of walking, and if this idea be firmly grasped, the details will be understood with comparative ease. One kind of leverage employed in walking is essentially the same with that employed in pulling forward the pole, as in figure 339. And the other, less exactly, is that employed in raising the handles of a wheelbarrow. Now, supposing the lower end of the pole to be

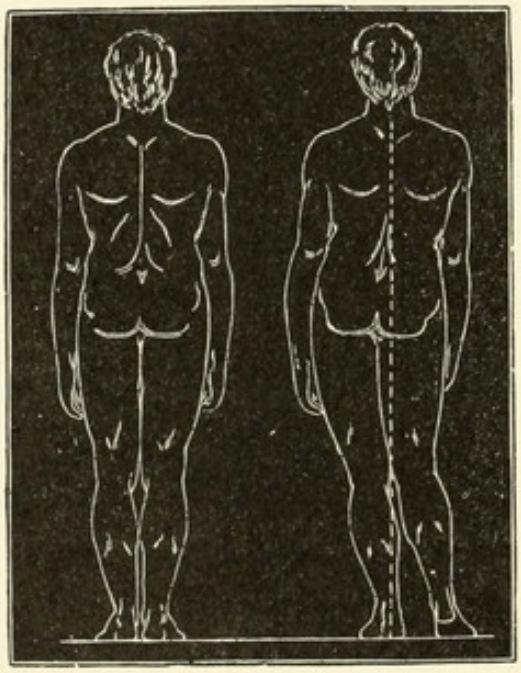


FIG. 341.

placed in the barrow, we should have a very rough and inelegant, but not altogether bad representation of the two main levers employed in the act of walking. The body is pulled forward by the muscles in front, much in the same way that the pole might be by the force applied at P, while the raising of the heel and pushing forward of the trunk by the calf muscles are roughly represented on raising the handles of the barrow. The manner in which these actions are performed alternately by each leg, so that one after the other is swung forward to support the trunk, which is at the same time pushed and pulled forward by the muscles of the other, may be gathered from the previous description.

There is one more thing to be especially noticed in the act of walking. Inasmuch as the body is being constantly supported and balanced on each leg alternately, and therefore on only one at the same moment, it is evident that there must be some provision made for throwing the center of gravity over the

line of support formed by the bones of each leg, as, in its turn, it supports the weight of the body. This may be done in various ways, and the manner in which it is effected is one element in the differences which exist in the walking of different people. Thus it may be done by an instinctive slight rotation of the pelvis on the head of each femur in turn, in such a manner that the center of gravity of the body shall fall over the foot of this side. Thus when the body is pushed onward and upward by the raising, say, of the *right* heel, as in figure 340, 3, the pelvis is instinctively by various muscles made to rotate on the head of the left femur at the acetabulum, to the left side, so that the weight may fall over the line of support formed by the left leg at the time that the right leg is swinging forward, and leaving all the work of support to fall on its fellow. Such a "rocking" movement of the trunk and pelvis, however, is accompanied by a movement of the whole trunk and leg over the foot which is being planted on the ground, figure 341, the action being accompanied with a compensatory outward movement at the hip, more easily appreciated by looking at the figure (in which this movement is shown exaggerated) than from the description.

Thus the body in walking is continually rising and swaying alternately from one side to the other, as its center of gravity has to be brought alternately over one or the other leg; and the curvatures of the spine are altered in correspondence with the varying position of the weight which it has to support. The extent to which the body is raised or swayed differs much in different people.

In walking, one foot or the other is always on the ground. The act of **leaping** or **jumping** consists in so sudden a raising of the heels by the sharp and strong contraction of the calf muscles that the body is jerked off the ground. At the same time the effect is much increased by first bending the thighs on the pelvis, and the legs on the thighs, and then suddenly straightening out the angles thus formed. The share which this action has in producing the effect may be easily known by attempting to leap in the upright posture, with the legs quite straight.

Running. Running is performed by a series of rapid low jumps produced by each leg alternately; so that, during each complete muscular act concerned, there is a moment when both feet are off the ground.

In all these cases, however, the description of the manner in which any given effect is produced, can give but a very imperfect idea of the infinite number of combined and harmoniously arranged muscular contractions which are necessary for even the simplest acts of locomotion.

II. THE PRODUCTION OF THE VOICE.

Before commencing the consideration of the Nervous System and the special Senses it will be convenient to consider first speech, the production of the human voice, and the physiology of the larynx as a muscular apparatus.

The Larynx. In nearly all air-breathing vertebrate animals there are arrangements for the production of sound, or *voice*, in some parts of the respiratory apparatus. In many animals, the sound admits of being variously modified and altered during and after its production; and, in man, one such modification occurring in obedience to dictates of the cerebrum, is *speech*.

It has been proven by observations on living subjects, by means of the laryngoscope, as well as by experiments on the larynx taken from the dead body, that the sound of the human voice is the result of the vibration of the inferior laryngeal ligaments, or the true vocal cords which bound the *glottis*, caused by currents of expired air impelled over their edges. If a free opening exists in the trachea, the sound of the voice ceases, but it returns if the opening is closed. An opening into the air-passages above the glottis, on the contrary, does not prevent the voice being produced. By forcing a current of air through the larynx in the dead subject, clear vocal sounds are elicited, though the epiglottis, the upper ligaments of the larynx or false vocal cords, the ventricles between the upper ligaments and the inferior ligaments, and the upper part of the arytenoid cartilages, be all removed. But the true vocal cords must remain entire with their points of attachment, and be kept tense and so approximated that the fissure of the glottis may be narrow.

The vocal ligaments or cords, therefore, are regarded as the proper organs for the production of vocal sounds. The modifications of these sounds are effected, as will be presently explained, by other parts, viz., by the tongue, teeth, lips, etc. The structure of the vocal cords is adapted to enable them to vibrate like tense membranes, for they are essentially composed of elastic tissue; and they are so attached to the cartilaginous parts of the larynx that their position and tension can be variously altered by the contraction of the muscles which act on these parts.

Thus it will be seen that the larynx is the organ of voice. It may be said to consist essentially of the two vocal cords and the various cartilaginous, muscular, and other apparatus by means of which not only can the aperture of the larynx (rima glottidis) be closed against the entrance and exit of air to or from the lungs, but also by means of which the cords themselves can be *stretched* or *relaxed*, brought together and separated in accordance with the conditions that may be necessary for the air in passing over them to set them vibrating to produce the various sounds. Their action in respiration has been already referred to.

Anatomy of the Larynx. The principal parts entering into the formation of the larynx, figures 342 and 343, are—the thyroid cartilage; the cricoid cartilage; the two arytenoid cartilages; and the two true vocal cords. The epiglottis, figure 343, has but little to do with the voice, and is chiefly useful in protecting the upper part of the larynx from the entrance of food and drink in deglutition. The false vocal cords and the ventricle of the larynx, which is a space between the false and the true cord of either side, need be only referred to.

Cartilages. *a*, The *thyroid* cartilage, figure 342, 1 to 4, does not form a complete ring

around the larynx, but only covers the front portion. *b*, The *cricoid* cartilage, figure 342, 5, 6, on the other hand, is a complete ring; the back part of the ring being much broader than the front. On the top of this broad portion of the cricoid are, *c*, the *arytenoid* cartilages, figure 342, 7, the connection between the cricoid below and arytenoid cartilages

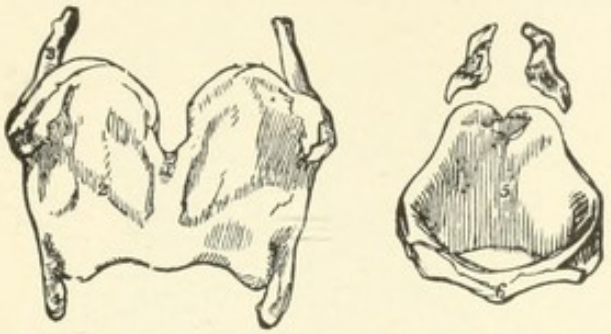


FIG. 342.—Cartilages of the Larynx Seen from the Front. 1 to 4, Thyroid cartilage; 1, vertical ridge or pomum Adami; 2, right ala; 3, superior, and 4, inferior cornu of the right side; 5, 6, cricoid cartilage; 5, inside of the posterior part; 6, anterior narrow part of the ring; 7, arytenoid cartilages. ×¾.

above being a joint with synovial membrane and ligaments, the latter permitting tolerably free motion between them.

Joints and Ligaments. The thyroid cartilage is also connected with the cricoid, not only by ligaments, but also by joints with synovial membranes; the lower *cornua* of the thyroid clasping the cricoid between them, yet not so tightly but that the thyroid can re-

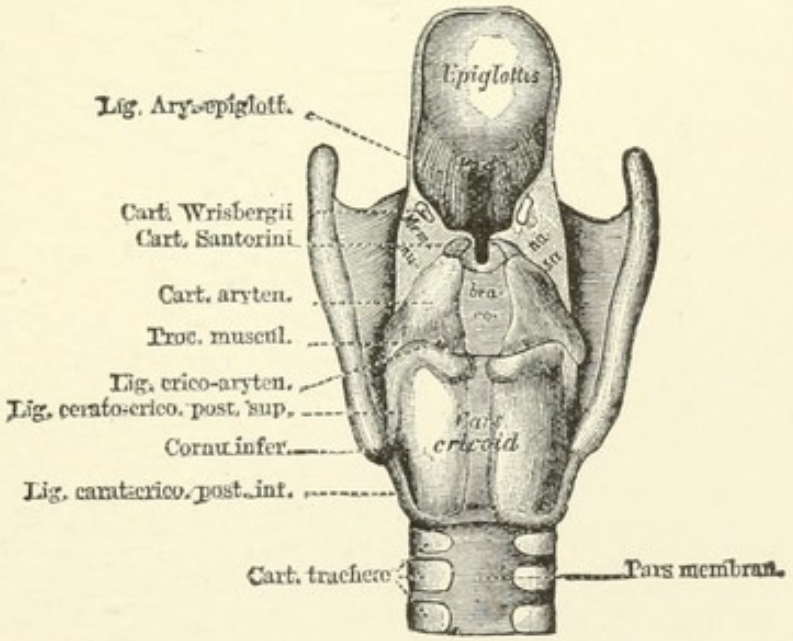


FIG. 343.—The Larynx as Seen From Behind after Removal of the Muscles. The cartilages and ligaments only remain. (Stoerk.)

volve, within a certain range, around an axis passing transversely through the two joints. The vocal cords are attached behind to the front portion of the base of the arytenoid cartilages, and in front to the re-entering angle at the back part of the thyroid; it is evident, therefore, that all movements of either of these cartilages must produce an effect on them of some kind or other. Inasmuch, too, as the arytenoid cartilages rest on the top of the back portion of the cricoid cartilage, and are connected with it by capsular and other ligaments, all movements of the cricoid cartilage must move the arytenoid cartilages, and also produce an effect on the vocal cords.

Intrinsic Muscles. The intrinsic muscles of the larynx are so connected with the laryngeal cartilages that by their contraction alterations in the condition of the vocal cords and glottis are produced. They are usually divided into four classes according to their action, viz., into *abductors*, *adductors*, *sphincters*, and *tensors*. The Abductors, the *crico-arytenoidei*, widen the glottis, by separating the cords; the Adductors, consisting of the *thyro-ary-epiglottici*, the *arytenoideus posticus seu transversus*, the *thyro-arytenoidei externi*,

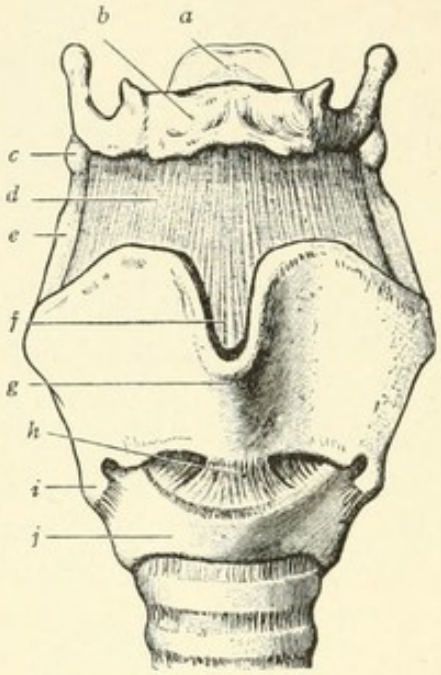


FIG. 344.—The Cartilages and Ligaments of the Larynx, Viewed from the Front. *a*, Epiglottis; *b*, hyoid bone; *c*, cartilago tritica; *d*, thyro-hyoid membrane; *e*, superior cornu of thyroid cartilage; *f*, thyroid notch; *g*, pomum Adami; *h*, crico-thyroid membrane; *i*, inferior cornu of thyroid cartilage; *j*, cricoid cartilage. (Cunningham.)

the *crico-arytenoidei laterales*, and the *thyro-arytenoidei interni*, approximate the vocal cords, diminish the rima glottidis, and act generally as sphincters and supporters of the glottis. Finally, the tensors of the cords put the cords on the stretch, with or without elongating them; the tensors are the *crico-thyroidei* and the *thyro-arytenoidei interni*.

The attachments and the action of the muscles will be readily understood from the following table. All the muscles are in pairs except the arytenoideus posticus.

TABLE OF THE SEVERAL GROUPS OF THE INTRINSIC MUSCLES OF THE LARYNX AND THEIR ATTACHMENTS.

GROUP.	MUSCLE.	ATTACHMENTS.	ACTION.
I. **Abductors.**	Crico-arytenoidei postici.	This pair of muscles arises, on either side, from the posterior surface of the corresponding half of the cricoid cartilage. From this depression their fibers converge on either side upward and outward to be inserted into the outer angle of the base of the arytenoid cartilages behind the crico-arytenoidei laterales.	Draw inward and backward the outer angle of arytenoid cartilages, and so rotate outward the processus vocalis and widen the glottis.

Group.	Muscle.	Attachments.	Action.
II. and III. Adductors and Sphincters.	In three layers:		
	a. *Outer layer*, Thyro-ary-epiglottici.	A pair of muscles. Flat and narrow, which arise on either side from the processus muscularis of the arytenoid cartilage, then passing upward and inward cross one another in the middle line to be inserted into the upper half of the lateral border of the opposite arytenoid cartilage and the posterior border of the cartilage of Santorini. The lower fibers run forward and downward to be inserted into the thyroid cartilage near the commissure. The fibers attached to the cartilage of Santorini are continued forward and upward into the ary-epiglottic fold.	Help to narrow or close the rima glottidis.
	b. *Middle layer.* i. Arytenoideus posticus.	A single muscle. Half-quadrilateral, attached to the borders of the arytenoid cartilages, its fibers running horizontally between the two.	Draws together the arytenoid cartilages and also depresses them. When the muscle is paralyzed, the inter-cartilaginous part of the cords cannot come together.
	ii. Thyro-arytenoidei externi.	A pair of muscles. Each of which consists of three chief portions. The lower and principal fibers arise from the lower half of the internal surface of the thyroid cartilage, close to the angle, and from the fibrous expansion of the crico-thyroid ligament, and are inserted into the lateral border of the arytenoid cartilage. The inner fibers to the lower half of this border, and the outer fibers into the upper half, some pass to the cartilage of Wrisberg and the ary-epiglottic fold.	
	iii. Crico-arytenoidei laterales.	A pair of muscles. They arise on either side from the middle third of the upper border of the cricoid cartilage and are inserted into the whole anterior margin of the base of the arytenoid cartilage. Some of their fibers join the thyroid-ary-epiglottici.	Approximate the vocal cords by drawing the processus muscularis of the arytenoid cartilages forward and downward and so rotate the processus vocalis inward.
	c. *Innermost layer*, Thyro-arytenoidei interni.	A pair of muscles. They arise on either side, internally from the angle of the thyroid cartilage, internal to the last described muscle, b. iii., and running parallel to and in the substance of the vocal cords are attached posteriorly to the processus vocalis and to the outer surface of the arytenoid cartilages.	Render the vocal cords tense and rotate the arytenoid cartilages and approximate the processus vocalis.

Group.	Muscle.	Attachments.	Action.
IV. Tensors.	Crico-thyroidei.	A pair of fan-shaped muscles attached on either side to the cricoid cartilage below; from the mesial line in front for nearly one-half of its lateral circumference backward the fibers pass upward and outward to be attached to the lower border of the thyroid cartilage and to the front border of its lower cornea.	The thyroid cartilage being fixed by its extrinsic muscles, the front of the cricoid cartilage is drawn upward, and its back, with the arytenoids attached, is drawn down. Hence the vocal cords are elongated antero-posteriorly and put upon the stretch. Paralysis of these muscles causes an inability to produce high notes.
	Thyro-arytenoidei interni.	The most posterior part is almost a distinct muscle and its fibers are all but horizontal: sometimes this muscle is described as consisting of two layers, superficial with cortical fibers, deep with oblique fibers, described under Group III.	

Nerve Supply. The sensory filaments of the *superior laryngeal branch* of the vagus supply the epithelial lining of the larynx, giving it that acute sensibility by which the glottis is guarded against the ingress of foreign bodies, or of irrespirable gases. The contact of these stimulates the nerve endings; and the sensory nerve impulse conveyed to the medulla oblongata, whether accompanied by sensation or not, arouses motor impulses through the filaments of the *recurrent or inferior laryngeal* branch, which excite contraction of the muscles that close the glottis. Both these branches of the vagi cooperate also in the pro-

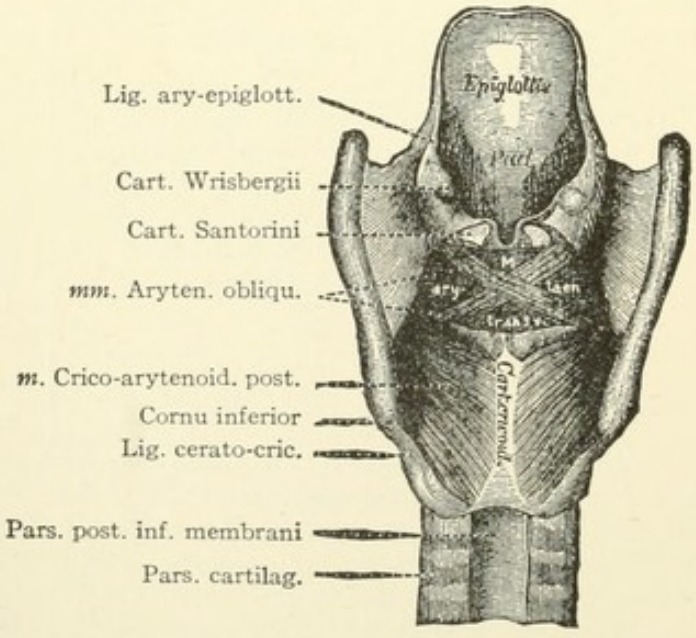


Fig. 345.—The Larynx as Seen from Behind. To show the intrinsic muscles posteriorly. (Stoerk.)

duction and regulation of the voice. The inferior laryngeal determines the degree of contraction of the muscles that vary the tension of the vocal cords, and the superior laryngeal conveys to the brain the sensation which indicates the state of contraction of these muscles. Both the branches co-operate also in the actions of the larynx in the ordinary slight dilatation and contraction of the glottis in the acts of expiration and inspiration, more evidently in the acts of coughing and other forcible respiratory movements.

The Laryngoscope. This is an instrument employed in investigating the condition of the pharynx, larynx, and trachea. It consists of a large concave mirror with perforated center and of a smaller mirror fixed in a long handle. In use the patient is placed in a chair, a good light (argand burner, or lamp) is arranged on one side of, and a little above his head. The operator fixes the concave mirror round his head in such a manner that

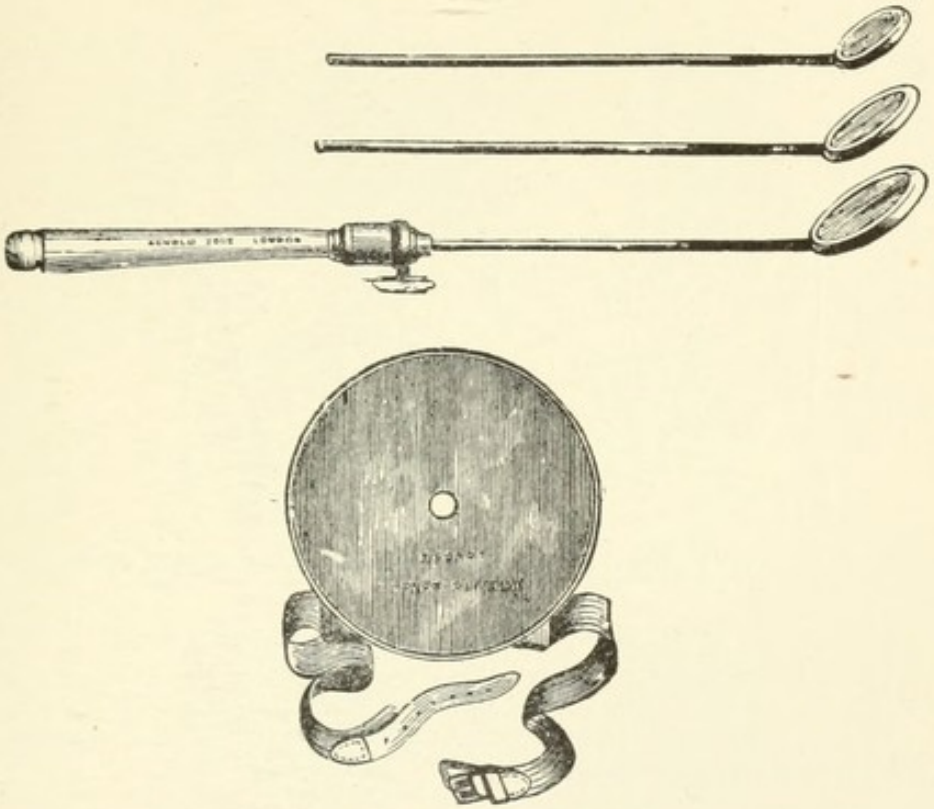


FIG. 346.—The Parts of the Laryngoscope.

he looks through the central aperture with one eye. He then seats himself opposite the patient, and so adjusts the position of the mirror, which is for this purpose provided with a ball and socket joint, that a beam of light is reflected on the lips of the patient.

The patient is now directed to throw his head slightly backward, and to open his mouth; the reflection from the mirror lights up the cavity of the mouth, and by a little alteration of the distance between the operator and the patient the point at which the greatest amount of light is reflected by the mirror—in other words its focal length—is readily discovered. The small mirror fixed in the handle is then warmed, either by holding it over the lamp, or by putting it into a vessel of warm water; this is necessary to prevent the condensation of breath upon its surface. The degree of heat is regulated by applying the back of the mirror to the hand or cheek, when it should feel warm without being painful.

After these preliminaries the patient is directed to put out his tongue, which is held by the left hand of the operator gently but firmly against the lower teeth by means of a handkerchief. The warm mirror is passed to the back of the mouth, until it rests upon and slightly raises the base of the uvula, and at the same time the light is directed upon it: an inverted image of the larynx and trachea will be seen in the mirror. If the dorsum of the tongue be alone seen, the handle of the mirror must be slightly lowered until the larynx comes into view; care should be taken, however, not to move the mirror upon the

uvula, as it excites retching. The observation should not be prolonged, but should rather be repeated at short intervals.

The structures seen will vary somewhat according to the condition of the parts as to inspiration, expiration, phonation, etc. They are the following: first, and apparently at the posterior part, the *base of the tongue*, immediately below which is the accurate outline of the *epiglottis*, with its cushion or tubercle, figure 348. Then are seen in the central line the *true vocal cords*, white and shining in their normal condition. In the inverted image the cords are closer together posteriorly. Between them is left an open slit, narrow while a high note is being sounded, wide during a deep inspiration. On each side of the true vocal cords, and on a higher level, are the *false vocal cords*. Still more externally than the false vocal cords is the *aryteno-epiglottidean* fold, in which are situated upon each side

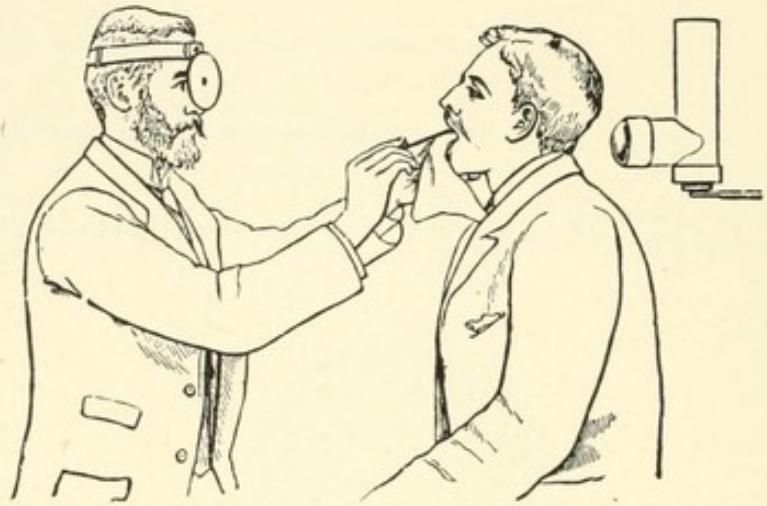


FIG. 347.—To Show the Position of the Operator and Patient when Using the Laryngoscope.

three small elevations; of these the most external is the *cartilage of Wrisberg*, the intermediate is the *cartilage of Santorini*, while in front and somewhat below the preceding is the summit of the *arytenoid cartilage* seen only during deep inspiration. The *rings of the trachea*, and even the bifurcation of the trachea itself, if the patient be directed to draw a deep breath, may be occasionally seen.

Movements of the Vocal Cords. The position of the vocal cords in ordinary tranquil breathing is so adapted by the muscles that the opening of the glottis is wide and triangular, figure 348, *B*, becoming a little wider at each inspiration, and a little narrower at each expiration. On making a rapid and deep inspiration the opening of the glottis is widely dilated, figure 348, *C*, and somewhat lozenge-shaped.

In Vocalization. At the moment of the emission of a note the opening is narrowed, the margins of the arytenoid cartilages being brought into contact and the edges of the vocal cords approximated and made parallel at the same time that their tension is much increased. The higher the note produced, the tenser do the cords become, figure 348, *A;* and the range of a voice depends, of course, in the main, on the extent to which the degree of tension of the vocal cords can be thus altered. In the production of a high note the vocal cords are brought well within sight, so as to be plainly visible with the help of the laryngoscope. In the utterance of low tones, on the other hand, the epiglottis

is depressed and brought over the vocal cords, figure 349. The epiglottis, by being somewhat pressed down so as to cover the superior cavity of the larynx, serves to render the notes deeper in tone and at the same time somewhat duller, just as covering the end of a short tube placed in front of caoutchouc tongues lowers the tone. In no other respect does the epiglottis appear to have any effect in modifying the vocal sounds.

The degree of approximation of the vocal cords also usually corresponds with the height of the note produced; but probably not always, for the width

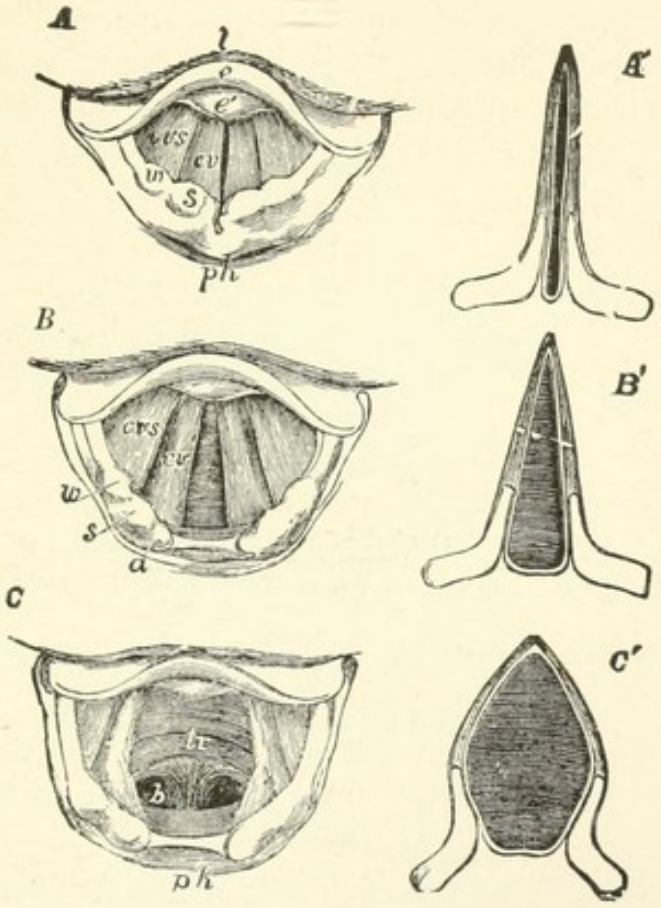


FIG. 348.—Three Laryngoscopic Views of the Superior Aperture of the Larynx and Surrounding Parts. *A*, The glottis during the emission of a high note in singing; *B*, in easy and quiet inhalation of air; *C*, in the state of the widest possible dilatation, as in inhaling a very deep breath. The diagrams *A'*, *B'*, and *C'*, show in horizontal sections of the glottis the position of the vocal ligaments and arytenoid cartilages in the three several states represented in the other figures. In all the figures, so far as marked, the letters indicate the parts as follows, viz.: *l*, the base of the tongue; *e*, the upper free part of the epiglottis; *e'*, the tubercle or cushion of the epiglottis; *ph*, part of the anterior wall of the pharynx behind the larynx; in the margin of the aryteno-epiglottidean fold *w*, the swelling of the membrane caused by the cartilages of Wrisberg; *s*, that of the cartilages of Santorini; *a*, the tip or summit of the arytenoi l cartilages; *cv*, the true vocal cords or lips of the rima glottidis; *cvs*, the superior or false vocal cords; between them the ventricle of the larynx; in *C*, *tr* is placed on the anterior wall of the receding trachea, and *b* indicates the commencement of the two bronchi beyond the bifurcation which may be brought into view in this state of extreme dilatation. (Quain, after Czermak.)

of the aperture has no essential influence on the pitch of the note, as long as the vocal cords have the same tension; only with a wide aperture the tone is more difficult to produce and is less perfect, the rushing of the air through the aperture being heard at the same time.

No true vocal sound is produced at the posterior part of the aperture of the glottis, the part of the aperture which is formed by the space between the arytenoid cartilages. For if the arytenoid cartilages be approximated in such a manner that their anterior processes touch each other, but yet leave an opening behind them as well as in front, no second vocal tone is produced by the passage of the air through the posterior opening, but merely a rustling sound. The pitch of the note produced is the same whether the posterior part of the glottis be open or not.

The Voice in Singing. The laryngeal votes may be produced in three different kinds of sequence. The first is the monotonous, in which the notes have nearly all the same pitch as in ordinary speaking; the variety of the sounds of speech being due to articulation in the mouth. In speaking, occasional syllables receive a higher intonation for the sake of accent. The second mode of sequence is the successive transition from high to low notes, and *vice versa*,

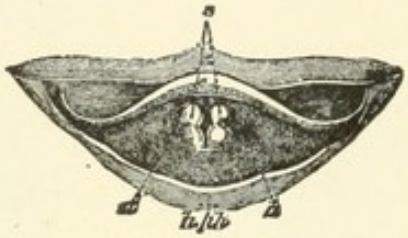


FIG. 349.—View of the Upper Part of the Larynx as Seen by Means of the Laryngoscope during the utterance of a grave note. *c*, Epiglottis; *s*, tubercles of the cartilages of Santorini; *a*, arytenoid cartilages; *z*, base of the tongue; *ph*, the posterior wall of the pharynx. (Czermak.)

without intervals; such as is heard in the crying in children and in the howling and whining of dogs. The third mode of sequence of the vocal sounds is the musical, in which each sound has a determinate number of vibrations, and the numbers of the vibrations in the successive sounds have the same relative proportions that characterize the notes of the musical scale.

The different sounds made by the musical voice are characterized by the three properties of tones in general, viz., the *pitch*, which is dependent on the rate of vibration of the vocal cords; the *loudness*, which depends on the force of the vibration, and the *quality* or *timber*, which is dependent on the resonance of the cavities of the respiratory apparatus, particularly of the mouth, pharynx, and nasal cavities.

The Vocal Range of the Voice. In different individuals this comprehends one, two, or three octaves. In singers, that is, in persons trained in singing, it extends to three or more octaves. But the male and female voices commence and end at different points of the musical scale. The lowest note of the female voice is about an octave higher than the lowest of the male voice; the highest note of the female voice about an octave higher than the highest of the male. The entire scale of the average human voice includes, from the lowest male note to the highest female, about three to three and a half octaves.

Some remarkable musical voices have had a range of three and a half octaves. A principal difference between the male and female voice is, therefore, in their *pitch*. But they are also distinguished by the quality of the *tone*. The voices of men and of women differ among themselves, both in the general pitch and in the quality. There are two kinds of male voices, technically called the *bass* and *tenor*, and two of female voices, the *contralto* and *soprano*, all differing from each other in general pitch. The bass voice reaches lower than the tenor, and its strength lies in the low notes. The contralto voice is lower range than the soprano, and is strongest in the lower notes of the female voice. The barytone and mezzo-soprano voices are intermediate in range; the barytone being intermediate between bass and tenor, the mezzo-soprano between the contralto and soprano. The difference in the pitch of the male and the female voices depends primarily on the different size of the larynx and the length of the vocal cords in the two sexes; their relative lengths in men and women are as three to two.

The boy's larynx resembles the female larynx. His vocal cords before puberty are not two-thirds the length of the adult cords; and the angle of the thyroid cartilage is as little prominent as in the female larynx. Boys' voices are *alto* and *soprano*, resembling in pitch those of women, but louder, and differing somewhat from them in tone. But, after the larynx has undergone the change produced during the period of development at puberty, the boy's voice becomes bass or tenor. While the change of form is taking place the voice becomes imperfect, frequently hoarse and crowing, and is unfitted for singing until the readjustment of the larynx is complete and the muscles which control the vocal cords are again coordinated. In eunuchs who have been deprived of the testes before puberty, the voice does not undergo this change. The voice of most old people is deficient in tone, unsteady, and more restricted in extent. The first defect is owing to the ossification of the cartilages of the larynx and the altered condition of the vocal cords; the want of steadiness arises from the loss of nervous power and command over the muscles, the result of which is here, as in other parts, a tremulous movement. These two causes combined render the voices of old people void of tone, unsteady, and weak.

Most persons have the power, if at all capable of singing, of modulating their voices through a double series of notes of different character: namely, the notes of the natural voice, or *chest-notes*, and the *falsetto notes*. The natural voice, which alone has been hitherto considered, is fuller, and excites a distinct sensation of much stronger vibration and resonance than the falsetto voice, which has more of a flute-like character.

The Quality of the Voice. The difference in quality of voices, seen when two or more persons sound the same note, is due to differences in resonance in the cavities of the mouth and larynx, also of the nose. The shape of the roof of the mouth, the regularity of the teeth, and the size of the tongue, and the size and clearness of the nasopharynx are all factors. The

size and shape of the larynx and mouth cavity which influence the voice quality can be controiled to some extent during singing, and this is a special point of training in voice culture.

Speech. Besides the musical tones formed in the larynx a great number of other sounds can be produced in the vocal tubes, between the glottis and the external apertures of the air-passages, the combination of which sounds into different groups to designate objects, properties, actions, etc., constitutes language. The languages do not employ all the sounds which can be produced in this manner, the combination between certain sounds being often difficult. Those sounds which are easy of combination enter, for the most part, into the formation of the greater number of languages. Each language contains a certain number of such sounds, but in no one are all brought together. On the contrary, different languages are characterized by the prevalence in them of certain classes of these sounds, while other sounds are less frequent or altogether absent.

Articulate Sounds. The sounds produced in speech, or the articulate sounds, are commonly divided into *vowels* and *consonants:* the distinction between which is that the sounds for the former are generated by the larynx, while those for the latter are produced by interruption of the current of air in some part of the air-passages above the larynx. The term consonant has been given to these because several of them are not properly sounded, except *consonantly with* a vowel. Thus, if it be attempted to pronounce aloud the consonants **b, d,** and **g,** or their modifications, **p, t, k,** the intonation follows them only in their combination with a vowel. To recognize the essential properties of the articulate sounds, it is necessary first to examine them as they are produced in whispering, and then investigate which of them can also be uttered in a modified character conjoined with vocal tone. By this procedure we find two series of sounds: in one the sounds are mute, and cannot be uttered with a vocal tone; the sounds of the other series can be formed independently of voice, but are also capable of being uttered in conjunction with it.

All the vowels can be expressed in a whisper without *vocal tone*, that is, *mutely*. These mute vowel sounds differ, however, in some measure, as to their mode of production, from the consonants. All the mute consonants are formed in the vocal tube above the glottis, or in the cavity of the mouth or nose, by the mere rushing of the air between the surfaces differently modified in disposition. But the sound of the vowels, even when mute, has its source in the glottis, though its vocal cords are not thrown into the vibrations necessary for the production of voice; and the sound seems to be produced by the passage of the current of air between the relaxed vocal cords. The same vowel-sound can be produced in the larynx when the mouth is closed, the nostrils being open, and the utterance of all vocal tone avoided. The sound, when the mouth is open, is so modified by varied forms of the oral cavity as to assume the characters of the vowels **a, e, i, o, u,** in all their modifications

The cavity of the mouth assumes the same form for the articulation of each of the mute vowels as for the corresponding vowel when vocalized; the only difference in the two cases lies in the kind of sound emitted by the larynx. It has been pointed out that the conditions necessary for changing one and the same sound into the different vowels are differences in the size of two parts—the oral canal and the oral opening; and the same is the case with regard to the mute vowels. By oral canal is meant here the space between the tongue and palate: for the pronunciation of certain vowels both the opening of the mouth and the space just mentioned are widened; for the pronunciation of other vowels both are contracted; and for others one is wide, the other contracted. Admitting five degrees of size, both of the opening of the mouth and of the space between the tongue and palate, Kempelen thus states the dimensions of these parts for the following vowel sounds:

Vowel.	Sound.	Size of Oral Opening.	Size of Oral Canal.
a	as in "far"	5	3
a	" "name"	4	2
e	" "theme"	3	1
o	" "go"	2	4
oo	" "cool"	1	5

Another important distinction in articulate sounds is that the utterance of some is only of momentary duration, taking place during a sudden change in the conformation of the mouth, and being incapable of prolongation by a continued expiration. To this class belong **b, p, d,** and the hard **g.** In the utterance of other consonants the sounds may be continuous; they may be prolonged, ad libitum, as long as a particular disposition of the mouth and a constant expiration are maintained. Among these consonants are **h, m, n, f, s, r, l.** Corresponding differences in respect to the time that may be occupied in their utterance exist in the vowel sounds, and principally constitute the differences between long and short syllables. Thus the **a** as in **far** and **fate,** the **o** as in **go** and **fort,** may be indefinitely prolonged; but the same vowels (or more properly different vowels expressed by the same letters), as in **can** and **fact,** in **dog** and **gotten,** cannot be prolonged.

All sounds of the first or explosive kind are insusceptible of combination with vocal tone (*intonation*), and are absolutely mute; nearly all the consonants of the second or continuous kind may be attended with intonation.

The tongue, which is usually credited with the power of speech, plays only a subordinate, although very important, part. This is well shown by cases in which nearly the whole organ has been removed on account of disease. Patients who recover from this operation talk imperfectly, and their voices are considerably modified; but the loss of speech is confined to those letters in the pronunciation of which the tongue is particularly concerned.

Stammering depends on a want of harmony between the action of the muscles (chiefly abdominal) which expel air through the larynx, and that of

the muscles which guard the orifice (rima glottidis) by which it escapes, and of those (of tongue, palate, etc.) which modulate the sound to the form of speech. Over either of the groups of muscles, by itself, a stammerer may have as much power as other persons, but he cannot harmoniously arrange their conjoint actions.

LABORATORY EXPERIMENTS ON MUSCLE AND NERVES.

Physiological experiments on living muscle serve to demonstrate many of the most fundamental particulars of the subject. The muscles, especially of cold-blooded animals, when isolated from the body retain their living attributes for several hours under the ordinary conditions which can be readily supplied in the laboratory. They, therefore, serve as specially favorable experimental material.

The muscles of frogs, turtles, and other cold-blooded animals illustrate practically all the facts which can be shown by the muscles of warm-blooded animals and are therefore most advantageously used.

1. **The Muscle-Nerve Preparation.** The classical muscle-nerve preparation is the gastrocnemius muscle and the sciatic nerve. Prepare it as follows: Kill the frog by pithing. This is done by grasping the frog firmly in one hand and with the other making a cut with a blunt scalpel through the cranium just over the medulla, turning the scalpel so as completely to destroy the medulla. Now take a slender knitting needle, quickly run it up into the cranial cavity to destroy the brain, and down the spinal canal to destroy the cord. After a brief spasmodic contraction of the muscles of practically the entire body, the frog remains limp and motionless. In making the muscle-nerve preparation it is better to isolate the tendon first, then the nerve, and finally the femur. The nerve should be prepared as long as possible and should not be allowed to come in contact with the skin. If the preparation is to be used in a moist chamber, the skin should be entirely removed; if it is to be used in the open air, the skin should be left on. Use care not to stretch the nerve, and protect it from evaporation.

2. **The Irritability of Nerve.** Prepare a muscle nerve with its skin on and do not cut away the foot. Mount it by inserting the femur in a muscle clamp, letting the leg extend vertically upward, and the foot hang over. The nerve should lie along the exposed moist femur, one end being slightly free. Stimulate the nerve in the following ways:

a. *Electrical Stimuli.* Apply the electrodes from the secondary coil of an induction apparatus to the tip of the nerve. When an induction current of sufficient strength is produced, the muscle to which the nerve is attached will give contractions, thus moving the foot. Notice that contractions occur with both make and break induction. Apply the electrodes from the two poles of a

dry battery. When the current of the battery is established a contraction will occur, but does not continue during the time of the flow of the current. When the current is stopped a second contraction occurs. The nerve is irritable to both galvanic and faradic currents.

b. *Mechanical Stimuli.* Pinch the nerve lightly with forceps, or give it a sudden stroke with the scalpel handle. With each mechanical impact there is a single contraction of the muscle.

c. *Thermal Stimuli.* Touch the end of the nerve with a glass rod heated in boiling water. At each time the nerve is brought in contact with the rod there will be muscular contraction, as in the preceding cases. The experiment succeeds better if the nerve comes in contact with the rod for several millimeters of length. If the tip of the nerve has ceased to respond, then snip it off with the scissors, and repeat the experiment on the fresh end.

d. *Chemical Stimulation.* Many chemical substances when brought in contact with living nerve fiber produce nerve impulses. Try crystals of sodium chloride, magnesium sulphate, dilute ammonia, acetic acid, 10 per cent nitric acid, 1 per cent mercuric chloride.

Tabulate your observations on all the forms of stimulation used above, by the following outline:

Kind of Stimulation.	Effect Produced.

3. **Irritability of Muscle.** Repeat the experiments in number 2 above, applying the stimuli, electricity, etc., directly to the muscle substance, choosing as far as possible portions of muscle which do not exhibit nerve fiber. The muscle will usually respond by a contraction to each of the above forms of stimulation.

These tests do not fully demonstrate the direct irritability of muscle substance, since in each case it is possible that nerves may have been stimulated. The nerve influences over the muscle can be eliminated by the use of drugs, as will be shown in the next experiment.

4. **Independent Irritability of Muscle.** The influence of curara on the muscle-nerve preparation is demonstrated as follows: Destroy the brain only of a frog by pithing, taking care not to injure the blood-vessels of the spinal canal. Place the animal on a glass plate with its back up and dissect out the sciatic nerve. Use care not to injure in any way the accompanying femoral artery. Pass a ligature of linen thread under the sciatic and around the muscles and blood-vessels of the leg so as completely to shut off the circulation on

that side. Now inject under the skin of the back three drops of 1 per cent curara, allowing twenty to thirty minutes for absorption. When the drug is completely absorbed, make the following observations:

a. Stimulate the muscles of the ligatured leg, also the muscles of the curarized leg, both will contract.

b. Stimulate the sciatic nerve of the ligated leg below the ligature where it has not come in contact with the curara; also the sciatic of the opposite side, which has come in contact with the curara. Stimulation of the first nerve produces contraction of its muscle; of the second nerve does not produce contraction of its muscle.

From this experiment of Claude Bernard's it is evident that the curara does not destroy the irritability of nerve fiber nor the irritability of the muscle fiber, yet it does destroy the influence of the nerve over the muscle, probably acting as a specific poison for the motor end-plates. If the motor end-plates are destroyed, then forms of stimuli which produce contractions of the muscle must act directly on muscle substance, proving that muscle substance, as such, is irritable.

5. **The Simple Muscle Contraction.** Striated muscle responds to electrical stimuli even of almost instantaneous duration. The response which the muscle gives to a single stimulus is called a simple muscle contraction, and is demonstrated as follows:

Make a muscle-nerve preparation with the tendon isolated and the skin removed, and mount it in a moist chamber, figure 350. Connect the tendon

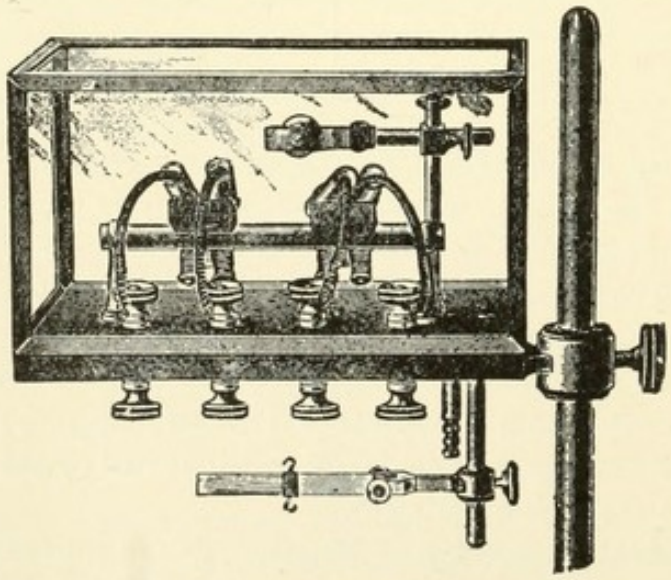


FIG. 350.—Moist Chamber.

with a recording lever by short copper-wire hooks. Lay the nerve across a pair of platinum electrodes, shake a little water on the sides of the cover of the moist chamber, and place it over the preparation so as to prevent drying of the nerve and of the muscle. Arrange an induction coil with its keys, battery,

and electrodes connected as shown in the diagram, figure 351. Set the secondary coil at a position which will give a strong contraction of the muscle, and record this contraction on the smoked paper of an ordinary recording cylinder. Whenever the induction shock is sent through the nerve there will be a single contraction of the muscle. If this contraction is recorded on the drum standing still, then the record will be a vertical line, the height of which can be measured. From it and the arms of the lever the exact shortening of the muscle can be computed. Repeat the stimulus with weaker and weaker currents, until no contraction is produced. As the stimulus becomes weaker a point

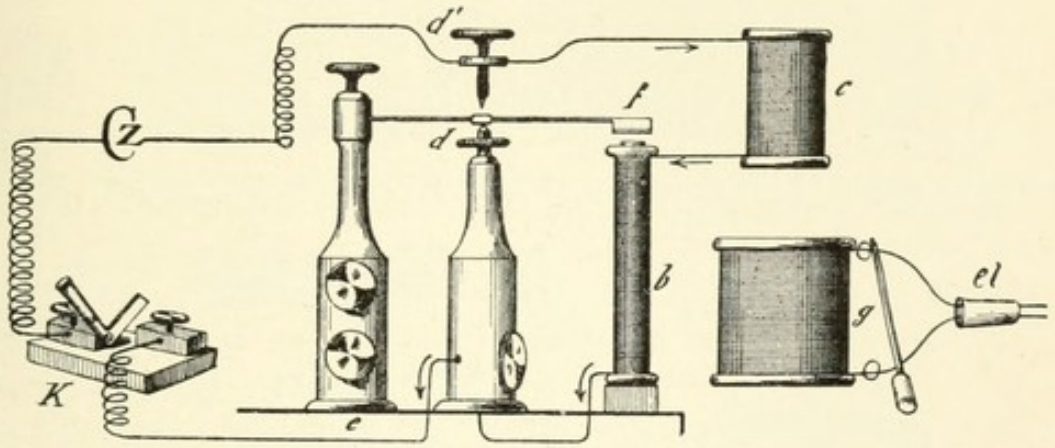


FIG. 351.—Arrangement of Apparatus in the Induction Coil, as Shown for Single Inductions.

is reached at which the contractions rapidly decrease in height and cease altogether. If, on the other hand, the stimulus is stronger the contractions only slightly increase.

Arrange the apparatus so as to stimulate the muscle by an automatic key attached to the recording drum. Adjust the apparatus and lever and revolve the drum at a rapid rate, allowing the automatic key to be opened while the drum is turning at a rapid speed. Or take a record on the pendulum myograph, which is especially constructed for this experiment, figure 352. The muscle contraction now is recorded as a wave which shows some considerable duration in time. Repeat the experiment, introducing a 100 double vibration tuning fork to record the speed of the drum, and taking care to mark the exact point on the record where the automatic key is opened. In this record the muscle contraction shows three different periods or phases. The first, a period of no activity, called the latent period, taking about 0.01 of a second; the second, the period of rapid shortening known as the contraction phase, taking about 0.04 of a second on the average; and the third, a period of rapid relaxation or return to the normal, which takes about 0.05 of a second, see figure 353.

The time and character of the simple muscle contraction will be influenced by: 1, load or tension; 2, the exact temperature; 3, by the amount of work

it has previously done, or fatigue; 4, by the time since it was isolated from the circulation. Perform a series of experiments varying these effects, and record the results by the following outline:

Number of the Experiment.	Muscle Used.	Temperature.	Load.	Total Time of Contraction, in Seconds.	Latent Period, in Seconds.	Contraction Period, in Seconds.	Relaxation Period, in Seconds.

6. **The Relation of the Contraction to the Strength of the Stimulus. Minimal and Maximal Stimuli.** Prepare a muscle-nerve of the frog and mount in the moist chamber and arrange for stimulating the muscle directly by means of the secondary current of the induction coil, with the ap-

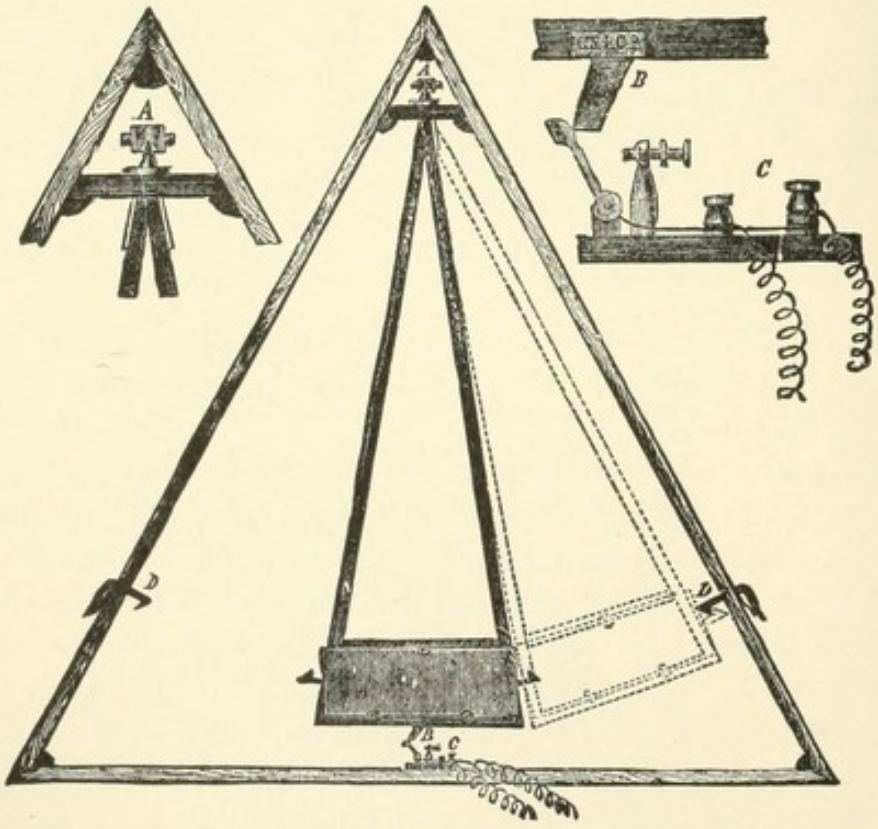


FIG. 352.—Simple Form of Pendulum Myograph and Accessory Parts. *A*, Pivot upon which pendulum swings; *B*, catch on lower end of myograph opening the key, *C*, in its swing; *D*, a spring-catch which retains myograph, as indicated by dotted lines, and on pressing down the handle of which the pendulum swings along the arc to *D* on the left of figure, and is caught by its spring.

paratus adjusted as in figure 351. Prepare a recording cylinder for making vertical records of the contractions. Adjust the writing point of the muscle lever to the drum and move the drum by hand 1 cm. after each succeeding contraction. Set the secondary coil of the induction apparatus so that it will be too weak to produce a stimulus. Now attempt to stimulate the muscle,

then move the induction coil toward the primary 1 cm. at a time and repeat until the first slight contraction appears. Continue to slide the secondary coil toward the primary, stimulate at each new position, moving the drum forward

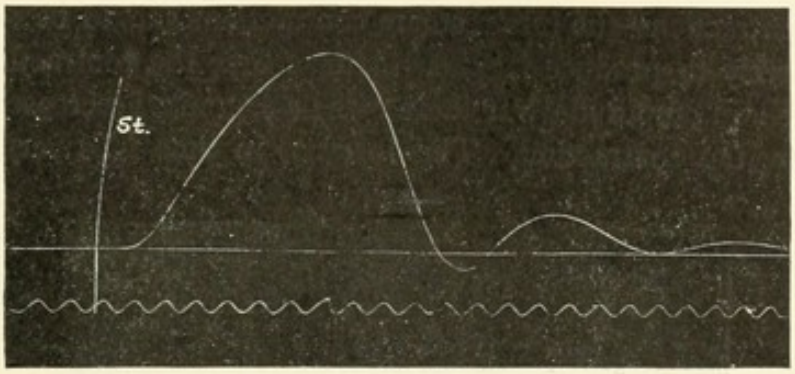


FIG. 353.—Record of a Simple Contraction of the Gastrocnemius of the Frog. Time in .01 of a second. *St*, Moment of stimulation. Record taken on a rapid drum that was provided with an automatic key.

for each stimulus as directed, until a series of contractions is obtained through the range of variation of induction of which the apparatus is capable, usually twenty to thirty contractions.

A typical tracing, figure 326, shows that as the strength of the stimulus is increased the amplitude of the contractions quickly mounts from the minimal to a maximal, after which all further increase in the strength of the stimulus produces contractions of practically the same height. The first perceptible contraction is called the minimal contraction, the strength of the current which produced it a minimal stimulus for that preparation. The contractions of the greatest amount are called maximal contractions. The weakest stimulus which produces a maximal contraction is called the maximal stimulus, and all stronger stimuli supramaximal.

7. **The Effect of Fatigue on the Amplitude of the Simple Muscle Contraction.** Prepare a gastrocnemius muscle for direct stimulation and mount it in a moist chamber. Arrange the induction apparatus for single stimuli. Adjust the recording lever of the muscle to a smoked-paper kymograph and set the speed of the kymograph to revolve at the rate of 1 mm. per second. Now stimulate the muscle with the make induction (short-circuiting the break) once every two seconds. The contractions will be recorded as vertical marks on the drum in regular order, at a distance of 2 mm. apart, hence very slight changes in amplitude are readily detected. The contractions gradually increase in height for the first ten or twenty, the phenomenon of *treppe*, then run for from fifty to one hundred contractions of practically uniform amplitude, after which there is a gradual but sharp decrease known as *fatigue*. Repeat the experiment after ten minutes' rest. The former variations occur now very rapidly, indicating that the fatigue effects are only partially recovered from.

8. **The Effect of Fatigue on the Time of the Simple Contraction.** Prepare a muscle-nerve and mount it in the moist chamber, arrange for the record as directed under 5 above. Make a series of records of the simple contraction when automatically stimulated, recording only every tenth or twentieth contraction—the intermediate contractions should be shunted and are used merely to produce fatigue. After a time the contractions will not only diminish in amplitude, but there will be a gradual increase in the time consumed by the contraction. This increase in time falls very slightly on

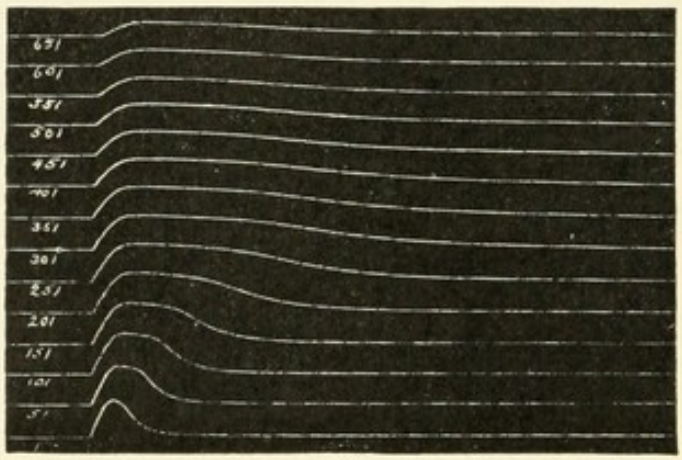


FIG. 354.—Contractions of the Gastrocnemius Muscle to Show Fatigue. The numbers printed on the figure indicate the contraction in the series which is recorded. (Lee.)

the latent period, is more pronounced in the contraction phase, but is very marked in the relaxation phase, figure 354.

9. **Fatigue of Voluntary Muscular Contraction.** The human voluntary muscles are used to demonstrate this experiment. Use a Mosso's ergograph, or any one of its numerous modifications. If the original form is used, then the muscle should be loaded with about 3 kilos, and contractions once a second recorded until the muscle can no longer lift the load. The load may have to be adjusted to the individual, but should be chosen so that exhaustion will be obtained with about fifty contractions. This experiment does not demonstrate complete exhaustion, but merely fatigue down to a certain level. If an apparatus is previously arranged for direct stimulation of the muscles by electric currents it will be found that the contractions of the muscles still occur after the voluntary power is lost, showing that at least a part of the phenomenon, possibly the chief part, is located in the nervous tissue rather than in the muscle substance.

10. **The Effect of Temperature on Muscle Contractions.** Prepare a muscle-nerve and mount it in Porter's latest form of temperature apparatus. Adjust the levers for vertical records on the smoked paper of the kymograph. Begin with a temperature of the tap water and gradually lower the temperature of the preparation by adding small amounts of crushed ice at first, later ice and some salt crystals, to the external chamber. Take care

to lower the external temperature very slowly and gradually,—say about one degree in two minutes. Stimulate the muscle with a supramaximal stimulus twice in rapid succession, for 1° C. of change. Record these contractions as pairs of vertical marks on the drum 1 mm. apart, separating each pair by a space of 1 cm. When 0° C. is reached, or before if the muscle fails to contract at a higher temperature, reverse the direction of the temperature change, gradually but slowly increase it until the muscle goes into heat rigor, which begins at from 38° to 40° C.

While the muscle is entering rigor, move the drum 1 cm. for each degree, as before, so as to record the development of that process.

11. **The Effect of Temperature on the Time of the Simple Contraction.** Repeat the preceding experiment, but record the contractions by the method described in experiment 5 above, recording a contraction for every change of 5° C. Measure the time and amplitude of the different contractions, and the phases of the simple contractions, and tabulate them as shown in experiment 5.

12. **Effect of Load on the Height of the Contraction and on the Work of Voluntary Muscle.** Make a muscle-nerve preparation and arrange it for stimulation, as in experiment 6 above. Set the induction coil of the stimulating apparatus for an effective supramaximal stimulus. Record the contractions as a series of vertical lines on the kymograph, separated by a distance of 1 cm. Begin with the load of the lever only for the first contraction, then increase the load by steps of 20 grams each until the muscle is no longer able to lift the weight used. Support the lever under a tension of 20 grams. Use care that no mechanical changes of the apparatus are recorded on the smoked cylinder. Repeat the experiment on a fresh muscle, but do not support the lever.

The amount of work done by the muscle at each contraction is the product of the load in grams times the height in centimeters. The height of the lift can be obtained in this experiment from the height of the record on the drum and the length of the recording arm and power arm of the lever, in which the length of the recording lever is to the length of the power lever as the height of the record obtained is to the actual shortening of the muscle. Compute the exact amount of work done by each contraction under varying loads, and tabulate on co-ordinate paper. Compare the variation in work done with the variation in amplitude of the contraction.

13. **Tetanus.** A continued contraction of a voluntary muscle can be shown to be a fusion of simple muscle contractions. This is called a tetanus. Prepare a muscle-nerve in the moist chamber and arrange the induction coil for stimulating with a series of rapidly repeated stimuli. The rate of the stimulation is obtained from the tetanometer, a form of key for rapidly interrupting the current, which should be connected with the primary coil instead of the key, *K*, figure 351. Stimulate the muscle at a rate of 10 per

second, record the contractions on the drum moving at a speed of about 2 cm. per second. Use care not to overfatigue the muscle, *i.e.*, stimulate it only 2 or 3 seconds at a time. Repeat this test, increasing the rate of stimulation each time by 5, that is, stimulate at 10, 15, 20, etc., per second. In the first stimulus there will be a series of simple contractions with almost complete intervening relaxations. As the rate is increased these relaxations become less and less until presently a rate is found which produces continuous, apparently uninterrupted contraction. This is a tetanus, the others are incomplete tetani. The frog's gastrocnemius at a temperature of 20° C. is tetanized with a stimulation of from 25 to 35 per second.

14. **Cardiac Muscle.** Cardiac muscle differs from voluntary in that the contractions occur rhythmically and automatically. This is shown

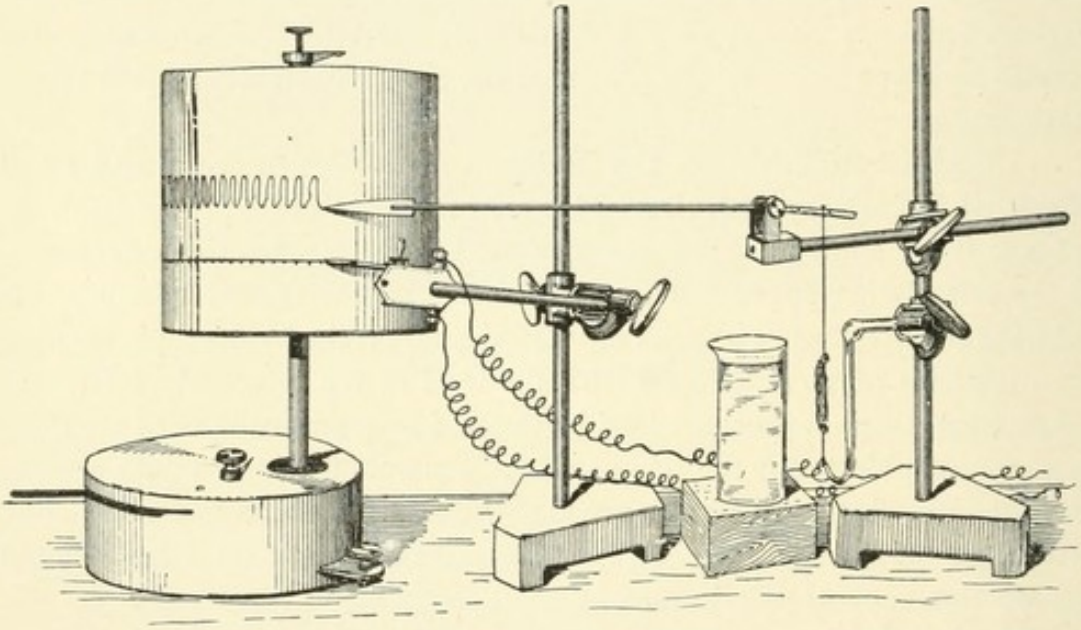


FIG. 354 A.—Arrangement of Apparatus for Studying the Contractions of the Strip of the Apex of the Ventricle.

by the isolated frog's heart, which continues to contract when bathed with blood or salt solution, often for hours. This isolated heart, however, has a complicated local nervous mechanism. The apex of the ventricle of the terrapin's heart is practically free from nerve ganglia and may be used to demonstrate the characteristics of pure cardiac muscle. Cut a strip off the apex of the terrapin's ventricle, as shown in figure 214, and mount it by means of light silk-thread ligatures tied around the two ends of a strip and attached to the apparatus shown in figure 215. When such ventricular strips are immersed in ordinary 0.7 per cent sodium chloride they will begin contractions in a few minutes, twenty minutes or so. The contractions will be regular in rate and will continue through two or three hours, gradually becoming smaller and smaller until the standstill is reached. If the strip is immersed in its own serum it will give only occasional contractions, but it re-

mains irritable and capable of contracting at any moment. If changed to salt solution, the salt solution apparently brings out the automatic rhythm by an increase in its irritability. Portions of the auricle and of the sinus, especially the latter, are more highly rhythmic than portions of the ventricle, due to a specific difference in the muscle cells themselves and not to the nervous mechanism.

Refer to the experiments on cardiac muscle at the end of the chapter on Circulation.

15. **Involuntary Muscle.** Strips of smooth or involuntary muscle, cut from the stomach of a frog or terrapin or from the intestine of a frog, may be used to show the physiology of this character of tissue. Mount a strip in the moist chamber, or in the apparatus shown in figure 354 A, using

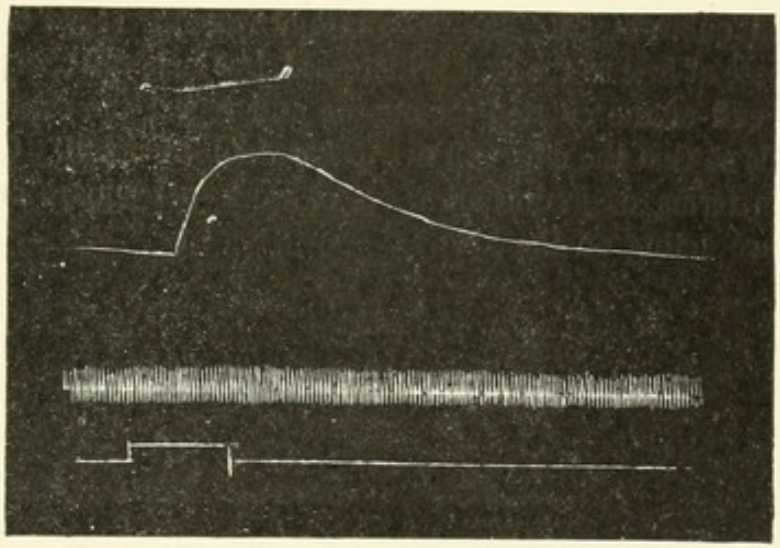


FIG. 355.—Figure Showing the Type of Contraction of a Strip of Muscle from the Stomach of a Frog. The muscle was stimulated with an interrupted current during the time indicated by the signal tracing, immediately below the time tracing. Time in seconds.

care not to load it too heavily; the weight of the ordinary muscle lever may produce too much tension. Stimulate the muscle for one or two seconds with interrupted induction currents of moderate strength. Contractions will follow, usually developing very, very slowly as compared with striated muscle, and lasting through many seconds, from thirty to one hundred seconds. By using very strong inductions occasionally a contraction may be secured with a single stimulus, but single-induction currents as a rule do not produce effective stimuli for smooth muscle, which requires a more slowly developed stimulus.

If the stomach muscle of the frog be used and it be handled with extreme care, it may happen that automatic contractions will develop in the muscle in the moist chamber. If so, these contractions will be found to be slow and of varying amplitude. The terrapin's stomach muscle will ordinarily not show automatic contractions, but by increasing the temperature to about

30° C. automatic contractions will sometimes occur in it. Smooth muscle responds like voluntary muscle to variations in temperature, to fatigue, strength of stimulus, etc., etc.

16. **Ciliary Contractions.** *Ciliated Epithelium.* Make a preparation of ciliated epithelium by cutting out the esophagus of a terrapin or frog, slitting it open longitudinally, and smoothing it out on a cork block. The cilia of this membrane will drive in the direction down the esophagus. Test the rate at which different loads are moved and measure the distance on the preparation as follows: Cut pieces of clean white paper about 4 and 6 mm. square. Select a favorable area on the ciliated surface as long as possible, place the 4 mm. square paper at the beginning of the area, and measure the time which it takes to travel the distance. Measure the speed in terms of seconds per centimeter. Now replace the paper at the point of beginning and load it with small weighed cubes of paraffin. The rate at which the load is carried will slightly increase at first as the load is increased, but later will sharply decrease. Elevate one end of the ciliated membrane and repeat the experiment with different loads so that the cilia will now carry the load uphill. Calculate the work done in terms of gramcentimeters of work per square centimeter of ciliated surface acting on the load.

CHAPTER XIV

THE NERVOUS SYSTEM

The nervous system consists of an extremely complex anatomical mass of nerve cells and fibers. It is usually described as made up of two main divisions, the cerebro-spinal system and the sympathetic. These two divisions must be regarded as parts of one great whole, and in no sense coordinate. The gross subdivision of the nervous system may be given as the following:—first, the cerebro-spinal axis, which consists of matter within the bony cranium and spinal column, constituting the brain and cord. Second, smaller masses for the most part in the abdominal and thoracic cavities, also in the neck and head, and constituting the sympathetic ganglia. Third, the nerves or bundles of nerve fibers which connect the central nerve axis with the periphery and with the sympathetic ganglia. Fourth, there are special peripheral organs in connection with the beginnings and endings of the nerve fibers, the one for receiving nerve stimuli, the other for transmitting stimuli to other tissues. These are properly parts of the nervous system. The peripheral organs for receiving stimuli constitute the sense organs and will be treated in a separate chapter.

I. FUNCTION OF THE NERVE CELL.

The Nerve Cell. The nerve cell, the neurone, may be considered the anatomical and physiological unit of the nervous system. The details of the structure of the nerve cell, both its body and its processes, have already been given in chapter II. It is sufficient to recall that the types of nerve cells found in various parts of the nervous system vary extremely. The peculiar feature, however, consists in the fact that the cell body has one or more processes. Sometimes these processes are short but complexly branched, sometimes they are exceedingly long as compared with the extent of the cell body. The cell processes may or may not be medullated and subdivided into nodes, but the axis-cylinder process is to be regarded as a continuity of the protoplasm of the cell body. In recent years the structure of the cell body and its branches has been very carefully investigated, with the result that we are finding that the intimate structure is very complex. Networks of neurofibrillæ have been described not only in the cell body, but extending throughout the course of the processes and, in fact, from cell to cell. We are not in a position at the present time fully to determine what bearing

these neurofibrillæ have on our accepted theories of nerve function, other than that they are assumed to be the conducting elements.

The Neurone Theory. Our knowledge of the function of the nervous system is best explained on the basis of the neurone theory, which considers the nerve cell as a physiological unit. By this view each gross division of the nervous system is supposed to consist of a large number of individual neurones, each of which is a more or less complete morphological unit capable of carrying on certain functions of its own. Each of these neurones maintains physiological continuity with its associates, presumably by protoplasmic contact rather than by continuity; so that well-marked paths of conduction are possible throughout the extent of the particular mass of

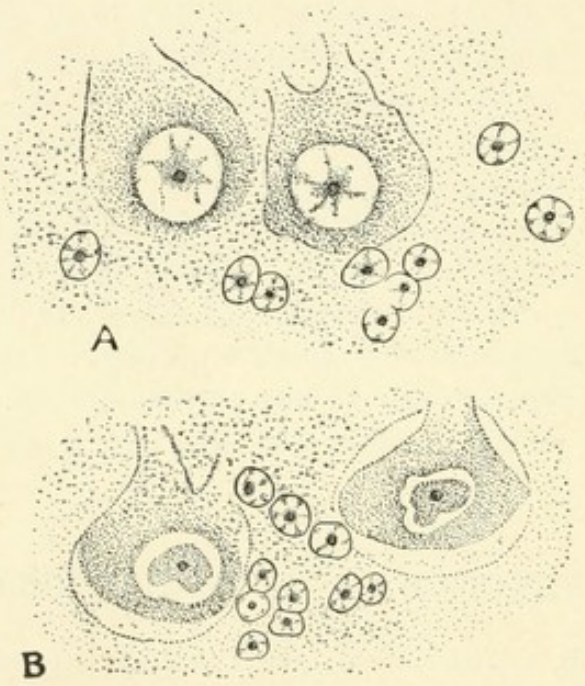


FIG. 356.—Purkinje Cells from the Cerebellum of the Swallow. A, Taken in the morning; B, taken in the evening. (Hodge.)

which the neurone is a part, and throughout the adjacent masses. By this view, paths of conduction are made up of series of individual neurones which are in physiological continuity.

The Characteristics of the Individual Nerve Cell. The function of the nerve cell may be discussed under two headings: The function of the cell body, and the function of the cell processes.

The cell body of the nerve cell is the part that contains the nucleus and is the center of those activities which influence the metabolism of the cell itself. If the cell body be isolated from its processes, the processes will degenerate, while the body continues to live. In other words, the cell body may be considered as the center of those trophic influences which regulate the nutrition of the processes. Although the nerve cell as a whole is in many, perhaps in

most, cases a conducting organ, still those physiological processes which go on in it produce marked changes in the protoplasm of the cell body. Hodge has demonstrated that nerve cells which have been active for several hours, in case of sparrows which have been flying about actively throughout the day, or in bees after a day's work, show marked evidences of fatigue. These evidences

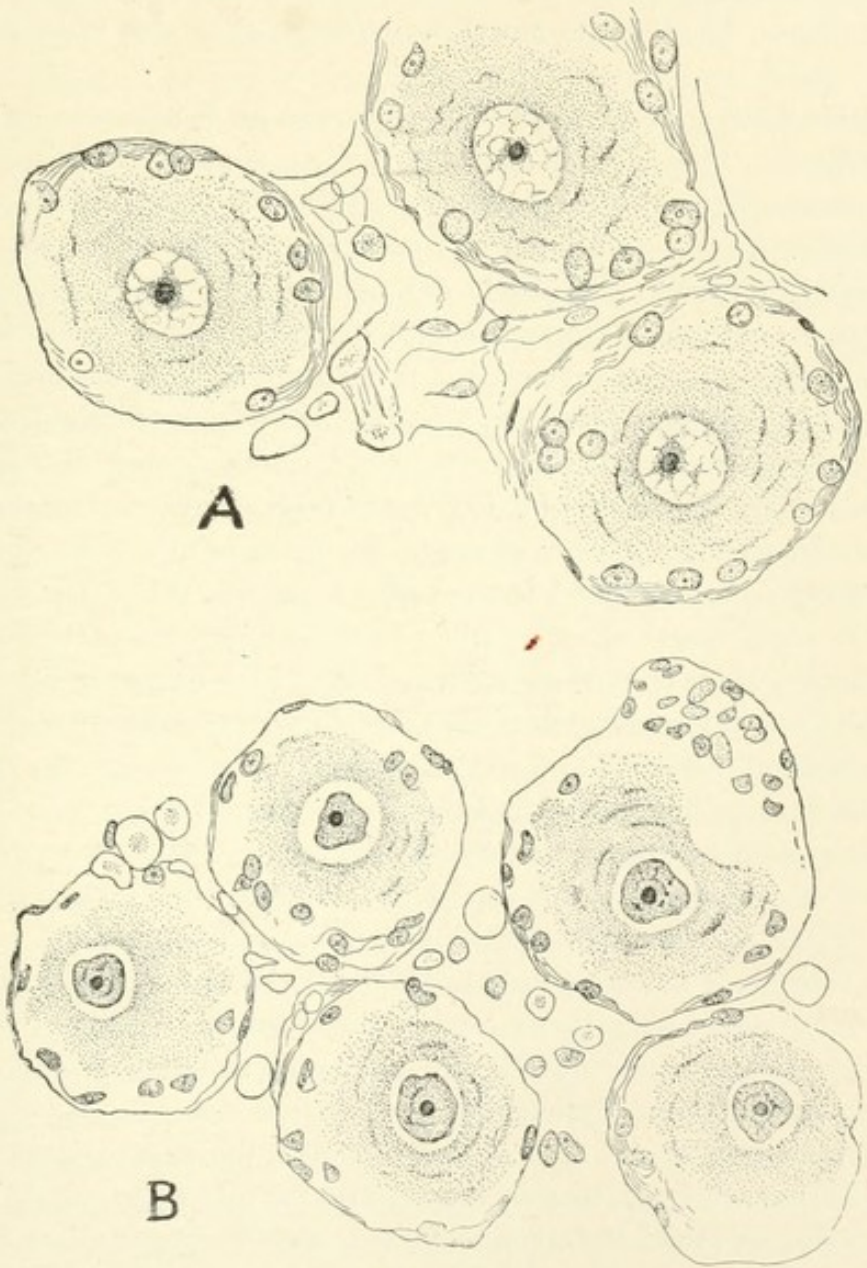


FIG. 356 A.—Spinal Ganglion Cells from the Cat. A, Normal taken before stimulation; B, taken after five hours' stimulation. From the right and left, eight thoracic ganglia. (Hodge.)

consist in the decrease in the size of the nucleus and the appearance of vacuoles in its structure, also in the shrinking of the protoplasm of the cell, which, in case of the cells of the spinal ganglia, draws away from its capsule. If the cells are examined early in the morning, then these fatigue changes will not be present, the cell having recuperated during the rest of the night. It

has also been found that the Nissl granules which are present in the cell body of resting cells decrease in number and show evidence of disintegration in cells that have been stimulated for several hours.

The nerve processes or fibers are primarily conducting structures. But their fibers are susceptible to artificial stimulation, as shown in the previous chapter, that is, they are irritable. They are influenced by certain changes in the environment, but they do not show evidence of fatigue upon prolonged functional activity.

Nutritive Influence of the Cell Body over its Processes—Wallerian Degeneration. The control of the cell body over the nutrition of the cell processes is demonstrated by the changes which occur when these processes are severed from connection with the cell body. Under such conditions the axis-cylinder process completely degenerates. Howell and Huber have followed the degenerative changes in medullated nerve fibers. The medullated fiber in the course of three or four days, in mammals, breaks up into elliptical segments of myelin, containing small fragments of the axis-cylinder. These changes in the cut-off section of nerve occur simultaneously throughout its whole extent. In the course of a few weeks regenerative changes begin, apparently under trophic influence of the nuclei of the primitive sheath. These nuclei increase in number and form small masses of protoplasm which ultimately produce a strand of embryonic protoplasm, which is described as the " band fiber." If the ends of the sectioned nerve have originally been brought together and sutured in place, then the axis-cylinder processes of the portion of the nerve fiber still attached to the cell body will grow down into the peripheral fibers, thus forming new axis-cylinder processes along the course of the band fiber. If the stumps of the nerves are not so brought together, then apparently the band fiber again degenerates, especially in adult tissues, though it has been claimed by Bethe and others that complete regeneration of the peripheral fiber will take place in very young animals. Even if complete regeneration takes place in the peripheral fiber, unless connection is established between it and the central end of the fiber it will ultimately disintegrate and can only temporarily carry on any physiological function.

The central end of the divided nerve, that is, the part maintaining connection with the cell body, usually degenerates for a few nodes only, then regeneration and growth of the original stump proceed. Instances are observed in certain cases where the degeneration of the entire central fiber, including its cell body, takes place. This happens particularly in those relations where the original neurone forms a link in a conducting path.

In conclusion, one may infer that the cell body exercises a nutritive or trophic control over the protoplasm of its branches, just as we have already seen the neurone as a whole exercises trophic control over the nutritive processes taking place in the tissue to which its branches are distributed.

Specific Energy of the Nerve Impulses. We have already discussed the fact that a nerve fiber, also its cell body, is irritable to various forms of mechanical, electrical, etc., stimuli. In the complex differentiation of the nervous system it is found that whatever the form of the external stimulus applied to a nerve the resulting nerve impulse produces the same effects in the central nervous system. This idea has been called the *specific energy of the nerve impulse*, and was first advanced by Johannes Müller.

Transmission of Nerve Impulses through the Nerve Cell. The theory has been advanced that in the nerve cell the primary function of some processes is to carry nerve impulses toward the cell body, and of other processes to carry nerve impulses away from the cell body. At the present time this view is advocated by perhaps the ablest living anatomists and neurologists. The *dendrites* conduct toward the cell body, and the *axones* away from it. That is, the former are cellulipetal, the latter cellulifugal.

Impressions made upon the terminations or upon the trunk of a cellulifugal nerve may cause, *a*, pain or some other kind of general sensation; *b*, special sensation; *c*, reflex action of some kind; or *d*, inhibition or restraint of action. Similarly impressions made upon a cellulipetal nerve may cause, *a*, contraction of muscle (motor nerve); *b*, it may influence nutrition (trophic nerve); *c*, it may influence secretion (secretory nerve); or *d*, inhibit, augment, or stop any other efferent action.

By artificial stimulation nerve impulses can be made to pass in both directions in all classes of nerve processes. That is to say, if a motor axone is stimulated in the middle of its course it will not only convey a nerve impulse to its distribution, but also a nerve impulse will pass back over the fiber to the cell body and out over the dendrites. Normally, in the complex of the body it is probable that such a neurone will be stimulated only at its points of contact with other neurones chiefly through its dendrites, and especially by means of the sensory cells. The dendrites will therefore receive the nerve stimulus, carry it through the cell body to the axone and its distribution. In such cells there is isolated, or uninterrupted, conduction throughout the extent of the neurone. The nerve impulse is able to pass from a given neurone to adjacent ones only at the termination of the axone or its branches, which may be considered as special organs for the transference of the nerve impulses. This activity involves isolated conduction in nerve fibers bound in a common nerve trunk. It has been supposed that the myelin sheath of a medullated nerve acts as an insulator of the axis-cylinder, but this can be only relatively true, for the reason that non-medullated nerves do not possess the myelin sheath. In non-medullated nerves we must suppose that the primitive sheath is sufficient to give insulated conduction, or that it is an inherent property of the axis-cylinder itself to carry the nerve impulse without transmission to adjacent fibers.

We have already, page 470, discussed the rate of transmission of the nerve

impulse in motor nerves. In sensory nerves the rate is said to be somewhat higher; in human nerve from 30 to 42 meters per second.

Physiological Types of Nerve Cells. Many classifications could be made of nerve cells, based on the differences in their functional relations, but at this place attention will be called to only one. Nerve cells may be classified as *afferent* or *sensory*, *efferent* or *motor*, and *connecting* or *transmitting* cells.

Under afferent neurones are classed all those neurones which transmit the effects of external stimuli received through the sense organs, both general and special sense organs. These neurones carry nerve impulses toward the central nervous system, ultimately producing those changes in the cerebral cortex which are associated with states of consciousness.

Under efferent neurones are included all those which transmit nerve impulses from any part of the central nervous system to the muscles, that is, motor nerves; or transmit nerve impulses to the glands, secretory nerves; or that transmit nerve impulse, which inhibit peripheral action, inhibitory nerves.

Under central or transmitting neurones may be included those units which act as connecting links within the central organ, especially within coordinate parts of the central nervous system, between the afferent and efferent neurones.

Nerve Centers. Whenever a number of neurones are gathered in one group to accomplish some specific function it is called a nerve center. The term usually applies to the aggregation of cell bodies and their dendritic processes in contradistinction to nerve trunks. There are aggregations of nerve cells into different specific groups, to which we cannot in every case ascribe a specific function. These groups are not called nerve centers, but are described by the general anatomical term, ganglia. Such ganglia are represented by the sympathetic chain, the spinal-root ganglia, the ganglia of certain cranial nerves, etc. The nerve centers are found in the spinal cord, the medulla, and the higher cranial groups. The medulla is particularly rich in nerve centers. The cerebro-spinal axis is in fact an aggregation of nerve centers of greater or less complexity.

It is by means of the nerve centers that the activities of the differentiated parts of the human body are brought into intimate correlation. The nerve centers exercise their influence through the power of inhibiting or decreasing activity; or, on the other hand, of augmenting or increasing the activity in the peripheral tissues or in other parts of the nervous system. For example, the vagus center regulates the activity of the heart muscle by its power to decrease or inhibit cardiac contractions. This center, we have already found, is in constant tonic activity; that is to say, in constant regulative control of the heart. The cardiac augmentory center, on the other hand, produces just the opposite effect, increasing the activity of the cardiac muscle. What is true for the heart is likewise true in general for other tissues of the body. The numerous nerve centers in the central nervous system are brought into correlation through an

exceedingly complex system of communicating fibers. The cerebro-spinal axis may in fact be regarded as a segmental chain of nerve centers, the complexity increasing from the cord toward the brain, and the coordinating control culminating in the cerebral cortex.

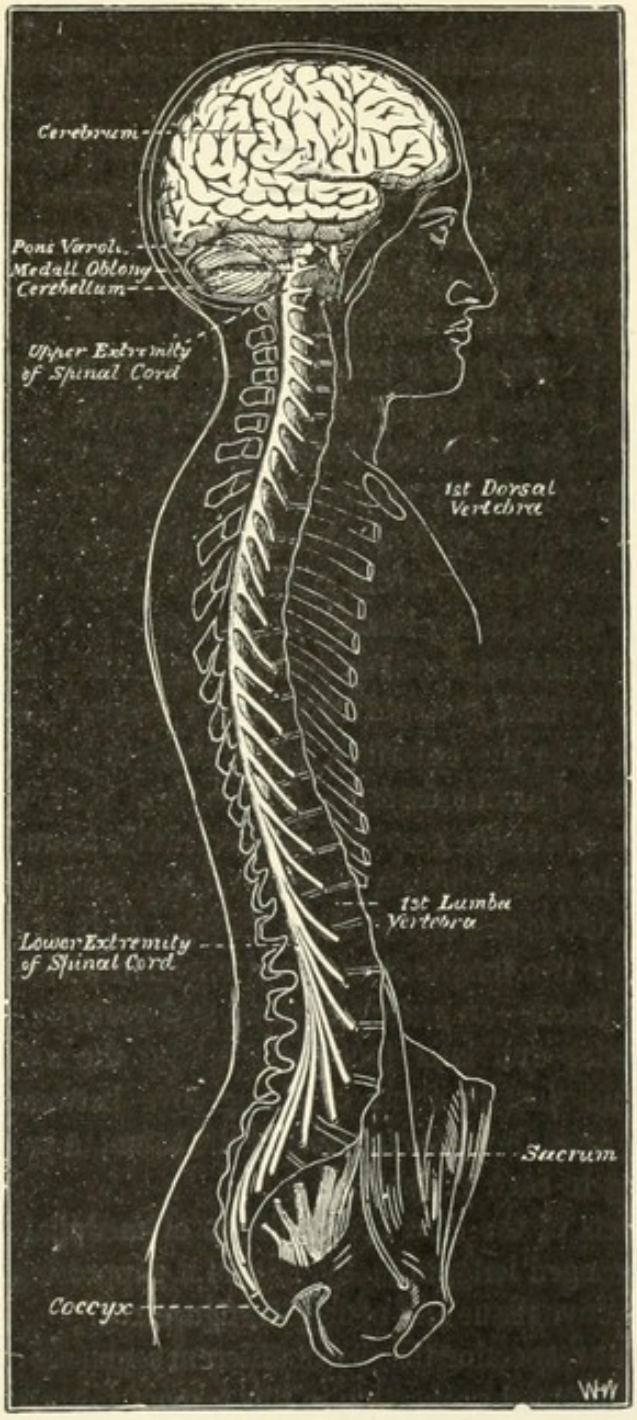


FIG. 357.—View of the Cerebro-spinal Axis of the Nervous System. The right half of the cranium and trunk of the body has been removed by a vertical section; the membranes of the brain and spinal cord have also been removed, and the roots and first part of the fifth and ninth cranial, and of all spinal nerves of the right side, have been dissected out and laid separately on the wall of the skull and on the several vertebræ opposite to the place of their natural exit from the cranio-spinal cavity (After Bourgery.)

II. THE STRUCTURE AND FUNCTION OF THE SPINAL CORD.

STRUCTURE.

The spinal cord is a cylindrical column of nerve-substance connected above with the brain through the medium of the bulb, and terminating below in a slender filament of nerve substance, the *filum terminale*, which lies in the midst of the roots of the many nerves forming the *cauda equina*.

General Features. The cord is composed of nerve fibers and nerve cells. The former are situated externally and constitute the chief portion of the cord, while the latter occupy its central or axial portion and are so disposed that on the surface of a transverse section of the cord two somewhat crescentic grayish masses connected by a narrower portion or isthmus appear, figure 358. Passing through the center of the cord in a longitudinal direction is a minute canal, the central canal, which is continued through the whole length of the cord, opening above into the space at the back of the medulla oblongata and pons Varolii called the fourth ventricle. The canal is lined by a layer of columnar ciliated epithelium.

The spinal cord consists of exactly symmetrical halves, separated anteriorly and posteriorly by vertical *fissures* (the posterior fissure being deeper but less wide and distinct than the anterior), and united in the middle by nervous matter which forms the commissures. The central part, which contains the central canal, is known as the *gray* commissure, and is bounded by the *anterior white* commissure in front, and the *posterior white* commissure behind. Each half of the spinal cord is marked on the sides (obscurely at the lower part, but distinctly above) by two longitudinal furrows, which divide it into three portions, columns, or tracts—an *anterior*, *lateral*, and *posterior*. From the groove between the anterior and lateral columns spring the *anterior roots* of the spinal nerves; and just in front of the groove between the lateral and posterior columns arise the *posterior roots* of the same; a pair of roots on each side corresponding to each vertebra.

The nerve tracts of the cord are made up of medullated nerve fibers of different sizes, arranged longitudinally, and of a supporting material of ordinary fibrous connective tissue and neuroglia, figure 105.

The general rule respecting the size of different segments of the cord appears to be that each is in direct proportion in this respect to the size and number of nerve roots given off from it, and has but little relation to the size or number of those given off below it. Thus the cord is very large in the middle and lower part of its cervical portion, whence arise the large nerve roots for the formation of the brachial plexuses and the nerve supply of the upper extremities; and again enlarges at the lowest part of its dorsal portion and the upper

part of its lumbar, at the origins of the large nerves which, after forming the lumbar and sacral plexuses, are distributed to the lower extremities. The chief cause of the greater size at these parts of the spinal cord is increase in the quantity of the gray matter; for there seems reason to believe that the white part of the cord becomes gradually and progressively larger from below upward, doubtless from the addition of a certain number of ascending fibers from each pair of nerves.

From careful estimates of the number of nerve fibers in a transverse section of the cord toward its upper end, and the number entering or issuing from it by the anterior and posterior roots of each pair of nerves, it has been shown

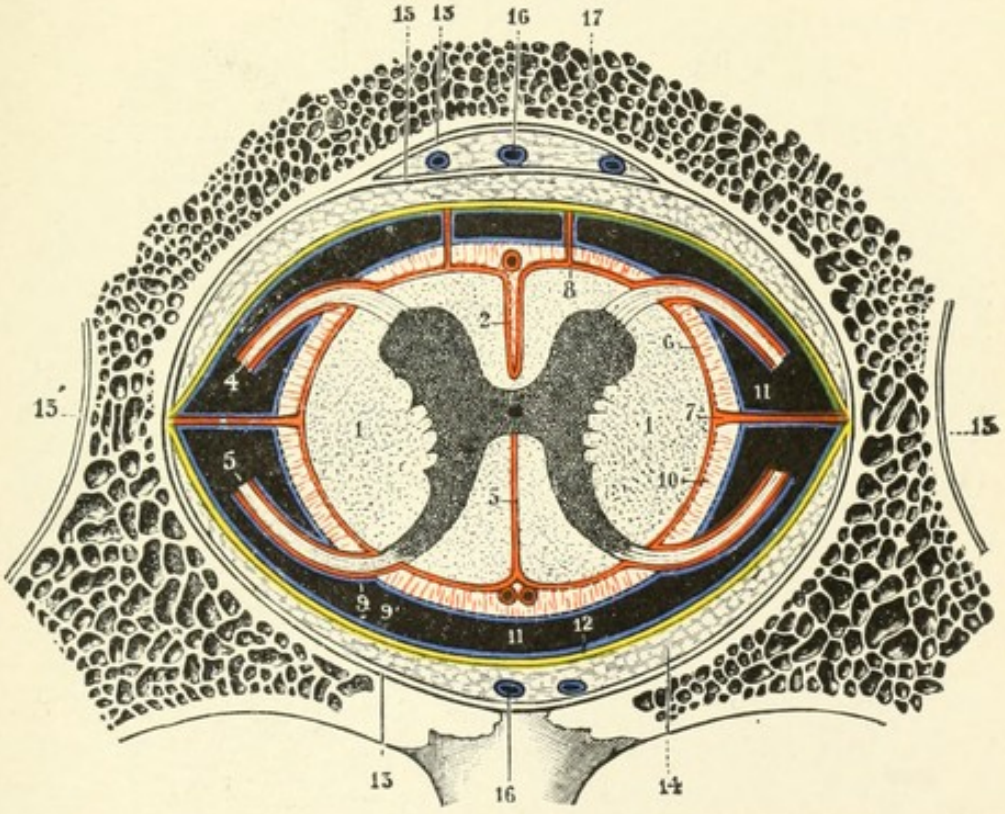


FIG. 358.—Horizontal Section of the Cord and its Envelopes, at the Middle of a Vertebral Body (Schematic). 1, Spinal cord with 2, its anterior median fissure; 3, its posterior median fissure; 4, anterior roots; 5, posterior roots; 6, pia mater (in red); 7, ligamentum dentatum; 8, connecting fibers passing from the pia to dura mater; 9, visceral layer, and 9′, parietal layer of the arachnoid (in blue); 10, subarachnoid space; 11, arachnoid cavity; 12, dura mater (in yellow); 13, periosteum; 13,′ external periosteum; 14, cellular tissue situated between the dura mater and the wall of the vertebral canal; 15, common posterior vertebral ligament; 16, intraspinal veins; 17, vertebra in section. (Testut.)

that in the human spinal cord not more than half of the total number of nerve fibers of all the spinal nerves are contained in a transverse section near its upper end. It is obvious, therefore, that at least half of the nerve fibers entering it must terminate somewhere in the cord itself.

The Arrangement of Nerve Cells in the Spinal Cord. The gray matter of the spinal cord consists of numerous groups of nerve cells and of a close meshwork of nerve fibers, most of which are very fine and delicate. Medullated fibers mingled with the small gray fibers about the borders of the

gray substance. Mingled with it and supporting it is the meshwork of the neuroglia.

The multipolar cells of the cord are either scattered singly or arranged in groups, of which the following are to be distinguished on either side, certain of the groups being more or less marked in all of the regions of the cord, viz., those, *a*, in the anterior cornu, *b*, those in the posterior cornu, and *c*, intrinsic cells distributed throughout the gray matter.

The cells in the anterior cornu are large and branching, and each gives rise to an axis-cylinder process which passes out in the anterior nerve root. These

FIG. 359.—From the Lower Lumbar Cord of Man, after a Preparation by Klönne and Müller, of Berlin (No. 11,153), stained by Weigert and Pal's method. A portion of the gray substance of the ventral cornu with the adjoining portions of the lateral column is represented, showing anterior-horn cells and the fine medullated fibers which enter the gray substance from the lateral column and surround the nerve cells, which here are provided with fine pigmented granules. High power. (Kölliker.)

cells are everywhere conspicuous, but are particularly numerous in the cervical and lumbar enlargements. In these districts they may be divided into several groups: 1, A group of large cells close to the tip of the inner part of the anterior cornu—all the cells of the anterior cornu in the dorsal or thoracic region are said to belong to this group; 2, several lateral groups, *2a*, *2b*, and *2c*, figure 360, on the outer side of the gray matter, and a certain number of cells at the base of the inner part of the anterior cornu particularly well marked in the thoracic region; 3, cells of the posterior cornu—these are not numerous. They

are small and branched, and each has an axis-cylinder process passing off; but these processes do not pass into the posterior nerve roots. The groups are two at least in number, viz., *a*, in connection with the edge of the gray matter externally, where it is considerably broken up by the passage of bundles of fibers through it, and called the *lateral reticular formation ;* and *b*, in connection with a similar reticular formation, more at the tip of the gray, known as the *posterior reticular formation.*

A group of cells, 3, figure 360, is situated at the base and median side of the posterior cornu. It is formed of fairly large cells, fusiform in shape, and constitutes the posterior vesicular column, or Clarke's column. It extends from the seventh cervical to the third lumbar segment. On the outer portion of the gray matter, midway between the anterior and posterior cornua,

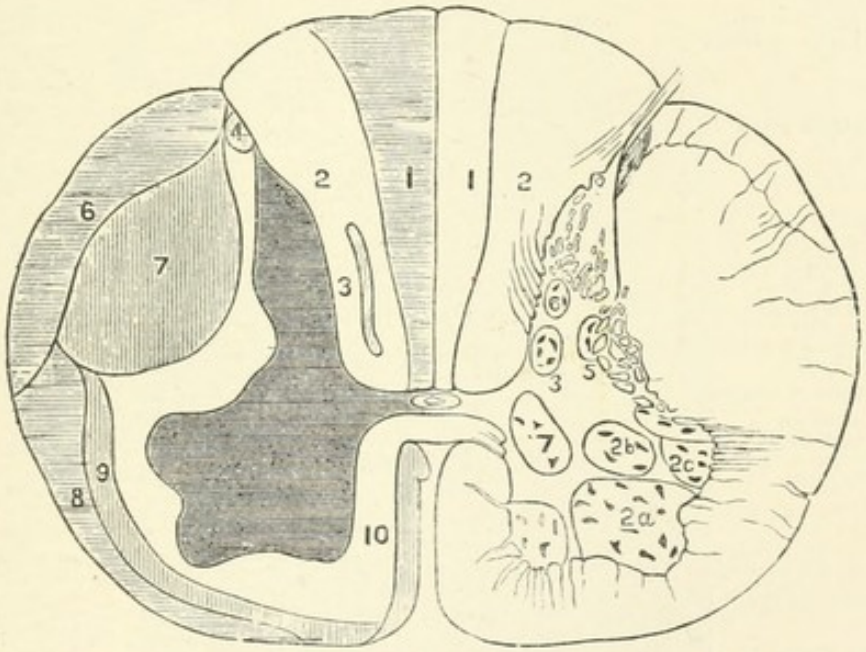


FIG. 360.—Section of Spinal Cord. One Half of Which (Left) Shows the Tracts of the White Matter, and the Other Half (Right) Shows the Position of the Nerve Cells in the Gray Matter. 7, 10, 9, and 3 are tracts of descending degeneration; 1, 4, 6 and 8, of ascending degeneration. Semi-diagrammatic. (After Sherrington.)

is a group of cells, known as the *cells of the lateral gray column.* These are small and spindle-shaped, and are more or less marked in the lumbar region, as well as in the thoracic region, 5, figure 360.

Besides these groups, which have their names largely on account of their location, there are distributed throughout the gray matter a very large number of other cells, which are known as *intrinsic cells.* These send out axones which pass into the adjacent ground bundles of the same or of the opposite side, and pass up and down the cord, to enter the gray matter again. They connect by their end-brushes with cells at different levels of the cord.

The function of these connecting cells, or intrinsic cells, is to unite the posterior and anterior regions of the cord, to serve as conductors between the lateral halves, or to connect segments at different levels. They are also dis-

tributing fibers in that they bring a single or at least a small number of posterior neurones into connection with a relatively large number of anterior neurones.

Columns and Tracts in the White Matter of the Spinal Cord. In addition to the columns of the white matter which are marked out by the points from which the nerve roots issue, and which are the *anterior*, the *lateral*, and *posterior*, the posterior is further divided by a septum of the pia mater into

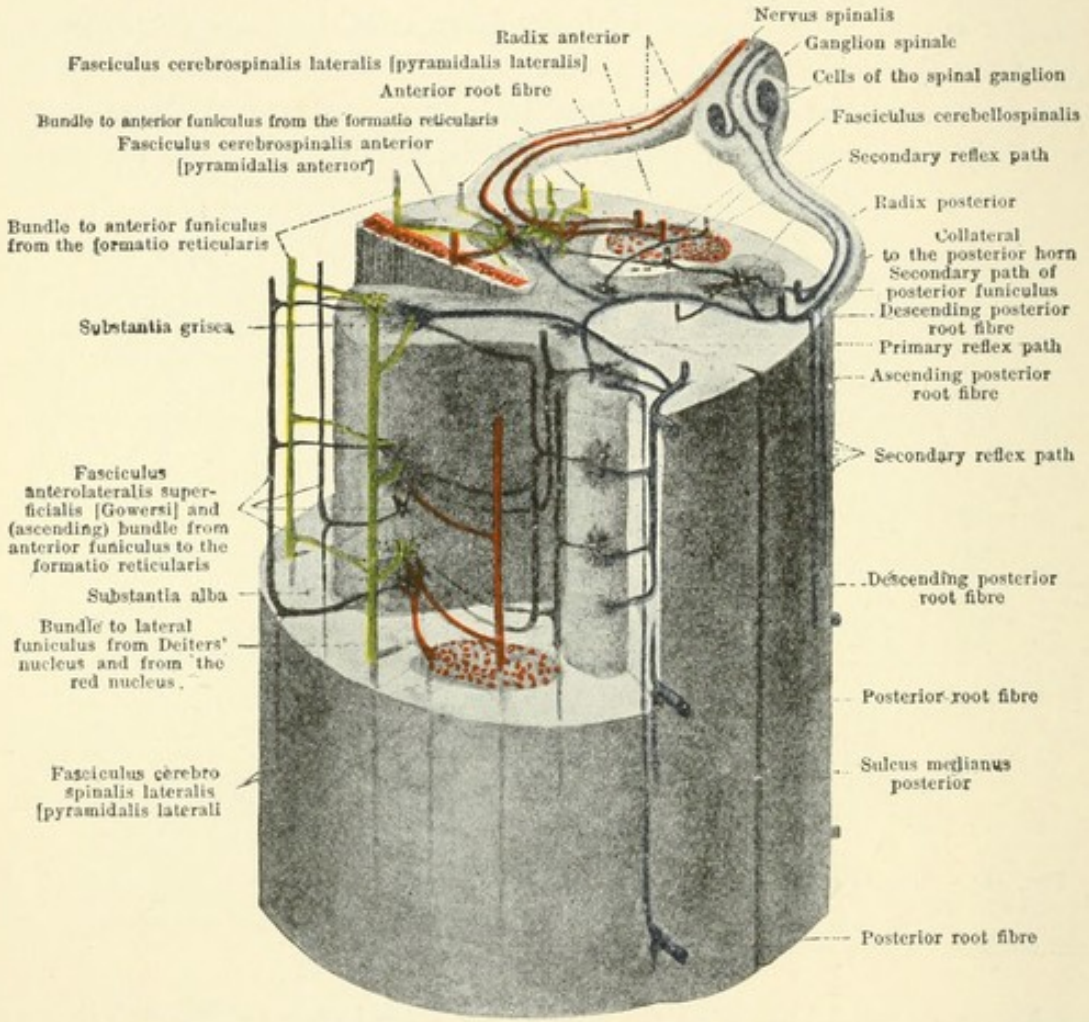


FIG. 361.—Reconstruction of a Segment of the Spinal Cord Representing Both a Transverse and Longitudinal Section. (Held, from Spalteholz's Anatomy.)

two almost equal parts, constituting the *postero-external* column, or *column of Burdach*, figure 360, 2, and the *postero-median*, or *column of Goll*. In addition to these columns, however, it has been shown that the white matter can be still further subdivided. This subdivision has been accomplished by evidence of several kinds that the parts or, as they are called, tracts in the white matter perform different functions in the conduction of impulses.

The methods of observation are the following:

The embryological method. It has been found that, if the development of the spinal cord be carefully observed at different stages, certain groups of

the nerve fibers acquire their myelin sheath at earlier periods than others, and that the different groups of fibers can therefore be traced in various directions. This is known as the method of Flechsig.

Wallerian or degeneration method. This method depends upon the fact already presented that if a nerve fiber is separated from its nerve cell it wastes or degenerates. It consists in tracing the course of tracts of degenerated fibers which result from an injury, to any part of the central nervous system. When fibers degenerate below a lesion the tract is said to be of *descending degeneration*, and when the fibers degenerate in the opposite direction the tract is one of *ascending degeneration*. By modern methods of staining of the central nervous system it has proved comparatively easy to distinguish degenerated parts in sections of the cord and of other portions of the central nervous system. Degenerated fibers have a different staining reaction when the sections are treated by what are called Weigert's and Marchi's methods. Accidents to the central nervous system in man have given us much information as to its organization, but this has of late years been supplemented and largely extended by the experiments on animals, particularly upon monkeys. Considerable light has by the method of section and degeneration been shed upon the path of conduction of impulses to and from the nervous system. Thus we not only have embryological evidence mapping out different tracts, but also confirmatory pathological and experimental observations.

The tracts which have been made out are the following:

Tracts of Descending Degeneration. *The Crossed Pyramidal Tract.* This tract is situated to the outer side of the posterior cornu of gray matter, figure 360, 7. It is found throughout the whole length of the spinal cord; at the lower part it extends to the margin of the cord, but higher up it becomes displaced inward from this position by the interpolation of another tract of fibers, the direct cerebellar tract. The crossed pyramidal tract is large, and may touch the tip of the gray matter of the posterior cornu, but it is separated from it elsewhere. It is oval in shape on cross-section, and diminishes in size from the cervical region downward. The tract is particularly well marked out, both by the degeneration and the embryological methods. The fibers are supposed to pass off as they descend, and to join the various local nervous mechanisms of nerve cells and their branchings which are represented in the cord. The tract of degeneration may be traced upward beyond the cord, in a way to be presently described. The fibers of which this tract is composed are moderately large, but are mixed with some that are smaller.

The Direct or Uncrossed Pyramidal Tract. This tract is situated in the anterior column by the sides of the anterior fissure, figure 360, 10. It is smaller than the crossed tract and is not present in all animals, though conspicuous in the human cord and in that of the monkey. It can be traced upward to the cerebral cortex, and downward as far as the mid or lower thoracic region, where it ends.

Antero-lateral Descending Tract. This is an extensive tract, elongated but narrow, and reaching from the crossed to the direct pyramidal tract. It is a mixed tract, since not all of its fibers degenerate below the lesions.

Comma Tract. This is a small tract of fibers which degenerate below the point of section or injury of the cord. Its presence has been demonstrated in the cervical and thoracic regions. It is supposed to consist of the descending collaterals of the posterior nerve roots as they pass into the postero-external columns.

Tracts of Ascending Degeneration. *Postero-median Column and Postero-lateral Column.* These tracts degenerate upward on injury or on section of the cord, also on section of the posterior nerve roots, figure 360, 1. They exist throughout the whole of the cord from below up, and can be traced into the bulb. They consist of fine fibers.

Direct Cerebellar Tract. This tract is situated on the outer part of the cord between the crossed pyramidal tract and the margin. It is found in the cervical, thoracic, and upper lumbar regions of the cord, and increases in size from below upward. It degenerates on injury or section of the cord itself, but not on section of the posterior nerve roots, since its fibers arise from the cells of Clarke's column. As its name implies, it is believed to pass up into the cerebellum.

Antero-lateral Ascending Tract, Tract of Gowers, figure 360, 8. This tract has been shown on injury to the spinal cord; it is situated at the margin of the cord outside of the corresponding descending tract. It is traceable throughout the whole length of the cord.

Tract of Lissauer, or Posterior Marginal Zone. A small tract of fine white fibers, situated at the apex of the posterior horn, is made up of fibers from the posterior nerve roots which enter the column and pass up and down for a short distance, finally entering the posterior horn, where they terminate in fine end-brushes around the cells of the posterior horn.

It will thus be seen that the white matter of the spinal cord has three general divisions—into the anterior, the lateral, and posterior columns. These columns are subdivided into tracts in which the fibers degenerate upward, those in which the fibers degenerate downward, and others in which the fibers degenerate neither way except for short distances when the cord is cut across. These parts of the cord are composed of commissural fibers which connect different levels of the cord. The commissural tracts form the antero-lateral columns and the lateral limiting layer. The arrangement of these tracts is shown well in figure 360.

The Spinal Nerves. The spinal nerves consist of thirty-one pairs, from the sides of the whole length of the cord, their number corresponding with the intervertebral foramina through which they pass. Each nerve arises by two roots, an anterior and a posterior, the latter being the larger. The roots emerge through separate apertures of the sheath of dura mater surrounding

the cord; and directly after their emergence, where the roots lie in the intervertebral foramen, a ganglion is found on the posterior root. The anterior root lies in contact with the anterior surface of the ganglion, but none of its fibers intermingle with those in the ganglion, figure 361. But immediately beyond the ganglion the two roots coalesce, and by the mingling of their fibers form a compound or mixed spinal nerve, which, after issuing from the intervertebral canal, gives off anterior and posterior (or *ventral* and *dorsal*) branches, each containing fibers from both the roots as well as a third or *visceral* branch, ramus communicans, to the sympathetic.

The anterior root of each spinal nerve arises by numerous separate and converging bundles from the anterior column of the cord; the posterior root

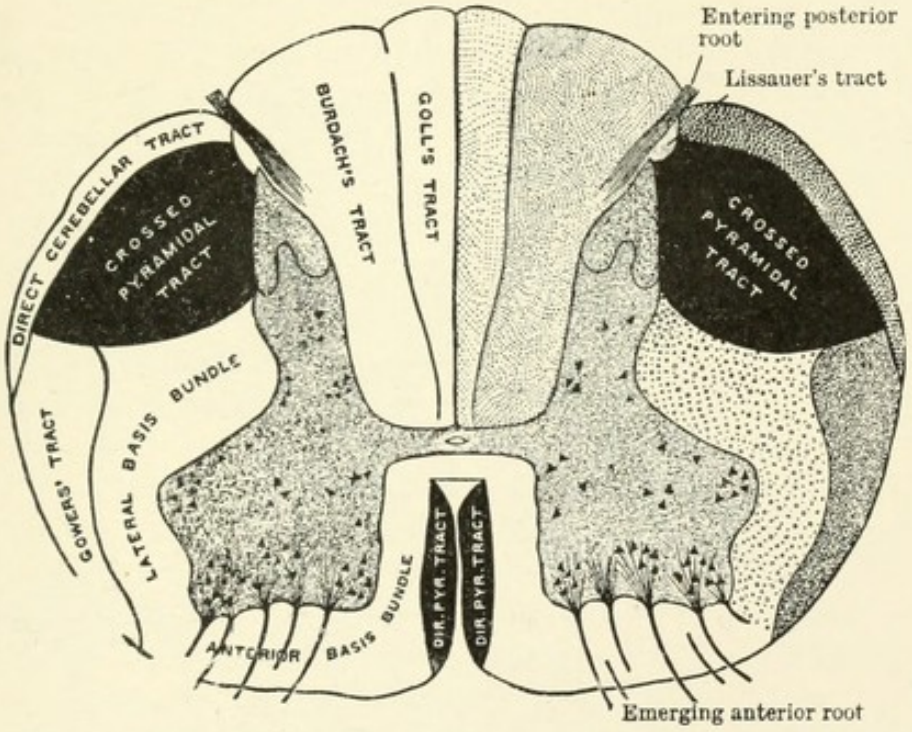


FIG. 362.—Diagrammatic Transverse Section of the Spinal Cord, Showing the Conduction Paths and Groups of Cells. (Cunningham.)

by more numerous parallel bundles, from the posterior column, or, rather, from the posterior part of the lateral column, for if a fissure be directed inward from the groove between the middle and posterior columns, the posterior roots will remain attached to the former. The anterior roots of each spinal nerve consist chiefly of efferent fibers; the posterior exclusively of afferent fibers.

Course of the Fibers of the Spinal Nerve Roots. *The Anterior Roots.* The anterior roots leave the cord in several bundles, which may be called: 1, Internal; 2, Middle; 3, External. All have their origin from the groups of multipolar cells in the anterior cornua. The *internal* fibers are originated partly in the internal group of nerve cells of the anterior cornu

of the same side; but some fibers can be traced through the anterior commissure to cells of the anterior cornu of the opposite side.

The Posterior Roots. The fibers of the posterior roots enter the spinal cord to the inner or median side of the posterior cornu. The fibers, as soon as they reach the cord, divide in a fork-like fashion, one branch passing down a short distance, about three centimeters, the other branch passing up for a shorter or longer distance. This upper branch sometimes reaches the whole extent of the cord, but generally it extends over only one or two segments of the cord. The divisions of the posterior root fibers give off in their course numerous collaterals, figure 368. The fibers

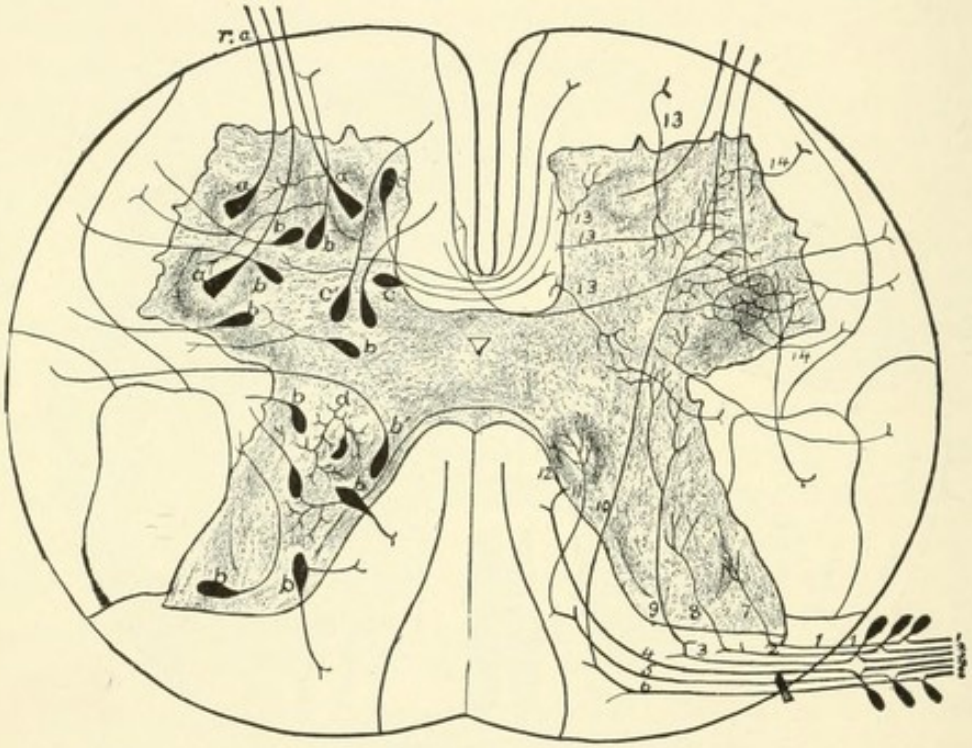


FIG. 363.—Section of the Spinal Cord, Showing the Grouping of Nerve-Cells and the Course of Nerve Fibers Entering in Posterior and Anterior Roots. (After Lenhossek.)

of the posterior roots are divided into two sets, an internal or median, an external or lateral group. The lateral set consists mostly of small fibers which enter the cord opposite the tip of the posterior horn. The fibers pass in part to the marginal column of Lissauer, where they ascend and descend; in part they penetrate the posterior horn, and come in relation with its cells. From the median set some fibers pass to Clarke's column, others pass by way of the posterior commissure to the median cells of the other side. Others pass through the gray matter to the *anterior horn cells* of the same side. Besides this, they are connected through collaterals with the intrinsic cells of the gray matter at different levels of the cord. One can realize that each nerve root has, in this way, an effective grip upon a large extent of the cord. This is seen well by studying figures 361 and 363.

The Peculiarities of Different Regions of the Spinal Cord. The outline of the gray matter and the relative proportion of the white matter vary in different regions of the spinal cord, and it is, therefore, possible to tell approximately from what region any given transverse section of the spinal cord has been taken. The white matter increases in amount from below upward. The amount of gray matter varies; it is greatest in the cervical and lumbar enlargements, viz., at and about the 5th lumbar and the 6th cervical nerves, and least in the thoracic region. The greatest development of gray matter corresponds with greatest number of nerve fibers passing from the cord.

In the cervical enlargement the gray matter occupies a large proportion of the section, the gray commissure is short and thick, the anterior horn is blunt, while the posterior is somewhat tapering. The anterior and posterior roots run some distance through the white matter before they reach the periphery.

In the dorsal region the gray matter bears only a small relation to the white, and the posterior roots in particular run a long course through the white matter before they leave the cord; the gray commissure is thinner and narrower than in the cervical region.

In the lumbar enlargement the gray matter again bears a very large proportion to the whole size of the transverse section, but its posterior cornua are shorter and blunter than they are in the cervical region. The gray commissure is short and extremely narrow.

At the upper part of the conus medullaris, which is the portion of the cord immediately below the lumbar enlargement, the gray substance occupies nearly the whole of the transverse section, as it is invested only by a thin layer of white substance. This thin layer is wanting in the neighborhood of the posterior nerve roots. The gray commissure is extremely thick.

At the level of the fifth sacral vertebra the gray matter is again in excess, and the central canal is enlarged, appearing T-shaped in section; while in the *upper portion of the filum terminale* the gray is uniform in shape without any central canal.

The Reflex Arc and Reflex Action. The spinal cord is morphologically a segmental or metameric structure. This is shown both by its development and by its comparative anatomy. The pairs of nerves are indicative of the component segments of the cord. The tracts of the cord are in a sense connectives from segment to segment, connecting the cells of both adjacent and of widely separated segments. The function of the cord is comprised in the function of the segments and in the function of the tracts.

From a physiological point of view, it may almost be considered as an axiom that before a nerve cell can send out a nerve impulse it must first receive a stimulus of some kind. This stimulus usually consists of an afferent impulse from the periphery. Its effect upon the receiving cell may be insufficient to cause any response, or the response may be delayed for a long period

and may involve many complicated nervous activities and even psychological processes. Where the response is approximately immediate, the reaction is known as a reflex.

A *reflex arc*, reduced to its simplest terms, consists of the following elements: *a*, a sensory surface; *b*, an afferent neurone; *c*, an efferent neurone; *d*,

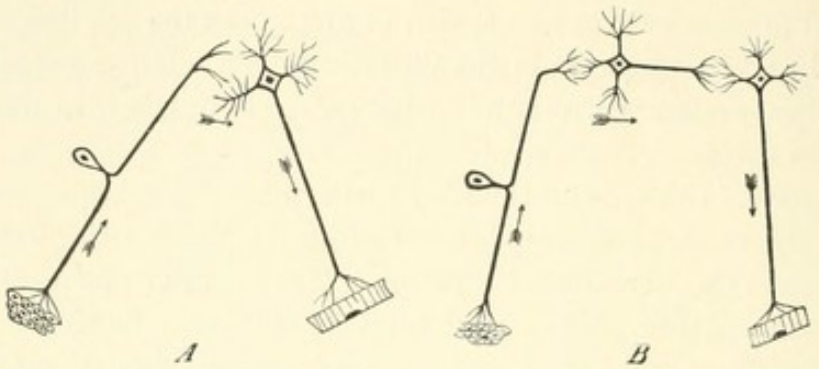


FIG. 364.—Schematic Sketch of a Reflex Arc. *A*, With two neurones, an afferent and an efferent; *B*, with three neurones, an afferent, efferent, and a connecting or intracentral neurone.

a muscle or gland. The simplest form of reflex arc is schematically shown in figures 364 and 365.

The gap between the termination of the afferent neurone and the dendron of the efferent neurone shown in figure 364 is called a *synapsis*. The reflex arc is probably seldom as simple as that shown in figure 365, where only two neurones are involved. More often, three or more neurones take part, as shown in figures 364 *B*, and 366.

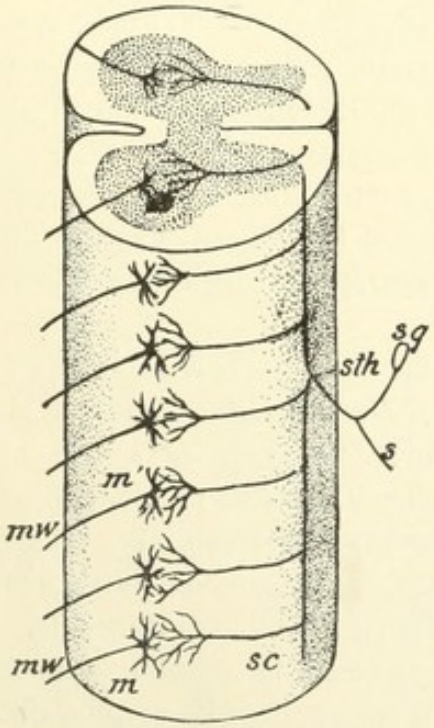


FIG. 365.—Showing the Arrangement of a Simple Reflex Mechanism Composed of a Motor and Sensory Neurone. *sg*, Posterior spinal ganglion; *s* and *sth*, sensory root; *m*, motor-nerve cell; *mw*, motor root. (Kölliker.)

The neurone connecting the afferent neurone with the efferent neurone belongs to the class of intracentral or connecting neurones. Since all parts of the cord, in fact of the entire cerebro-spinal axis, are indirectly connected with one another by intracentral neurones, figure 361, the possibility of increasing the number of efferent limbs of the reflex arc can be readily understood.

A physiological reaction in a tissue produced by efferent nerve impulses which have been discharged from a nerve center under the stimulus of a sensory or afferent nerve impulse, is called a *reflex act*. Where the nervous apparatus involved is of the type represented in figures 364 and 365, the activity is called a *simple reflex*. Most reflexes

are more complex in character. The afferent nerve impulse passes through more than one simple channel in the cord, so that a series of coordinated acts occurs in what may be called a *complex reflex*.

The transmission of impulses within the cord occurs over the pathways of least resistance. Increasing the number of synapses, or the number of neurone links in the chain of conduction, increases the resistance so that reflexes will occur most readily, other conditions being equal, where the least number of neurones is involved, *i.e.*, in the same segment of the cord in which the sensory impulse enters, or in immediately adjacent segments. In addition to the number of synapses in the reflex arc, other factors are of importance in determining reflex reaction; *e.g.*, the intensity of the exciting stimulus; the quality of the stimulus; the rapidity of the recurrence of the stimulus; and the duration of its application. Thus, a strong stimulus will bring about a reflex reaction sooner than a weak stimulus of the same kind. A single weak stimulus which will cause no reflex may do so if often enough and rapidly enough repeated, the phenomenon of *summation of stimuli*.

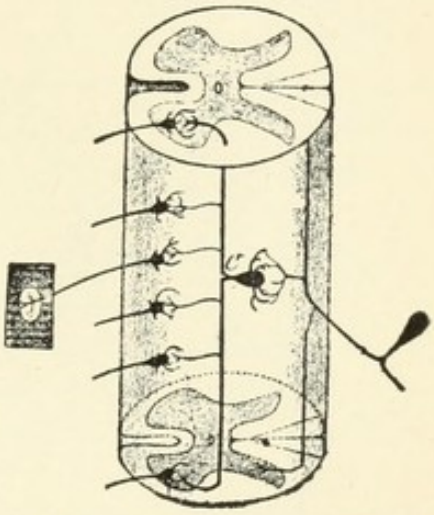


FIG. 366.—Showing the Arrangement of the Reflex Mechanism, with a Neurone Intercalated between the Sensory and Motor Neurones.

A reflex act once started may result in efferent impulses which continue for some time after the exciting cause has been removed. The same phenomenon is observed where groups of nerve cells are stimulated directly. It has been found, by observing electrical changes in nerve fibers by means of the capillary electrometer, that when their cells of origin are stimulated they discharge impulses in a rhythmical manner.

Usually, impulses are transmitted to a nerve cell only over its dendrons, but it must be also assumed that such a conveyance of impulses may take place over the collaterals of its axone near the cell body, or the cell body may be stimulated directly by the afferent neurone. The peripheral fiber of the spinal ganglion cell, although it has the structure of an axone, may be looked upon physiologically as a dendron, since homologues in lower vertebrates and in man himself (olfactory-nerve cells) have this structure, the nerve cell body being situated near the sensory surface from which impressions are received.

Irradiation of Impulses within the Cord. Taking as an example a frog whose brain has been destroyed, a simple reflex may be demonstrated by irritating the skin of one foot with a weak stimulus. In response to such a stimulus the foot is flexed upon the leg, due to a contraction of the muscles of the reflex arc corresponding to the sensory surface irritated. If the strength or duration of the stimulus be increased, other groups of muscles are involved

in the following order: 1, Those of the leg and thigh of the same side; 2, homologous muscles of the opposite side; 3, the arms of the same side and of the opposite side.

The increasing complexity of the reflexes aroused by stimulation of one and the same sensory spot is not easy of explanation. We know that there is almost an infinite number of morphological paths in the cord, yet the responses are orderly and observe a certain sequence in their increasing complexity. The reflexes have a mechanical definiteness which, in a living structure, seems almost purposeful, yet there is no consciousness in a frog which has its brain destroyed.

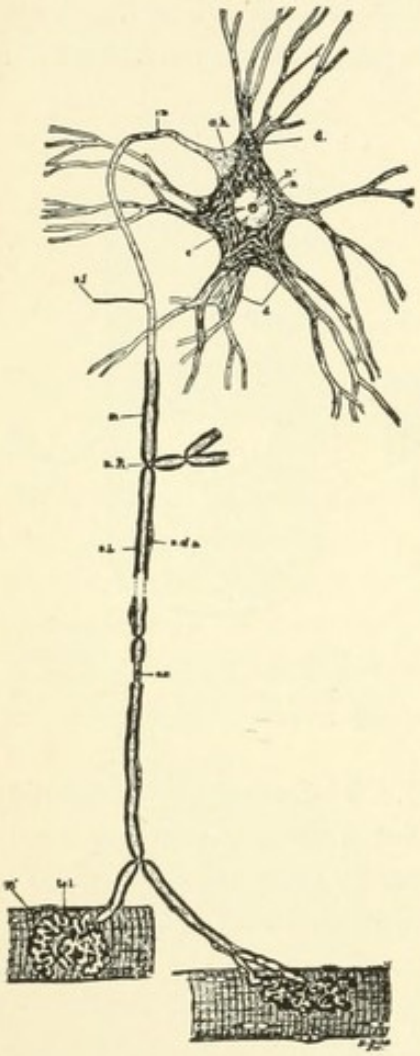


Fig. 367.—Scheme of Lower Motor Neurone. The cell body, protoplasmic processes, axone, collaterals, and terminal arborizations in muscle are all seen to be parts of a single cell and together constitute the *neurone*. (Barker.) *c*, Cytoplasm of cell body containing chromophilic bodies, neurofibrils, and perifibrillar substance; *n*, nucleus; *n'*, nucleolus; *d*, dendrites; *ah*, axone hill free from chromophilic bodies; *ax*, axone; *sf*, side fibril (collateral); *m*, medullary sheath; *nR*, node of Ranvier where side branch is given off; *sl*, neurilemma and incisures of Schmidt; *m*, striated muscle fiber; *tel*, motor end plate.

The fact is that in the development of the nervous system certain physiological paths of slight resistance have been established between the sensory areas and the muscles which move the parts for their protection. Apparently other physiological nerve pathways exist, but it requires a stronger sensory stimulus to arouse nerve impulses along these paths. In explanation we may suppose that the stronger afferent impulses are sufficient to overcome the resistance of increasingly complex paths, that they diffuse through greater and greater extents of the cord. But we may repeat that in the normal state of the cord this diffusion is in an orderly physiological sequence.

Orderly reflexes can be called forth only by stimulating sensory nerve endings, the first of the essential structures of the reflex arc. If artificial stimuli are applied to a nerve trunk, as the sciatic, uncoordinated muscular responses occur because the sensory stimuli are diffuse and general and are not specific and local.

An involvement of multiple pathways may also be accomplished through decreasing the resistance within the cord, as through the use of some drug such as strychnine. In the strychninized frog a slight stimulus brings about multiple and violent reflex spasms. These contractions have lost their orderliness and are uncoordinated. The entire musculature contracts. It is as though the strychnine removed all

differences in the facility with which afferent stimuli spread through the cord, and that the resistance was reduced to the minimum. The strychnine effect is possibly due to a decrease in the resistance at the synapses, and possibly also to an increase in the irritability of the discharging nerve cells.

We must also suppose that the centers are particularly sensitive to certain kinds of stimuli, sometimes producing very extensive and violent muscular actions in response to a slight stimulus of a special kind. Such a condition is illustrated in the violent and general muscular spasms occurring when a small particle of food passes into the larynx, violent expiratory spasms accompanied by contractions of other muscles taking place.

The time taken in a reflex action for the eye in man has been found to be 0.066 to 0.058 of a second, but this estimate includes the entire time from the instant of stimulation to the beginning of the contraction of the muscle.

Functions of the Spinal Nerve Roots. The anterior spinal nerve roots are efferent in function and the posterior are afferent. The fact is proved in various ways. Division of the anterior roots of one or more nerves is followed by complete loss of motion in the parts supplied by the fibers of such roots, but the sensation of the parts remains perfect. Division of the posterior roots destroys the sensibility of the parts supplied by their fibers, while the power of motion continues unimpaired. Moreover, stimulation of the ends of the distal portions of the divided anterior roots of a nerve excites muscular movements. There are sometimes slight evidences of sensory impulses due to recurrent fibers that are distributed through the anterior root to the spinal meninges. Stimulation of the proximal ends of the anterior roots, which are still in connection with the cord, is followed by no appreciable effect. It must be remembered, however, that in the anterior or efferent nerves other fibers besides motor are contained, *e.g.*, vaso-motor, secretory, heat fibers, and when the distal end of a divided nerve is stimulated, the effects are exercised not only upon muscles, but upon glands, blood-vessels, etc. Stimulation of the distal portions of the divided posterior roots, on the other hand, produces no muscular movements and no manifestations of pain; for, as already stated, sensory nerves convey impressions only toward the nerve centers. Stimulation of the proximal portions of these roots elicits signs of intense suffering. Muscular movements also ensue; but these are the result of the reflex stimulation of the motor neurones of the anterior horn of the cord or are movements in response to the afferent impulses passing to higher centers from the roots stimulated.

Functions of the Ganglia on Posterior Roots. The cells of the posterior ganglia act as centers for the nutrition of the nerve fibers given off from them. When these are cut, the parts of the nerves so severed degenerate, while the parts which remain in connection with the cells of the ganglia do not. Thus on section of the posterior nerve root beyond the ganglion the peripheral part degenerates and the central does not, and on section of the root between

the ganglion and the cord the central part degenerates and the peripheral is unaffected.

Spinal Reflexes in Man and Mammals. Much of our knowledge of the reflexes of the cord is derived from experiments on dogs, though paralysis of the lower extremities in man, by accident or otherwise, has given confirmatory information. In man the spinal cord is so much under the control of the higher nerve centers that its own individual functions in relation to reflex action are apt to be overlooked. But if the skin of the foot is stimulated, in a man whose lumbar cord is completely separated by injury or disease, the

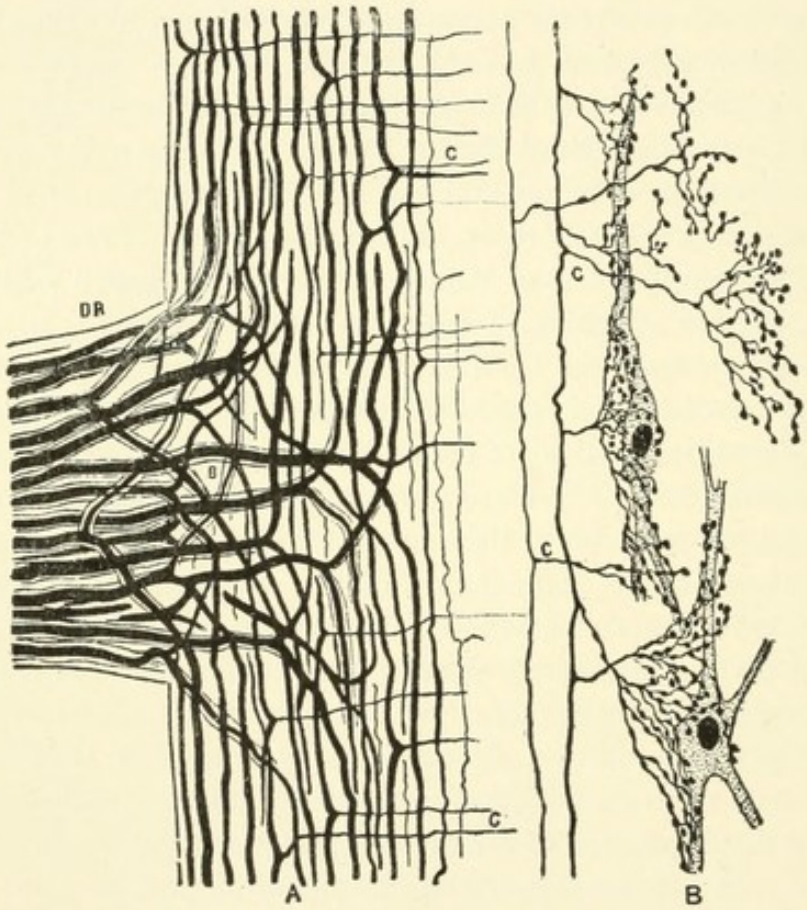


FIG. 368.—Scheme of the Relation of the Posterior Root Fibers upon Entering the Cord. *A*, The branch of the dorsal root fibers upon entering cord; *B*, terminal arborization about cell bodies of the cord; *DR*, axones of the dorsal root; *B*, their ascending and descending branches; *C*, collaterals. (After Cajal.)

foot will be drawn away from the stimulus; or, if the stimulus be strong enough, the entire leg will be moved. In both cases the movement may be orderly and well coordinated, and shows that the sensory stimulus has produced a coordinated reflex through the lumbar cord. The injured person feels no sensation of pain nor of action, and the phenomenon is independent of the higher nerve regions. The stimulus that is applied to man must be carefully graded, since when too intense it calls forth muscular spasms or convulsive action.

When the cord is first cut, the shock is very great, the lower or isolated portion of the cord remains for a time quite non-irritable. The vaso-motor and thermogenic centers are cut off so that there is great vascular dilatation and marked fall of temperature, the effects of which are likely to lead to death unless the operated animal is carefully attended. But these effects are slowly recovered from, and man, as well as lower mammals, soon regains the vascular tone. The general tonus of the muscular system, which is lost at first, is also regained.

In this partially recovered condition man, and such animals as the cat, the dog, and the monkey, perform certain of the lower functions with a remarkable degree of perfection. Of course these functions are under constant coordinative regulation and control in the normal animal, but experiments and observation have shown how much of such activity really is a primary function of the cord. Of these activities the following may be especially mentioned: Muscular tonus, general reflexes, the special reflexes of micturition, defecation, erection and the sexual reflex, and parturition, some of which will be briefly discussed.

The Center of the Tone of Muscles. The tonic influence of the spinal cord on the sphincter ani and sphincter urethræ will be presently mentioned. The cord maintains these muscles in permanent tonic contraction. The condition of the sphincters, however, is not altogether exceptional. Their contraction is the same in kind, though it exceeds in degree, that condition of muscles which has been called *tone*, a condition of slight contraction which they always maintain during health. This tone of all the muscles of the trunk and limbs depends on the spinal cord, just as does the contraction of the sphincters. If an animal be killed by injury or removal of the brain, the muscles retain their tenseness, but if the spinal cord be destroyed, the sphincter ani relaxes, and all the muscles become loose, flabby, and atonic, remaining so till *rigor mortis* commences.

If an animal, such as the dog, be held off the ground in the erect position assumed by the human body, when the trunk and hind limb muscles are not in voluntary contraction the limbs will assume a normal pendular position. In the pendular position the legs of a dog with cord severed hang more limp and are more completely extended. The muscles of the former exhibit that tone which keeps antagonistic muscles always slightly tense, the muscles of the latter have lost the tenseness.

Whether or not muscular tone is maintained through the constant subminimal action of sensory nerve impulses on the tonic centers of the cord, or whether these centers are automatic in their action, is a question that can be answered only by inference. The probability is that tone is a reflex activity, though it may be contributed to by the normal healthy nutritional condition of the muscles themselves—a condition which is itself dependent on the trophic influence of the nerve cells of the cord and brain stem.

The Ano-Spinal or Defecation Center. The mode of action of the ano-spinal center appears to be this: The mucous membrane of the rectum is stimulated by the presence of feces or of gas in the large bowel. The stimulus passes up by the afferent nerves of the hemorrhoidal and inferior mesenteric plexuses to the center situated in the lumbar enlargement of the cord, and is reflected through the pudendal plexus to the anal sphincter, and to the muscular tissue in the wall of the lower bowel. In this way there is produced a relaxation of the first and a contraction of the second, and expulsion of the contents of the bowel follows. The center in the spinal cord is partially under the control of the will, so that its action may be either inhibited or augmented. The action may be helped by the abdominal muscles, which are voluntary muscles, but are also stimulated to contract by reflex action.

The Vesico-Spinal or Micturition Center. The vesico-spinal center acts in a very similar way to that of the ano-spinal. The center is also in the lumbar enlargement of the cord. It is stimulated to action reflexly by the presence of urine in the bladder. The action may be voluntary and is excited by the sensation of distention of the bladder by the urine. The sensory fibers concerned are the posterior roots of the lower sacral nerves. The action of the spinal center is double, or it may be supposed that the center consists of two parts, one of which is usually in action and maintains the tone of the sphincter, and the other which causes contraction of the bladder and other muscles. When evacuation of the bladder occurs impulses pass to that part of the center which discharges impulses to the bladder and to certain accessory muscles which cause their contraction; and impulses pass to that part of the center which inhibits the tonic action on the sphincter urethræ which procures its relaxation. The way having been opened by the relaxation of the sphincter, the urine is expelled by the combined action of the bladder and accessory muscles. The cerebrum may exert its influence on the reflex not only by stimulating the center to action, but also by inhibiting its action.

The Genito-Spinal Center. The presence of the genito-spinal center is proven by the fact that dogs, and even man, are known to discharge semen when the lumbar cord is severed and all voluntary motion and sensibility are lost. The center situated in the lumbar enlargement of the spinal cord is stimulated to action by sensory impressions from the glans penis. Efferent impulses from the center excite the successive and coordinate contractions of the muscular fibers of the vasa deferentia and vesiculæ seminales and of the accelerator urinæ and other muscles of the urethra; and a forcible expulsion of semen takes place, over which the cerebral centers have little or no control, and which, in cases of paraplegia, are not felt.

The Erectal Center. This center is also situated in the lumbar region and is a vascular center, already described in the chapter on Circulation. It is reflexly excited to action by the sensory nerves of the penis, and also in the

normal animal by impulses passing down from the cerebrum. Efferent impulses produce dilatation of the vessels of the penis.

The Parturition Center. The center for the expulsion of the contents of the uterus in parturition is situated in the lumbar spinal cord rather higher up than the other centers already enumerated. The stimulation of the uterus may, under certain conditions, excite the center to send out impulses which produce a contraction of the uterine walls and expulsion of the contents of the cavity. The center is independent of the will since delivery takes place in paraplegic women, and also while a patient is under the influence of chloroform. Again, as in the cases of defecation and micturition, the abdominal and thoracic muscles assist; their action being for the most part reflex and involuntary.

Inhibition of Reflex Actions. Movements such as are produced by stimulating the skin of the lower extremities in the human subject, after division or disorganization of a part of the spinal cord, do not always occur when the cerebrum is active and the connection between the cord and the brain is intact. The reflex which would occur in the animal with spinal cord only is suppressed or inhibited in the normal animal through the regulative action of the higher cerebral centers. When one is anxiously thinking, even slight stimuli may produce involuntary and reflex movements. So, also, during sleep, such reflex movements may be observed, when the skin is touched or tickled; for example, when one touches the palm of the hand of a sleeping child, the impression on the skin of the palm producing a reflex movement of the muscles which close the hand. But when the individual is awake no such reflex is produced.

Further, many reflex actions are capable of being more or less controlled or even altogether prevented by the will, of which the following may be quoted as familiar examples:

When the foot is tickled we can, by an effort of will, prevent the reflex action of jerking it away. So, too, the involuntary closing of the eyes and starting back, when a blow is aimed at the head, can be similarly restrained. Darwin has mentioned an interesting example of the way in which such an instinctive reflex act may override the strongest effort of the will. He placed his face close against the glass of the cobra's cage in the Reptile House at the Zoological Gardens, and, though of course thoroughly convinced of his perfect security, could not by any effort of the will prevent himself from starting back when the snake struck with fury at the glass.

It can be readily shown, by comparing a spinal frog and a normal uninjured frog, that stimuli which call forth definite reflexes in the one often produce no movement of the other.

Cutaneous and Muscle Reflexes as Diagnostic Signs. In the human subject two classes of reflex actions dependent upon the spinal cord are usually distinguished, the alterations of which, either of increase or of diminution, are indications of some abnormality, and are used as a means of diag-

nosis in nervous and other disorders. They are termed respectively *cutaneous reflexes* and *muscle reflexes*. Cutaneous reflexes are set up by a gentle stimulus applied to the skin. The subjacent muscle or muscles contract in response. Although these cutaneous reflex actions may be demonstrated almost anywhere, yet certain of such actions as being most characteristic are distinguished, *e.g.*, plantar reflex; gluteal reflex, *i.e.*, a contraction of the gluteus maximus when the skin over it is stimulated; cremaster reflex, retraction of the testicle when the skin of the inside of the thigh is stimulated, and the like. The ocular reflexes, too, are important. They are contraction of the iris on exposure to light, and its dilatation on stimulating the skin of the cervical region. All of these cutaneous reflexes are true reflex actions. They differ in different individuals, and are more esaily elicited in the young.

Muscle reflexes or tendon reflexes consist of a contraction of a muscle under conditions of more or less tension, when its tendon is sharply tapped. The so-called patellar-tendon reflex is the best known of this variety of reflexes. If one knee be slightly flexed, as by crossing it over the other, so that the quadriceps femoris is extended to a moderate degree, and the patella tendon be tapped with the fingers, the muscle contracts and the foot is jerked forward. Another variety of the same phenomenon is seen if the foot is flexed so as to stretch the calf muscles, and the tendo Achillis is tapped; the foot is extended by the contraction of the stretched muscles. It appears, however, that the tendon reflexes are not exactly what their name implies. The interval between the tap and the contraction is said to be too short for the production of a true reflex action. It is suggested that the contraction is caused by local stimulation of the muscle, but that this would not occur unless the muscle had previously been stimulated by the tension applied, and placed in a condition of excessive irritability. It is probable that the condition on which it depends is a reflex change in the spinal irritability acting on the muscle or exaggerated muscular tone, which is admitted to be a reflex phenomenon in the spinal cord.

Conduction in the Spinal Cord. With the differentiation of the central nerve axis in vertebrates the conduction in the spinal cord becomes of increasing importance, reaching its maximum in man. It is evident that the cord is the path by which all nerve impulses arising in the trunk or in the arms and legs must reach the brain, or *vice versa*. Impulses of peripheral origin can and do produce reflexes, but they can arouse sensations and be perceived only after they have been conducted to the cerebral cortex. Motor impulses arising in the brain can reach the anterior-horn cells of the cord only through the cord as a conducting path. The continuity of the cord, therefore, while not necessary for the execution of reflexes, is absolutely necessary for the higher coordinations of the reflexes and for the excitation and controlling influence of the brain.

Illustrations of this are furnished by various examples of paralysis, but

by none better than by the common paraplegia, or loss of sensation and voluntary motion in the lower part of the body, in consequence of destructive disease or injury of a section including the whole thickness of the spinal cord. Such lesions destroy the communication between the brain and all parts of the spinal cord below the seat of injury, and consequently cut off from their connection with the brain the various organs supplied with nerves issuing from those parts of the cord.

It is not probable that the conduction of motor or sensory impulses is effected, under ordinary circumstances, to any great extent, as was formerly supposed, through the gray substance of the cord, *i.e.*, from cell to cell through the short filaments lying wholly within the gray substance. But cells with fibers running for short distances in the ground bundles are numerous, and these short connectives are capable of conducting impulses along the cord. All parts of the cord are not alike able to conduct all impressions; and as there are separate nerve fibers for motor and for sensory impressions, so in the cord separate and determinate tracts serve to conduct always the same kind of impressions. The sensations of touch, and perhaps of temperature and pain, do not appear to have such sharply limited tracts as do the motor impulses.

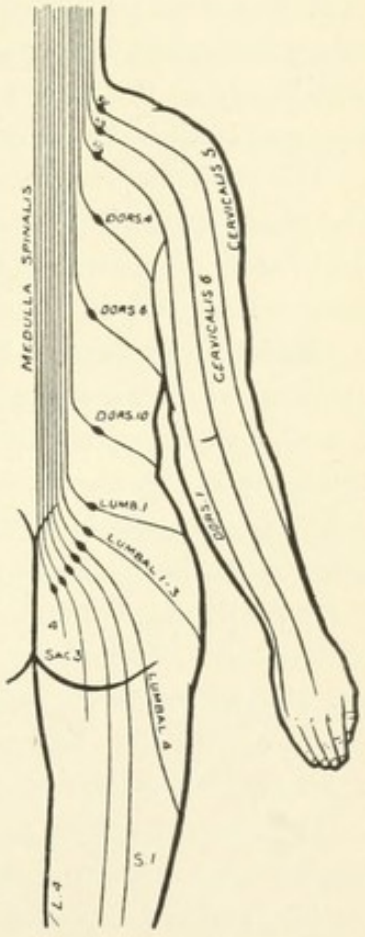


FIG. 369.—Diagram to Show the Manner in Which the Fibers of the Posterior Nerve Roots Enter and Ascend the Posterior Columns of the Cord. (Edinger.)

Experimental and other observations point to the following conclusions regarding the conduction of sensory and motor impressions through the spinal cord. Many of these conclusions must, however, be received with considerable reserve.

Sensory Impulses. The sensory impressions of touch, pain, heat and cold, and of the muscular sense are conducted to the spinal cord by the posterior nerve roots. Certain sensory impressions are then carried directly into the postero-median column on the same side, and thence up to the nucleus of this column in the medulla. It is mainly the impulses of the muscle sense and of the sense of touch that take this course through the cord, though the sense of touch is not wholly interrupted upon injury to the posterior columns. In lower animals it is scarcely interfered with at all. The posterior columns unquestionably are the primary muscle sensory paths. Visceral sensations are carried by the posterior root fibers to the cells of the column of Clarke in the posterior horn, figure 361. From there the impulses pass to the direct

cerebellar tract on the same side, and thence up through the medulla to the cerebellum, figure 396. The impressions of pain, and of heat and cold, are conveyed to the nerve cells in the posterior cornua of the same side in part, and in part to the nerve cells in the posterior cornu and median gray matter of the opposite side. From this point, the impulses are taken up again by intermediary neurones and conveyed through the anterior and lateral columns of the cord to the brain in the ascending tract of Gowers. By reason of the great number of collaterals and the interpolation in the course of the sensory impulse of many intermediary neurones, it has been difficult to make out very sharply defined tracts in the spinal cord for the conduction of the sensations of temperature, pain, and touch. If one set of fibers is destroyed by disease, others seem able, through the collaterals, to take up its function. We can say that injury to the lateral columns has resulted in loss of the sense of pain, heat and cold, but with only partial disturbance of touch sensations.

It is probable, also, that pain and temperature sensations cross over at once to a considerable extent and pass up in the opposite side of the cord to which they enter. Touch and the muscle sense impressions, especially the latter, pass up largely upon the same side until they reach the medulla or cerebellum.

Motor Impulses. Motor impulses are conveyed downward from the cerebral cortex of the brain along the pyramidal tracts, viz., the crossed or lateral, and the direct or anterior, chiefly the former. In the crossed pyramidal tract the impressions pass down chiefly on the side opposite to which they originate, having crossed over in the decussation in the medulla. But some motor impulses do not cross in the medulla, but descend in the direct pyramidal tract to lower levels of the cord, where they cross in the anterior commissure. The motor fibers for the legs partially pass downward in the lateral columns of the same side without decussation. This is also probably the case with the bilateral muscles, *i.e.*, muscles of the two sides that act together, such as the intercostal muscles and other muscles of the trunk.

It is quite certain, as was just now pointed out, that the fibers of the anterior nerve roots are more numerous than the fibers proceeding downward from the brain in the pyramidal tracts, or the so-called pyramidal fibers. This is because each pyramidal fiber is really a very long nerve process or axone, and is supplied in its course with a large number of collaterals, which go off at different points, and thus put it in relation with different groups of nerve cells in the anterior cornua at various levels. Each nerve fiber of the pyramidal tract, by means of its collaterals, can control a number of nerve cells, and can thus coordinate the action of impulses sent out through the anterior roots to a number of groups of muscles. In other words, the gray matter of the anterior cornua contains an apparatus with various complicated coordinating powers, which apparatus is under the regulative control of the neurones whose cells of origin are in the cortex of the brain. This is the same apparatus that is also reflexly influenced by sensory impressions passing to the cord.

Division of a single anterior pyramid of the medulla at a point just above the decussation is followed by paralysis of voluntary motions in the muscles of the opposite side in all parts below. Disease or division of any part of the cerebro-spinal axis below the seat of decussation of the pyramids is followed by impairment or loss of voluntary motion on the same side of the body. The paralysis is never quite complete, and the opposite side usually shows some slight impairment of function of the muscle.

When one-half of the spinal cord is cut through in monkeys, the results are as follows (Mott): Motor paralysis of the muscles of the same side (never complete paralysis of the muscles used in bilateral associated action), followed by gradual recovery of muscular movement, except of the finer movements of the hand and foot; wasting and flabbiness of the muscles; sensory paralysis of the same side (temperature, touch, pain, and pressure); temporary vaso-motor paralysis on the same side. The temperature of the affected side is depressed 1 to 3° F.

III. THE BRAIN STEM.

General Arrangement of Parts of the Brain. The great relative and absolute size of the cerebral hemispheres in the adult man and in mammals to a great extent masks the real arrangement of the several parts of the brain. An examination of the accompanying diagram, figures 370, 371, reveals that the parts of the brain are disposed in a linear series, as follows (from before backward): Olfactory lobes, cerebral hemispheres, thalamencephalon (optic thalami and third ventricle), the mid-brain (corpora quadrigemina and crura cerebri), medulla oblongata and cerebellum.

This linear arrangement of parts actually occurs in an early stage of the development of the human fetus, and it is permanent in some of the lower Vertebrata. In fishes the cerebral hemispheres are represented by a pair of ganglia intervening between the olfactory and the optic lobes, and considerably smaller than the latter, their adult development is fairly well represented by the figure 387. In Amphibia the cerebral lobes are further developed, and are larger than any of the other ganglia.

In reptiles and birds the cerebral ganglia attain a still further development, and in Mammalia the cerebral hemispheres exceed in weight all the rest of the brain. As we ascend the scale, the relative size of the cerebrum increases, till in the higher apes and man the hemispheres, which commenced as two little lateral buds from the anterior cerebral vesicle, have grown upward and backward, completely covering in and hiding from view practically all the rest of the brain. At the same time the smooth surface of the cerebral cortex of many lower mammalia, such as the rabbit, is replaced by the labyrinth of convolutions of the human brain.

When the cerebral hemispheres are removed, several large basal masses of

nerve substance are revealed: the *optic thalami*, the *corpora quadrigemina*, and the *crus cerebri*. These structures, together with the pons and the medulla, form a direct continuation forward of the spinal cord and sometimes are designated under the general term of the *brain stem*.

For convenience of description, the physiology of the brain will be presented by discussing the three main subdivisions: the *brain stem*, the *cerebral hemispheres*, and the *cerebellum*.

The human brain on superficial examination does not seem to follow the general plan outlined above, but when the cerebral hemispheres and the

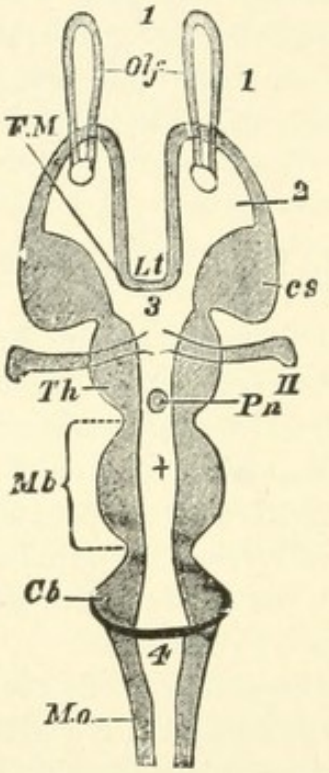


FIG. 370.—Diagrammatic Horizontal Section of the Vertebrate Brain. The figures serve both for this and the next diagram. *Mb*, mid-brain; what lies in front of this is the fore-, and what lies behind the hind-brain; *Lt*, lamina terminalis; *Olf*, olfactory lobes; *Hmp*, hemispheres; *Th. E*, thalamencephalon; *Pn*, pineal gland; *Py*, pituitary body; *F.M.*, foramen of Munro; *cs*, corpus striatum; *Th*, optic thalamus; *CC*, crura cerebri; the mass lying above the canal represents the corpora quadrigemina; *Cb*, cerebellum; *I–IX*, the nine pairs of cranial nerves; 1, olfactory ventricle; 2, lateral ventricle; 3, third ventricle; 4, fourth ventricle; +, iter a tertio ad quartum ventriculum. (Huxley.)

cerebellum are removed then it is found that what remains closely follows the plan presented. This central axis, or *brain stem*, is shown in part in figure 377.

The morphological parts of the brain usually given are:

1. The *fore-brain*, which consists of the corpora striata and the cerebral hemispheres.

2. The *inner-brain*, which consists of the optic thalami and the parts enclosing the greater part of the third ventricle.

3. The *mid-brain*, which comprises the crura cerebri and the corpora quadrigemina enclosing the aqueduct of Sylvius.

4. The *hind-brain*, which comprises the pons Varolii, forming the floor of the fourth ventricle, and the cerebellum, forming the roof.

5. The *after-brain*, the medulla oblongata or bulb.

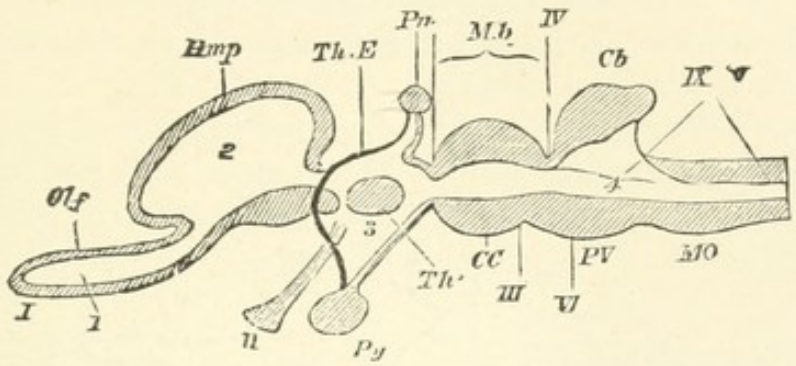


FIG. 371.—Longitudinal and Vertical Diagrammatic Section of a Vertebrate Brain. Letters as before. Lamina terminalis is represented by the strong black line joining *Pn* and *Py*. (Huxley.)

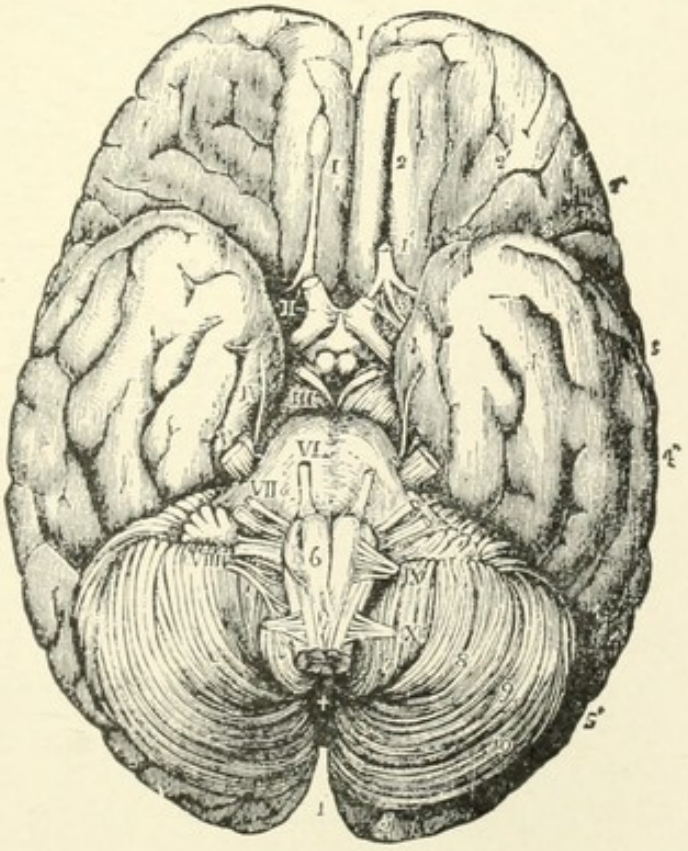


FIG. 372.—Base of the Brain. 1, Superior longitudinal fissure; 2, 2', 2'', anterior cerebral lobe; 3, fissure of Sylvius, between anterior and 4, 4', 4'', middle cerebral lobe; 5, 5', posterior lobe; 6, medulla oblongata. The figure is in the right anterior pyramid; 7, 8, 9, 10, the cerebellum; +, the inferior vermiform process. The figures from *I.* to *IX.* are placed against the corresponding cerebral nerves; *III.* is placed on the right crus cerebri. *VI.* and *VII.* on the pons Varolii; *X.*, the first cervical or suboccipital nerve. (Allen Thomson.) × ½.

THE MEDULLA OBLONGATA OR BULB.

Anatomical Structure. The medulla oblongata is continuous with the spinal cord at its upper end. It lies within the cranial cavity and forms the first part of the brain stem. The medulla consists of masses of nerve cells situated in the interior, but pretty generally distributed throughout the mass. The cell-masses are subdivided by laminæ of nerve fibers into groups, or nuclei, which give origin to or form the terminations of the various ranks of nerve fibers.

The nerve fibers are arranged partly in columns and partly in fasciculi traversing the central cellular matter. The medulla oblongata is larger than

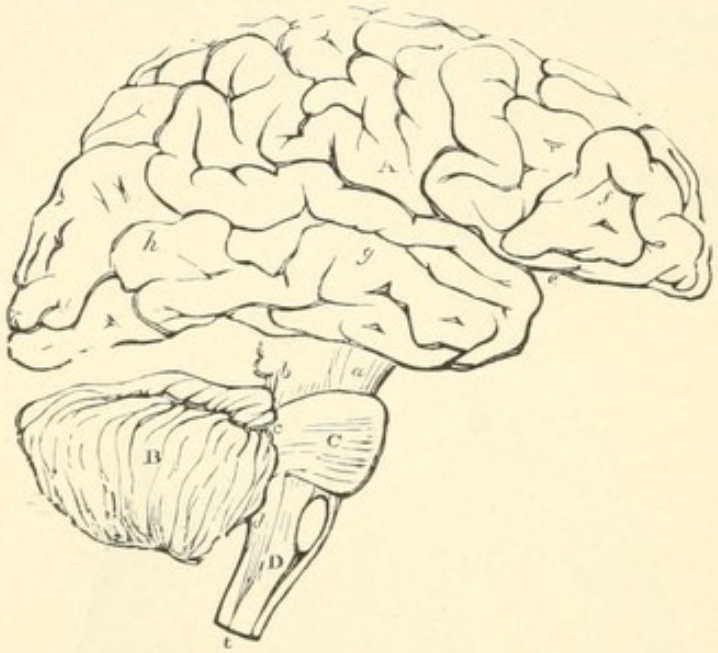


FIG. 373.—Plan in Outline of the Brain as seen from the Right Side. ×½. The parts are represented as separated from one another somewhat more than natural, so as to show their connections. *A*, Cerebrum; *f*, *g*, *h*, its anterior, middle, and posterior lobes; *e*, fissure of Sylvius; *B*, cerebellum; *C*, pons Varolii; *D*, medulla oblongata; *a*, peduncles of the cerebrum; *b*, *c*, *d*, superior, middle, and inferior peduncles of the cerebellum. (From Quain.)

any part of the spinal cord. Its columns are pyriform, enlarging as they proceed toward the brain, and are continuous with those of the spinal cord. Each half of the medulla, therefore, may be divided into three columns or tracts of fibers, continuous with the three columns of which each half of the spinal cord is made up, but the columns are more prominent than those of the spinal cord, and are separated from each other by deeper grooves. The *anterior*, continuous with the anterior columns of the cord, are called the *pyramids*. The postero-median and postero-external columns are also represented at the posterior or dorsal aspect of the cord as the *fasciculus gracilis* and the *fasciculus cuneatus*. The posterior pyramids of the medulla, which include these two columns of white matter, soon become much increased in width by the addition of a new column of white matter outside the other two, which is known

as the *fasciculus of Rolando*. In the upper portion of the medulla the gracile, cuneati, and Rolandic fasciculi are replaced by the restiform bodies (the inferior peduncles of the cerebellum). The lateral columns of the cord are scarcely represented as such in the bulb.

It may be said then that the bulb at its commencement differs only slightly in size from the cord, with which it is continuous. It soon becomes larger both laterally and antero-posteriorly. It opens out on the dorsal surface into a space which is known as the fourth ventricle, and from being a cylinder with a central canal it is flattened out on the dorsal surface by the gradual approach of the central canal to that surface, where it is directly continuous with the fourth ventricle.

If the bulb be examined on its anterior or ventral surface, it is found that the anterior fissure, which is a continuation of the same fissure in the cord, is

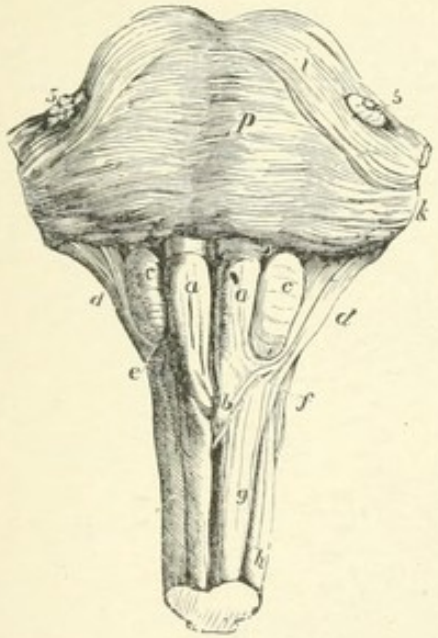


FIG. 374.

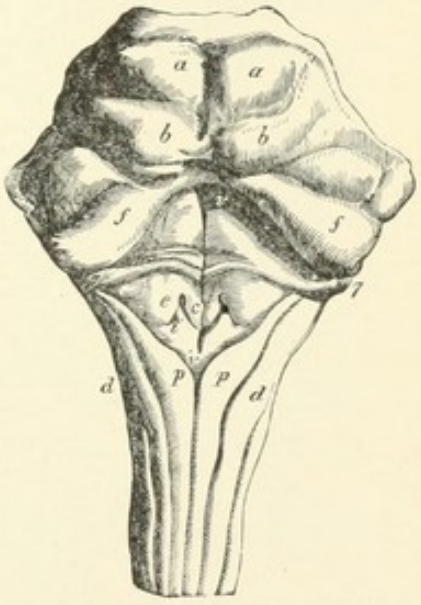


FIG. 375.

FIG. 374.—Ventral or Anterior Surface of the Pons Varolii and Medulla Oblongata. *a*, *a*, Anterior pyramids; *b*, their decussation; *c*, *c*, olivary bodies; *d*, *d*, restiform bodies; *e*, arciform fibers; *f*, fibers passing from the anterior column of the cord to the cerebellum; *g*, anterior column of the spinal cord; *h*, lateral column; *p*, pons Varolii; *i*, its upper fibers; 5, 5, roots of the fifth pair of nerves.

FIG. 375.—Dorsal or Posterior Surface of the Pons Varolii, Corpora Quadrigemina, and Medulla Oblongata. The peduncles of the cerebellum are cut short at the side. *a*, *a*, the upper pair of corpora quadrigemina; *b*, *b*, the lower; *f*, *f*, superior penduncles of the cerebellum; *c*, eminence connected with the nucleus of the hypoglossal nerve; *e*, that of the glosso-pharyngeal nerve; *i*, that of the vagus nerve; *d*, *d*, restiform bodies; *p*, *p*, posterior pyramids; *v*, *v*, groove in the middle of the fourth ventricle, ending below in the calamus scriptorius; 7, 7, roots of the auditory nerves.

occupied at the most posterior part by fibers which are crossing from one side to the other. This is what is known as the *decussation* of the pyramids. It is formed of the fibers which occupy the postero-lateral region in the cord, and are called the crossed pyramidal fibers. The lateral pyramidal fibers of either side after crossing the middle line become part of the pyramid of the opposite side; the rest of the pyramid is made up of the fibers which in the anterior

column of the cord are known as the direct or uncrossed pyramidal tract. These two pyramidal strands of fibers are those which degenerate after lesions of the parts of the cerebrum known as the motor areas of the cortex. They can therefore be traced downward after such lesions as tracts of degeneration. They are the descending fibers of communication between the cerebral motor cells of the cortex and the different segments of the spinal cord. The outer borders of the anterior pyramids of the bulb are marked by the exit from that part of the nervous axis of the twelfth or hypoglossal nerve. Still more laterally than this nerve there is on either side a rounded elevation or column which

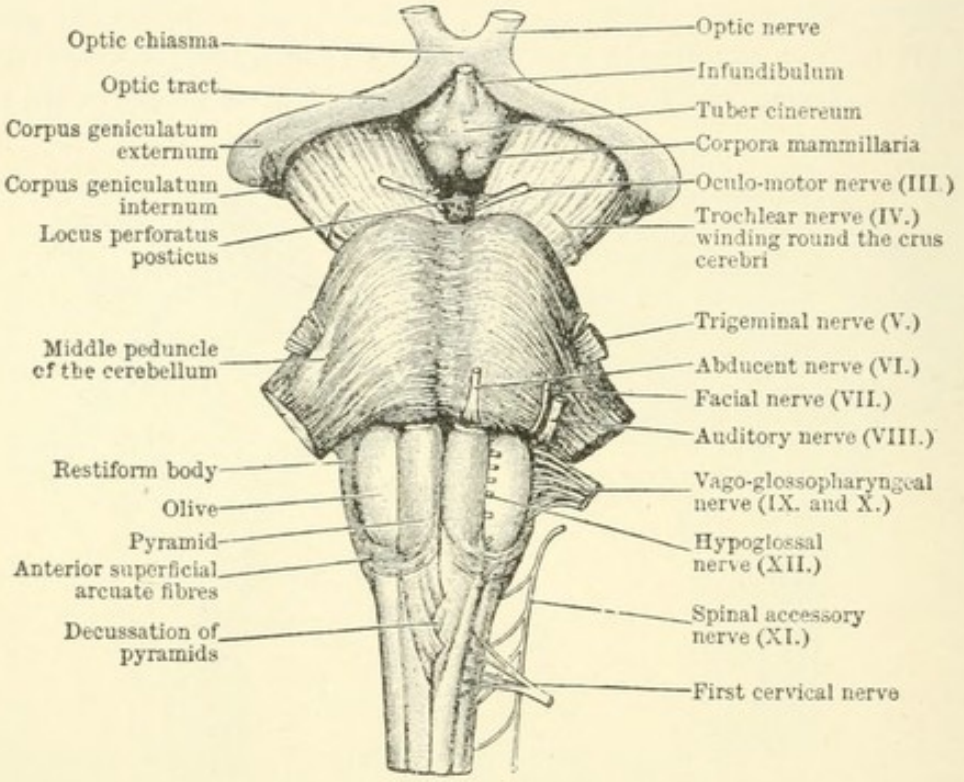


FIG. 376.—Front View of the Medulla, Pons, and Mesencephalon of a Full-Term Human Fetus. (Cunningham.)

is known as the *olivary body*. It begins at a level a little lower than the opening of the fourth ventricle. On the dorsal side of the olivary body is the line of origin of the eleventh, tenth, and ninth nerves, and from this to the posterior fissure is the posterior pyramid.

The changes in structure which are noticed in a series of sections of the bulb from below upward may be summarized: In the dorsal or posterior region, the posterior cornua are pushed more to each side by the large number of sensory fibers ascending in the posterior columns, and terminating in the gracile and cuneate nuclei. The substance of Rolando is increased and becomes rounded, reaching almost to the surface of the bulb on each side, only a small tract of longitudinal fibers of the root of the fifth nerve intervening.

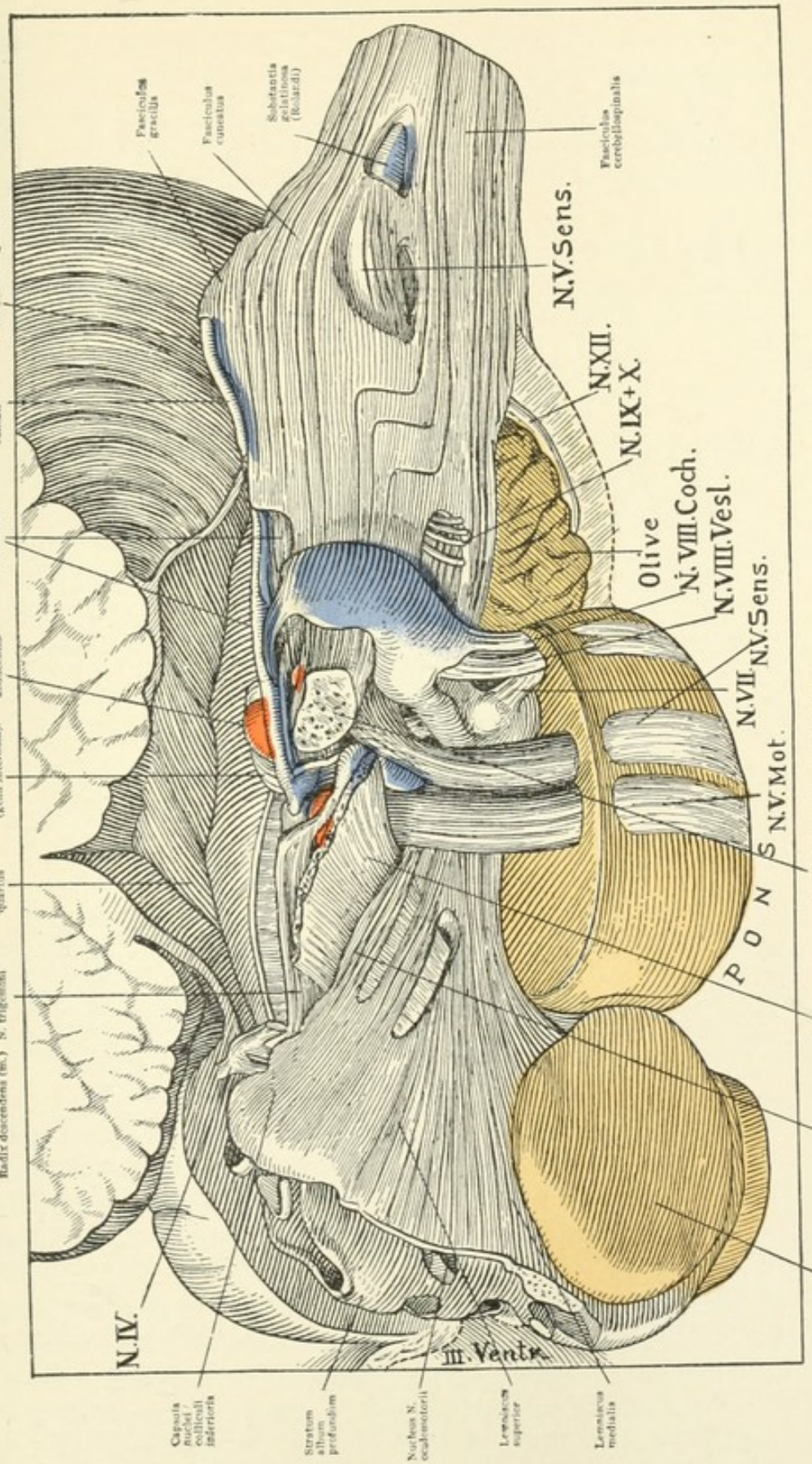


FIG. 377.—Reconstruction of the medulla, pons, and mid-brain of the new-born babe. Motor nuclei, red; sensory, blue. (Florence R. Sabin.)

There is a great increase of the reticular formation around the central canal, and the lateral approaches the anterior cornu. Then at the ventral or anterior aspect the decussation of the pyramids begins. By this crossing over of the fibers, the tip of the gray anterior cornu is cut off from the rest of the gray matter. The central canal is pushed farther toward the posterior surface, first of all by the decussation of the anterior pyramids just mentioned, and later on, *i.e.*, above, by another decussation of more dorsal fibers. These fibers of the second decussation as they cross form a median raphe and also help to break up the remaining gray matter into what is called a *reticular formation.*

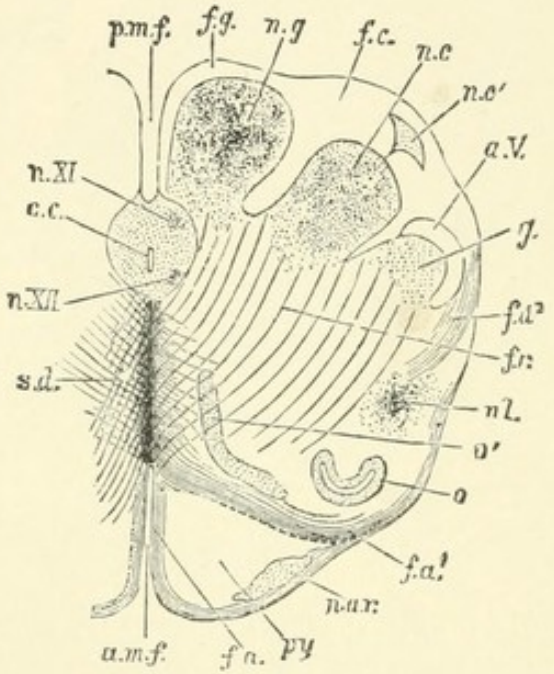


FIG. 378.—Anterior or Dorsal Section of the Medulla Oblongata in the Region of the Superior Pyramidal Decussation. *a.m.f.*, Anterior median fissure; *f.a.*, superficial arciform fibers emerging from the fissure; *py*, pyramid; *n.ar.*, nuclei of arciform fibers; *f.a.*, deep arciform becoming superficial; *o*, lower end of olivary nucleus; *n.l.*, nucleus lateralis; *f.r.*, formatio reticularis; *f.a.*², arciform fibers proceeding from the formatio reticularis; *g.*, substantia gelatinosa of Rolando; *a. V.*, ascending root of fifth nerve; *n.c.*, nucleus cuneatus; *n.c.'*, external cuneate nucleus; *n.g.*, nucleus gracilis; *f.g.*, funiculus gracilis; *p.m.f.*, posterior median fissure; *c.c.*, central canal surrounded by gray matter, in which are *n.XI.*, nucleus of the spinal accessory, and *n.XII.*, nucleus of the hypoglossal; *s.d.*, superior pyramidal decussation. (Modified from Schwalbe.)

These fibers arise from the nuclei of the fasciculus gracilis and fasciculus cuneatus of either side, and they are looked upon as a sensory decussation.

There are to be made out various masses of cells in addition to the reticular formation, viz., the nuclei of the fasciculus gracilis and fasciculus cuneatus, figure 379, *n.g.* and *n.c.*

The olivary bodies extend forward almost to the level of the pons. They consist of cells and fibers. The cellular matter consists of a plicated thinnish layer of small nerve-cells, folded upon itself in the form of a loop, with the ends turned inward and slightly dorsal, figure 379, *o.* The gray loop is filled with and covered by white fibers.

Internal to the olivary body on either side are two small masses of gray

matter, one more ventral to the other, called accessory olives, external and internal, and on the surface of the anterior pyramid on either side a small mass of gray matter, external arcuate nucleus; laterally another mass of the same material, the representative of the lateral nucleus of the cord, is seen, viz., the antero-lateral nucleus, which gives origin to the spinal accessory nerve.

It will be necessary to follow as shortly as possible the fibers of the spinal cord upward into the bulb and beyond.

Tracts Through the Medulla. The crossed and direct pyramidal tracts have already been described. Nothing definite is known of the antero-lateral descending tracts. The direct cerebellar tracts pass laterally into the restiform

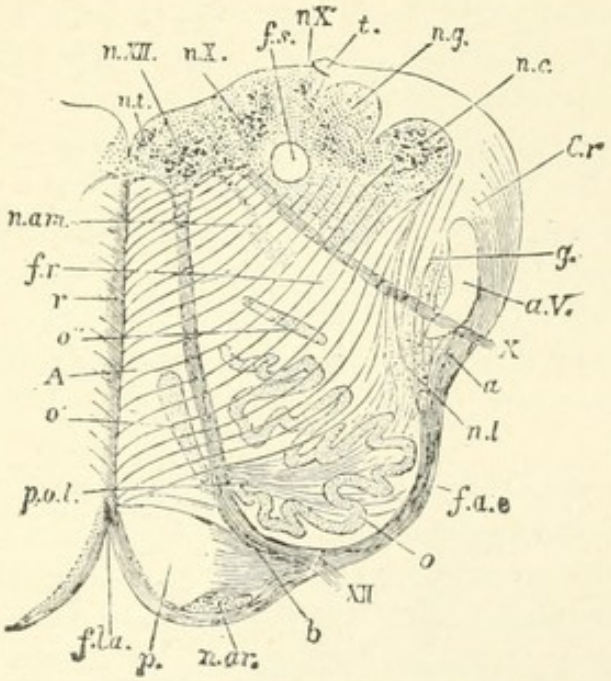


FIG. 379.—Section of the Medulla Oblongata at about the Middle of the Olivary Body. *f.l.a.*, Anterior median fissure; *n.ar.*, nucleus arciformis; *p.*, pyramid; *XII.*, bundle of hypoglossal nerve emerging from the surface; at *b*, it is seen coursing between the pyramid and the olivary nucleus, *o.*; *f.a.e.*, external arciform fibers; *n.l.*, nucleus lateralis; *a.*, arciform fibers passing toward restiform body, partly through the substantia gelatinosa, *g.*, partly superficial to the ascending root of the fifth nerve, *a.V.*; *X.*, bundle of vagus root emerging; *f.r.*, formatio reticularis; *c.r.*, corpus restiforme, beginning to be formed, chiefly by arciform fibers, superficial and deep; *n.c.*, nucleus cuneatus; *n.g.*, nucleus gracilis; *t*, attachment of the ligula; *f.s.*, funiculus solitarius; *n.X.*, *n.X.'*, two parts of the vagus nucleus; *n.XII.*, hypoglossal nucleus; *n.t.*, nucleus of the funiculus teres; *n.am.*, nucleus ambiguus; *r.*, raphe; *A.*, continuation of the anterior column of cord; *o'*, *o''*, accessory olivary nucleus; *p.o.*, pedunculus olivæ. (Modified from Schwalbe.)

bodies and go to the cerebellum. The antero-lateral ascending tracts (Gowers) appear to have the same destination, but pass indirectly into the cerebellum by way of the superior medullary velum; some of the fibers probably pass upward to higher centers. The fibers of the postero-median and postero-external columns of Goll and Burdach, of the cord, end in the nuclei of the fasciculus gracilis and cuneatus respectively; at any rate, ascending degeneration of these columns cannot be traced above these nuclei. The rest of the fibers of the cord appear to end in the reticular formation of the bulb.

Connections of the Bulb with the Cerebrum and Cerebellum. The

pyramidal tracts connect the bulb with the cerebrum; and the direct cerebellar and the antero-lateral ascending tract, tract of Gowers, connect it with the cerebellum. Other connections of the bulb with the cerebrum and with the cerebellum are:

1. Fibers from the nucleus gracilis and nucleus cuneatus, which, as we have said, are the endings of the fibers of the columns of Goll and Burdach of the cord, pass in sets in the following manner:

a. Internal arcuate fibers pass down and inward to the opposite side in the reticular formation, composing in part the superior or sensory decussation, and in the inter-olivary region enter the *mesial fillet*, which passes upward through the pons to end about the cells in the mid-brain and in the optic thalami. These fibers are probably augmented by the addition of fibers from the anterior columns of the cord, and by fibers arising from cells in the sensory nuclei of the cranial nerves ending in the bulb.

b. External arcuate fibers, after decussating in the same way, pass outward superficially over the anterior pyramid and olivary body, reaching the restiform body and passing to the side of the cerebellum opposite to their nuclei of origin. These fibers appear to be interrupted, at least in part, in the external arcuate nuclei. They connect one side of the spinal cord with the opposite side of the cerebellum through the gracile and cuneate nuclei.

c. Direct lateral fibers pass to the restiform body and so to the same side of the cerebellum.

2. Fibers from the olivary body pass to the opposite side of the cerebellum through the reticular formation and restiform body.

3. Fibers from the vestibular nucleus of the eighth or auditory nerve in the floor of the fourth ventricle pass to the same side of the cerebellum.

Functions of the Medulla Oblongata. The chief functions of the medulla are those of carrying impulses, *i.e.*, conduction, between the cord and brain; of carrying on activities distinctly reflex in character; and of producing automatic activity.

The Medulla as a Conducting Path. The medulla is the pathway of all ascending and descending nerve impulses between the spinal cord and most of the peripheral sensory and motor apparatus on the one hand, and the cerebellum and the cerebral centers on the other. These conducting paths are described in the tracts that have already been discussed at some length. They are represented graphically in the diagrams, figures 380 and 396.

Reflex Centers of the Medulla. The larger number of the cranial nerves, as we shall presently see, take their origin from the medulla and pons. Some of these nerves have both sensory and motor roots, while others are either motor or sensory exclusively. A large percentage of the afferent or sensory impulses that enter the medulla produce reflex effects on the motor nuclei so richly represented in the medulla. The nuclei, or centers, regulating some of the most important functions of the body are

among those in this group. When certain of these centers are interfered with, death follows.

Life may continue when the spinal cord is cut away in successive portions from below upward as high as the point of origin of the phrenic nerves. In amphibia, the brain has been all removed from above, and the cord removed as far as the medulla oblongata from below; yet so long as the medulla oblon-

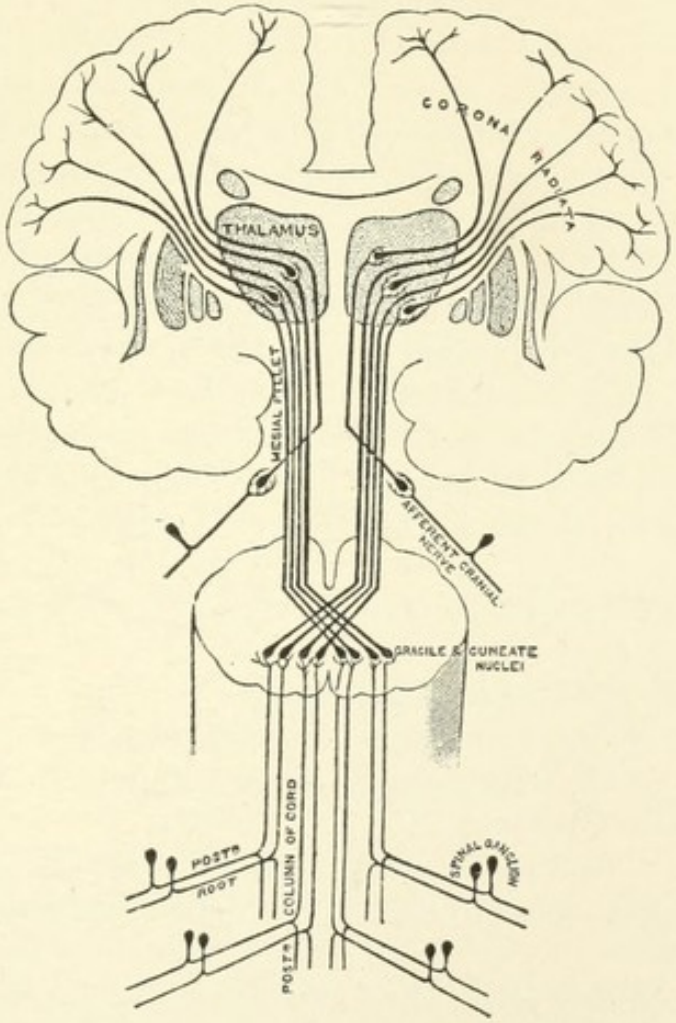


FIG. 380.—Diagram of Ascending Conduction Paths from the Cord through the Medulla and the Thalamus to the Cerebral Cortex. (Cunningham.)

gata was left intact, respiration and life were maintained. But if the medulla oblongata is wounded, particularly if it is wounded in its central part opposite the origin of the vagi, the respiratory movements cease, and the animal dies from asphyxiation. This effect ensues even when all parts of the nervous system except the medulla oblongata are left intact.

Injury and disease in men are accompanied by the same nerve disturbances as are exhibited by these experiments on animals. Numerous instances are recorded in which injury to the medulla oblongata has produced instantaneous

death; and, indeed, it is through injury to it, or of the part of the cord connecting it with the origin of the phrenic nerve, that death is commonly produced in fractures attended by sudden displacement of the upper cervical vertebræ.

The majority of the medullary centers are reflex centers simply, and are stimulated by afferent or by voluntary impulses. Some of them are automatic centers and are capable of sending out efferent impulses without previous stimulation by afferent or by voluntary impulses. The automatic centers are, however, normally influenced by reflex or by voluntary impulses.

Some of these reflex centers are: 1. Bilateral centers for the movements of *deglutition*. The medulla oblongata contains in the motor nuclei of the ninth and tenth nerves the centers whence are derived the motor impulses enabling the muscles of the palate, pharynx, and esophagus to produce the successive coordinated and adapted movements necessary to the act of deglutition, page 313. This is proved by the persistence of the act of swallowing in some of the lower animals after destruction of the cerebral hemispheres and cerebellum; its existence in anencephalous monsters; and by the complete arrest of the power of swallowing when the medulla oblongata is injured in experiments.

2. Bilateral centers for the combined muscular movements of *sucking*, the nerves concerned being the facial for the lips and mouth, the hypoglossal for the tongue, and the inferior maxillary division of the fifth for the muscles of the jaw.

3. Bilateral centers for the *secretion of saliva*, which have been already mentioned, page 305.

4. Bilateral centers for *vomiting*, page 330.

5. Bilateral centers for *coughing*, which is a reflex act quite independent of the respiratory act. The coughing center is situated above the inspiratory part of the respiratory center.

6. Bilateral centers for the *dilatation of the pupil*, the fibers from which pass out through the spinal cord in the two upper dorsal nerves into the cervical sympathetic.

7. The *respiratory center* of the medulla has already been discussed as regards its automatic action. It is only necessary to repeat here that although it is automatic in its action, being capable of direct discharge of respiratory impulses with no other stimulus than the condition of the blood circulating within it, yet it is constantly reflexly influenced by afferent impulses. The respiratory center has been proven to be bilateral. It also consists of an inspiratory part and of an expiratory part. The center is influenced by voluntary impulses, but one can not voluntarily control this center to the point of death. The vagus influence is probably the most constant of those stimulating the respiratory center. But the respiratory reflexes are going on constantly in response to afferent impulses flowing into the medulla from numerous other sensory nerves over the entire body.

8. The *cardio-inhibitory centers*. The medulla contains the centers which maintain the proper rhythm of the heart, these centers acting through the vagus fibers. These terminate in a local intrinsic mechanism which has been already discussed. It is claimed that the center can be stimulated directly, as by the condition of the blood circulating within it. It is constantly exerting a tonic influence over the heart, which is the chief reason for considering it an automatic center. But the cardio-inhibitory center is primarily a reflex center. Sensory or afferent impulses arriving over the sensory paths in the vagus itself, by abdominal paths through the sympathetic, and through cutaneous nerves, are constantly causing reflex discharges of inhibitory impulses from this center.

9. *Accelerator centers* for the heart are present in the medulla. They are reflexly stimulated by sensory impulses arising from the same general source as in the preceding center.

10. *Vaso-motor* centers which control the unstriped muscle of the arteries, are also situated in the medulla. The nerve cells constituting the center are under the constant influence of nerve impulses flowing in from the sensory and motor structures throughout the whole body. The reflexes produced by the afferent impulses bring about the variations in vaso-motor tone that not only regulate the general vascular responses of the body, but control and coordinate the local changes in the size of the blood-vessels.

11. Centers for the secretion of *sweat* exist in the medulla. The medullary centers control the subsidiary spinal sweat centers. They may be excited unequally so as to produce unilateral sweating.

The reflex medullary centers described above are comparable to the spinal reflex centers previously described. If the medulla were completely isolated from the higher cerebral centers, and the spinal cord removed with the exception of those paths which are necessary to maintain respiration, these medullary reflex centers would be able to coordinate afferent impulses in the same general way that isolated segments of the cord do. In the living body, however, the medullary centers are under the influence of changes going on in regions of the nervous system both above and below, changes which constantly influence the details of the reactions. The activities are unconscious reflexes in the same sense that the motor reflexes of the spinal cord are unconscious and machine-like. The main difference is one of complexity and not of kind.

The Pons Varolii. The pons Varolii is generally spoken of as a great commissure of fibers; of fibers which connect with the two halves of the cerebellum and which connect the bulb and spinal cord with the upper part of the brain. It must not be forgotten that the pons contains several smaller collections of nerve cells. Sections reveal the following parts or structures, beginning from the anterior or ventral surface.

1. Transverse or commissural fibers connect one side of the cerebellum with the other through the middle peduncle. These fibers connect the cere-

bellar cortex with the cells of the pontine nuclei; some are afferent, some efferent; some end in the gray matter of the pons on the same side near the ventral surface; others cross to the opposite side of the pons and then become longitudinal, passing on to the *tegmentum*.

2. Fibers longitudinal in direction are arranged in larger or smaller bundles and are separated by gray matter. Most of these fibers are pyramidal fibers which pass down to the pyramids of the medulla.

3. The dorsal portion of the pons is made up to a considerable extent of the

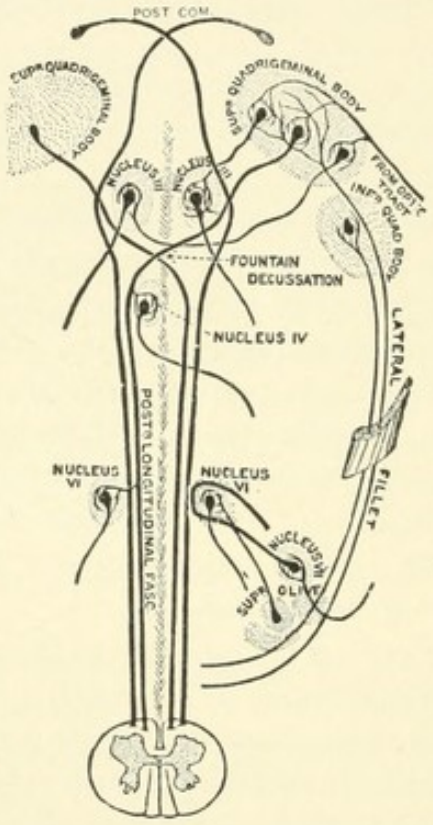


FIG. 381.—Scheme to Show the Connections of the Posterior Longitudinal Bundle. (Cunningham, modified from Held.)

reticular formation of the tegmental region together with one or two distinct bundles of longitudinal fibers. The chief longitudinal bundle, situated at the junction of the ventral two-thirds with the dorsal third, is the *fillet*, including *a* the larger mesial fillet, a sensory tract previously described arising in the gracile and cuneate nuclei, and by the lateral fillet, an auditory tract. The second, the *posterior longitudinal bundle*, is situated on each side of the mid-line, just internal to the mesial fillet.

4. In the upper part of the pons a mass of gray matter containing pigment, the *locus ceruleus*, forming a part of the origin of the fifth nerve and in the back part a second mass of gray matter, the *superior olive*.

THE MID-BRAIN.

The mid-brain includes the crura cerebri, the corpora quadrigemina, and the geniculate bodies.

The Crura Cerebri. The crura diverge from the anterior edge of the pons Varolii and pass upward on either side toward the cerebral hemispheres. At their anterior termination each of them appears to have upon its dorsal surface, to the inner and outer sides respectively, two large masses of gray matter which have been already spoken of, viz., the optic thalamus and the corpus striatum. The crus is made up of two principal parts. The *crusta*

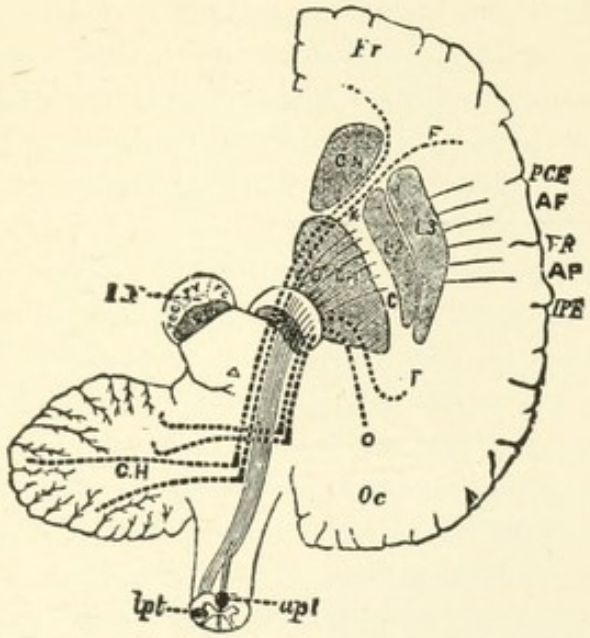


FIG. 382.—Diagram of the Motor Tract as Shown in a Diagrammatic Horizontal Section through the Cerebral Hemispheres, Crura, Pons, and Medulla. *Fr.*, Frontal lobe; *Oc.*, occipital lobe; *AF.*, ascending frontal, *AP.*, ascending parietal convolutions; *PCF.*, pre-central fissure, in front of the ascending frontal convolution; *FR.*, fissure of Rolando; *IPF.*, inter-parietal fissure, a section of crus is lettered on the left side; *SN.*, substantia nigra; *Py.*, pyramidal motor fiber which on the right is shown as continuous lines converging to pass through the posterior limb of *IC.*, internal capsule (the knee or elbow of which is shown thus), upward into the hemisphere and downward through the pons to cross the medulla in the anterior pyramids. (Gowers.)

or *pes* is in the ventral position, and the *tegmentum* in the dorsal position. The two are separated by the *substantia nigra.*

The *pes* consists of longitudinal fibers which pass anteriorly between the optic thalamus and the posterior part (lenticular nucleus) of the corpus striatum, and also more anteriorly. In this situation the fibers form a compact mass which spreads out dorsally in the *corona radiata.* The fibers thus have the form of a fan bent upon itself as they rise to pass into the cerebral hemisphere. This constitutes the *internal capsule*, and that portion of it which forms the angle at which the fibers are bent is called the *genu* of the capsule. The fibers of the internal capsule are connected with different districts of the cerebral cortex. Briefly the connections are, *a*, the fronto-pontine fibers are in the

anterior limb of the capsule; *b*, the pyramidal fibers in the genu and the anterior part of the posterior limb; *c*, the temporo-pontine fibers in the posterior part of the posterior limb. Fibers connecting the optic thalami and corpora striata with the cerebral cortex run in the capsule. The *pes* and the *corona radiata* form the great sensory and motor highway to and from the cerebral cortex.

The *tegmentum* is the continuation anteriorly of the reticular formation of the medulla. It ends for the most part in the neighborhood of the optic thalamus and in the parts beneath. The tegmentum of either side is supposed to be concerned chiefly with afferent impulses. It is made up to a very considerable extent of collections of gray matter, the most important of which are the *substantia nigra*, separating the pes and tegmentum, and the *nucleus ruber*, which is a rounded mass situated more toward the aqueduct of Sylvius; it serves as a way-station in the cerebello-cerebral conduction paths and also has important connections with the spinal cord. The locus niger extends back as far as the posterior corpus quadrigeminum. Posteriorly, the tegmentum is chiefly reticular in structure.

Corpora Quadrigemina. There are two corpora quadrigemina on each side, the anterior and posterior. They form prominences on the dorsal surface of the mid-brain, dorsal to the aqueduct of Sylvius. The posterior corpora quadrigemina receive through the lateral fillet fibers from the cochlear division of the eighth nerve. They are closely associated with the median corpora geniculata, and, like these, give origin to fibers which continue the auditory conduction path upward to the auditory center. The anterior corpora quadrigemina receive fibers from the optic nerve, the mesial fillet, and also from the occipital cortex, as will be more fully described later. They are closely associated with the external corpora geniculata. They also form reflex centers for eye muscles in the ocular adjustments.

Corpora Geniculata. These are two on each side of the brain stem, the external or outer and the median or inner. The external corpus geniculatum is at the side of the crus and appears to be a swelling on the lateral division of the optic tract, and actually receives terminations of the optic fibers, thus constituting a way-station in the optic conduction paths. Similarly the median appears to be the termination of the median division of the optic tract, from which it receives some fibers, figure 416, but it is more intimately connected with the auditory tracts, forming a way-station between the lateral fillet and the auditory cortical center, figure 389.

The Optic Thalami. The optic thalami are oval in shape, and rest upon the crura cerebri. They form part of the floor of the lateral ventricles and their inner sides bound the third ventricle. They are connected by a transverse tract, the middle commissure.

Each thalamus has several collections of gray matter, forming somewhat indistinctly defined masses separated by white fibers. These masses of gray

matter are known as the *nuclei of the thalamus*, and are six in number. They are called the anterior nucleus, the median nucleus, the lateral nucleus, the ventral nucleus, the pulvinar, and the posterior nucleus. The corpora geniculata are also closely associated with the optic thalamus. The anterior nucleus is composed of large nerve cells which receive the terminations of axones of cells of the corpora mammillaria at the base of the brain (bundle of Vicq d'Azyr). There they meet the fibers of the fornix, which establish a relation between this tubercle of the thalamus and the hippocampal convolutions. The median nucleus is connected by its axones with the cortex of the island of Reil and the second and third frontal convolutions. The lateral nucleus is quite large and lies against the internal capsule, into which it sends fibers. It is connected with the central convolutions. The ventral nucleus lies beneath the preceding; it is relatively small. It is connected with the cortex of the frontal lobe and with the operculum, the central convolutions, and the supramarginal gyrus. The fifth nucleus, known as the *pulvinar*, forms the posterior tip of the thalamus, and is connected with the optic tract. The posterior nucleus, lying just below the pulvinar, is a small mass and is connected with the cortex of the interior parietal convolution. The cells of the optic thalamus are thus seen to be connected with a large area of the cerebral cortex. The axones spread out in a great fan in the corona radiata, the thalamus sending more fibers to the cortex than are received from it.

The collections of nerve cells in the optic thalamus are shown by anatomical investigations and by methods of physiological degeneration to be on the pathway of ascending or afferent nerve tracts. Large masses of sensory fibers pass through the optic thalami, the majority of which form synapses about the nerve cells in the thalamus. Even in those cases where there is no distinct ending of the nerve fiber, collaterals are given off which establish physiological connection with the nuclei.

The optic thalamus is thus closely connected with large areas of the cortex. It must at least form an important relay in all those activities which involve the conscious perception of sensory stimuli wherever they may arise. Flechsig even claims that in the optic thalamus there are definite points of sensory localization corresponding to every sensory point in the periphery of the body (including the special senses). The optic thalamus also receives fibers from various parts of the cerebral cortex, thus establishing a double relation with this region.

Owing to the difficulty of those operations which establish isolation of the thalamus, it is not clear to what extent reflex actions may take place through these nuclei. It is probable, however, that extensive coordinations of afferent impulses may be mediated by the nuclei of the thalami. Such activities as walking, riding, writing, speaking, etc., are possibly coordinated reflexes through the optic thalami, perhaps with the assistance of the medulla in the case of walking.

Corpora Striata. The corpora striata are situated in front and to the outside of the optic thalami, partly within and partly without the lateral ventricles.

Each corpus striatum consists of two parts: An intraventricular portion, the *caudate nucleus*, which is conical in shape, with the base of the cone forward (this consists chiefly of gray matter), and an extraventricular portion, the *lenticular nucleus*, separated from the other portion by the internal capsule. The lenticular nucleus is shown in a horizontal section of the hemisphere to consist of three parts, the two internal called *globus pallidus major* and *minor*, and the outer called the *putamen*.

The cells of the corpora striata are somewhat evenly distributed, and not grouped in nuclei. Their axones pass for the most part into the internal capsule. It is doubtful if these ganglia have any direct anatomical relations with the cortex of the brain, but they are intimately connected by fibers to and from the optic thalami, and are connected with the substantia nigra (Flechsig). These nuclei are developed from the walls of the embryonic brain tube and are probably therefore homologous with the areas of the cortex. Their lesion is said to be accompanied by disturbance in muscular coordination. Lesion of the left lenticular nucleus is said to cause some disturbance in the power of speech, though this has not been observed in the case of the right nucleus. Lesions of the corpora striata produce disturbances in heat regulation, causing a rise of body temperature, the rise amounting to as much as 2° or 3° C. in the rabbit. The rise of temperature in man after lesion of the corpus striatum on one side is said to be chiefly on the opposite side of the body (Kaiser).

THE CRANIAL NERVES.

The cranial nerves consist of twelve pairs; they appear to arise (superficial origin) from the base of the brain in a double series, which extends from the under surface of the anterior part of the cerebrum to the lower end of the medulla oblongata. Traced into the substance of the brain and medulla, the roots of the nerves are found to take origin from various masses of gray matter.

The roots of the first or olfactory and of the second or optic nerves will be discussed elsewhere. The third and fourth nerves arise from gray matter beneath the corpora quadrigemina; and the roots of origin of the remainder of the cranial nerves can be traced to gray matter in the floor of the fourth ventricle, and in the more central part of the medulla, around its central canal, as low down as the decussation of the pyramids.

According to their several functions the cranial nerves may be thus arranged:

Nerves of special sense.....	Olfactory, Optic, Auditory, part of the Glosso-pharyngeal, and part of the Trigeminal.
Nerves of common sensation...	The greater portion of the Trigeminal.

Nerves of motion.....	The Motor Oculi; Trochlearis, lesser division of the Trigeminal, Abducens, Facial, and Hypoglossal.
Mixed nerves.....	Facial, Glosso-pharyngeal, Vagus, and Spinal Accessory.

The physiology of the first, second, and eighth nerves will be considered with the Organs of Special Sense.

The Third Nerve or Motor Oculi. *Origin.* The third nerve arises in three distinct bands of fibers from the gray nuclei surrounding the aqueduct of Sylvius near the middle line, but ventral to the canal. The nucleus of origin consists of large multipolar ganglion cells, and extends to the back part of the third ventricle as far as the level of the superior corpora quadrigemina. The

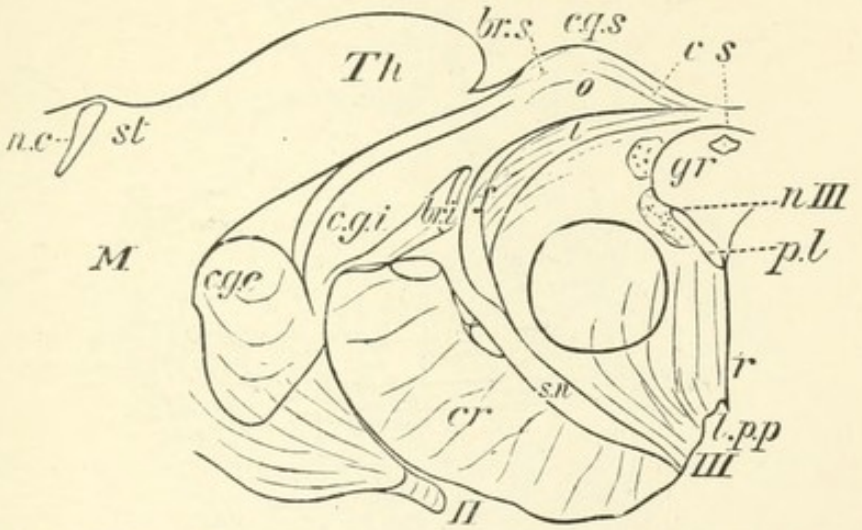


FIG. 383.—Section through Anterior Corpus Quadrigeminum and Part of Optic Thalamus. *s*, Aqueduct of Sylvius; *gr*, gray matter of the aqueduct, *c.q.s*, quadrigeminal eminence; *l*, stratum lemnisci; *o*, stratum opticum, *c*, stratum cinereum; *Th*, pulvinar of optic thalamus; *c.g.e*, *c.g.i*, lateral and median corpora geniculata; *br.s*, *br.i*, superior and inferior brachia, *f*, fillet; *p.l*, posterior longitudinal bundle; *r*, raphé; *III*, third nerve, and *n.III*, its nucleus; *l.p.p*, posterior perforated space; *s.n*, substantia nigra—above this is the tegmentum with the circular area of the red nucleus; *cr*, crusta; *II*, optic tract; *M*, medullary center of hemisphere; *n.c*, nucleus caudatus; *st*, stria terminalis. (After Quain, from Meynert.)

fibers pass from their origin partly through the red nucleus to their superficial origin in front of the pons at the median side of each crus. They decussate in the middle raphe.

Function. The third nerve supplies the levator palpebræ superioris muscle, and all of the muscles of the eyeball, except the superior oblique, to which the fourth nerve is appropriated, and the rectus externus, which receives the sixth nerve. Through the medium of the ophthalmic or lenticular ganglion, of which it forms what is called the short root, it also supplies motor filaments to the iris and ciliary muscle. The fibers which subserve the three functions, accommodation, contraction of the pupil, and nerve-supply to the external ocular muscles, arise from three distinct groups of cells. Optic reflexes involving movements of the eyeballs are through fibers from cells of the superior corpora quadrigemina (which receive fibers from the optic nerve). These

fibers from the corpora quadrigemina descend (chiefly through the posterior longitudinal bundle) to the nuclei of the third, fourth, and sixth nerves, thus rendering possible coordinated reflex movements of the eye muscles.

When the third nerve is stimulated within the skull, all those muscles to which it is distributed are convulsed. When it is *paralyzed* or *divided*, the following effects ensue: 1, The upper eyelid can be no longer raised by the levator palpebræ, but droops, *ptosis*, and remains gently closed over the eye, under the unbalanced influence of the orbicularis palpebrarum, which is sup-

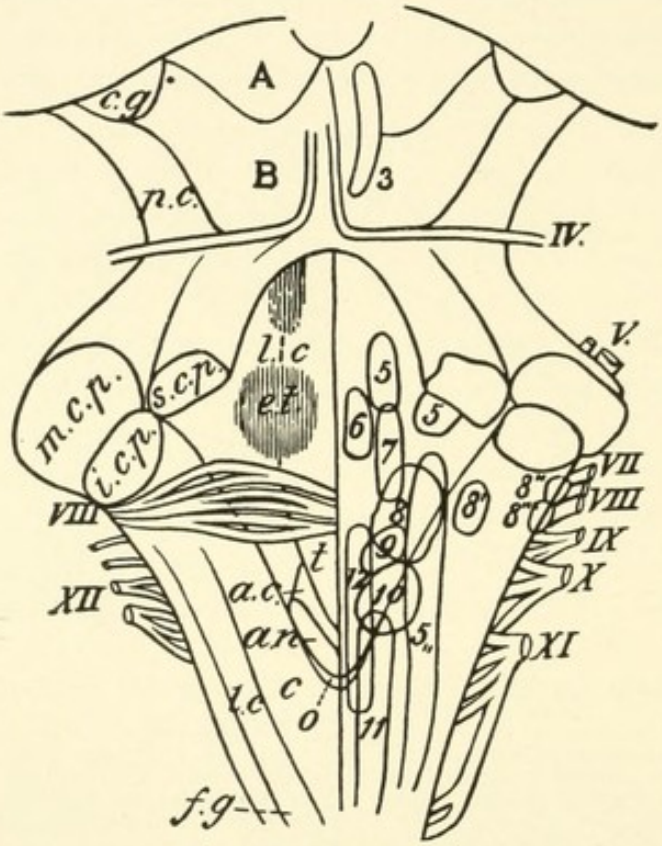


FIG. 384.—Fourth Ventricle with the Medulla Oblongata and the Corpora Quadrigemina. The roman numbers indicate superficial origins of the cranial nerves, while the other numbers indicate their deep origins, or the position of their central nuclei. 8, 8′, 8″, Auditory nuclei nerves; *t*, funiculus teres; *A*, *B*, corpora quadrigemina; *c.g*, corpus geniculatum; *p.c*, pedunculus cerebri; *m.c.p*, middle cerebellar peduncle; *s.c.p*, superior cerebellar peduncle; *i.c.p*, inferior cerebellar peduncle; *l.c*, locus ceruleus; *e.t*, eminentia teres; *a.c*, ala cinerea; *a.n*, accessory nuleus; *o*, obex; *c*, clava; *f.c*, funiculus cuneatus; *f.g*, funiculus gracilis.

plied by the facial nerve. 2, The eye is turned outward and downward, *external strabismus*, by the unbalanced action of the rectus externus and superior oblique, to which the sixth nerve is appropriated; and hence, from the irregularity of the axes of the eyes, double sight, *diplopia*, is often experienced when a single object is within view of both the eyes. 3, The eye cannot be moved upward, downward, or inward. 4, The pupil becomes dilated, *mydriasis*. 5, The eye cannot accommodate for short distances.

The Fourth Nerve, or Trochlearis. *Origin.* The fourth nerve arises from a nucleus consisting of large multipolar ganglion cells situated

ventral to the aqueduct of Sylvius, and the inferior corpus quadrigeminum. The fibers from both sides sweep dorsally around the central gray matter, and reach the valve of Vieussens, where they decussate in the mid-line of the roof, then pass forward along the lateral aspect of the crus. The nucleus of the fourth nerve on either side is connected with those of the third and sixth nerves and with the optic reflex center previously described.

Functions. The fourth nerve is exclusively motor, and supplies only the trochlearis or superior oblique muscle of the eyeball.

The Fifth Nerve, or Trigeminal. *Origin.* The fifth or trigeminal nerve resembles the spinal nerves in that it has two roots; namely, the larger

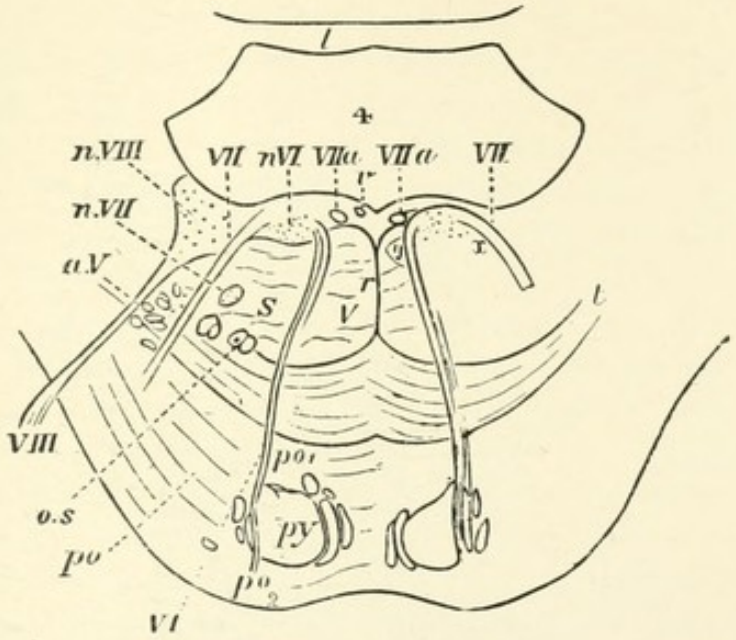


FIG. 385.—Section Across the Pons, About the Middle of the Fourth Ventricle. *py*, Pyramidal bundles; *po*, transverse fibers passing po_1, behind, and po_2, in front of *py*; *r*, raphé; *o.s*, superior olive; *a.V*, bundles of ascending root of *V*. nerve enclosed in a prolongation of the substance of Rolando; *VI*, the sixth nerve; *nVI*, its nucleus; *VII*, facial nerve; *VII.a*, intermediate portion, *nVII*, its nucleus; *VIII*, auditory nerve, *nVIII*, lateral nucleus of the auditory. (After Quain.)

or *sensory*, in connection with which is the Gasserian ganglion, and the small or *motor* root, which has no ganglion, and which passes under the ganglion of the sensory root. The fibers of origin of the fifth nerve come from the floor of the fourth ventricle. The motor root arises to the inside of the sensory, about the middle of each lateral half of the fourth ventricle. The sensory fibers, however, can be traced down in the medulla oblongata as far as the upper part of the cord. The motor nucleus stretches forward as far as the superior corpus quadrigeminum, giving rise to a bundle of long fibers termed the descending root. It is also connected with the locus ceruleus. The sensory nucleus receives a tract of sensory fibers from the trigeminus extending as low as the second cervical nerve, and this forms a tract at the tip of the posterior cornu, between it and the restiform body. The cells of origin of the sensory tract

are in the Gasserian ganglion. The nerve appears at the ventral surface of the pons near its front edge, at some distance from the mid-line.

Motor Functions. The first and second divisions of the nerve, which arise wholly from the larger root, are purely sensory. The third division is joined by the motor root of the nerve and is of course both motor and sensory.

Motor branches of the lesser or non-ganglionic portion of the fifth supply the muscles of mastication, namely, the temporal, masseter, two pterygoid, anterior part of the digastric, and mylohyoid. Filaments are also said to supply

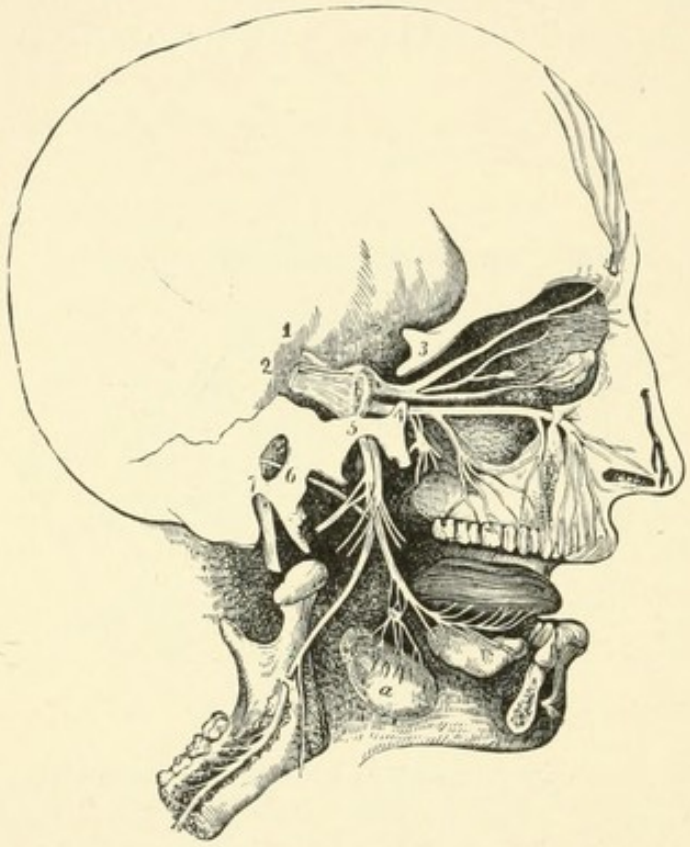


FIG. 386.—General Plan of the Branches of the Fifth. × ½. 1, Lesser root of the fifth; 2, greater root passing forward into the Gasserian ganglion; 3, placed on the bone above the ophthalmic nerve, which is seen dividing into the supra-orbital, lachrymal, and nasal branches, the latter connected with the ophthalmic ganglion; 4, placed on the bone close to the foramen rotundum, marks the superior maxillary division, which is connected below with the spheno-palatine ganglion, and passes forward to the infra-orbital foramen; 5, placed on the bone over the foramen ovale, marks the inferior maxillary nerve, giving off the anterior auricular and muscular branches, and continued by the inferior dental to the lower jaw, and by the gustatory to the tongue; *a*, the submaxillary gland, the submaxillary ganglion placed above it in connection with the gustatory nerve; 6, the chorda tympani; 7, the facial nerve issuing from the stylomastoid foramen. (Charles Bell.)

the tensor tympani and tensor palati (Kölliker). The motor function of these branches is proved by the violent contraction of all the muscles of mastication in experimental irritation of the third or inferior maxillary division of the fifth nerve; by paralysis of the same muscles when the nerve is divided or disorganized; and by the retention of the power of these muscles when the facial nerve is paralyzed. Whether the branch of the fifth nerve which is supplied to the buccinator muscle is entirely sensory, or in part motor also, must remain for the present doubtful. From the fact that this muscle, besides

its other functions, acts in concert or harmony with the muscles of mastication in keeping the food between the teeth, it might be supposed from analogy that it would have a motor branch from the same nerve that supplies them. However, the so-called buccal branch of the fifth is, in the main, sensory.

Sensory Functions. All the anterior and antero-lateral parts of the face and head, with the exception of the skin of the parotid region, acquire common sensibility through branches of the ganglionic division of the fifth nerve. The muscles of the face and lower jaw acquire muscular sensibility through the filaments of the ganglionic portion of the fifth nerve distributed to them with their proper motor nerves.

Through its ciliary branches and the branch which forms the long root of the ciliary or ophthalmic ganglion, it exercises some influence on the movements of the iris. When the trunk of the ophthalmic portion is divided, the pupil becomes, according to Valentin, contracted in men and rabbits, and dilated in cats and dogs, but in all cases becomes immovable even under all the varieties of the stimulus of light. How the fifth nerve affects the iris is unexplained; it has been suggested the influence of the fifth nerve on the movements of the iris may be ascribed to the affection of vision in consequence of the disturbed circulation or nutrition in the retina.

Trophic Influence. The morbid effects which division of the fifth nerve produces in the organs of special sense make it probable that the fifth nerve exercises some special or *trophic* influence on the nutrition of all these organs, although the effects may in part be due to the loss of sensibility which is the natural protective safeguard. Thus, after such division and within a period varying from twenty-four hours to a week, the cornea begins to be opaque, and later it grows completely white. A low destructive inflammatory process ensues in the conjunctiva, sclerotic coat, and in the interior parts of the eye. The sense of smell may be at the same time lost or gravely impaired. Commonly, whenever the fifth nerve is paralyzed, the tongue loses the sense of taste in its anterior and lateral parts, and according to Gowers in the posterior part as well.

In Relation to Taste. The tactile sensibility of the tongue is due to the lingual branch of the fifth nerve, which supplies the anterior and lateral parts of the tongue. The sense of taste in the lateral and anterior portions of the tongue have recently been traced back to the pars intermedia and chorda tympani of the seventh, figures 387 and 388. It forms also one chief sensory link in the nervous circle for reflex action in the secretion of saliva. But, deferring this question until the glosso-pharyngeal nerve is to be considered, it may be observed that in some brief time after complete paralysis or division of the fifth nerve, the power of all the organs of the special senses may be impaired. They may lose not merely their sensibility to common impressions, for which they all depend directly on the fifth nerve, but also their sensibility to the special stimuli to which they are adapted.

The Sixth Nerve, the Abducens. *Origin.* The sixth nerve arises from a compact oval nucleus, situated somewhat deeply at the back part of the pons near the middle of the floor of the fourth ventricle. The eminentia teres marks its position. It contains moderately large nerve cells with large axis-cylinder processes. It is connected, figure 373, with the nuclei of the third, fourth, and seventh nerves, and with reflex centers of the optic tracts, as previously mentioned. The root is thin, and passes ventrally and laterally through

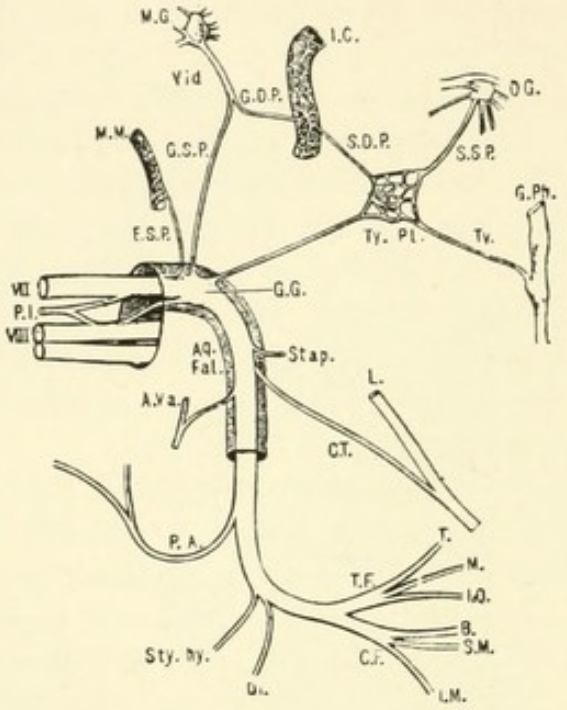


FIG. 387.—The Seventh Nerve and Its Branches. *VII*, Facial nerve; *P.I*, pars intermedia; *VIII*, auditory nerve; *Aq.Fal*, aqueduct of Fallopius; *G.G*, geniculate ganglion; *E.S.P*, external superficial petrosal nerve; *M.M*, middle meningeal artery; *G.S.P.*, great superficial petrosal nerve; *G.P.D*, great deep petrosal nerve; *I.C*, internal carotid artery; *Vid*, Vidian nerve; *M.G.*, Meckel s ganglion; *Ty.Pl*, tympanic plexus; *S.D.P*, small deep petrosal nerve; *G.Ph*, Glosso-pharyngeal nerve *Ty*, tympanic branch; *S.S.P.*, small superficial petrosal nerve; *O.G*, optic ganglion; *Stap*, nerve to stapedius; *C.T*, chorda tympani nerve; *L*, lingual nerve; *A.Va*, communication with auricular branch of vagus; *P.A*, posterior auricular nerve; *Sty.hy*, nerve to stylo-hyoid; *Di*, nerve to digastric (posterior belly); *T.F*, temporal-facial division; *C.F*, cervico-facial division; *T*, temporal *M*, malar; *I.O*, infra-orbital; *B*, buccal, *S.M*, supra-mandibular; *I.M*, infra-mandibular branches. (Cunningham.)

the reticular formation, to the surface, which it reaches at the lower edge of the pons, opposite the front end of the pyramid.

Functions. The sixth nerve is exclusively motor, and supplies only the rectus externus muscle of the eye. The muscle is paralyzed when the nerve is divided. In all such cases of paralysis the eye squints inward and cannot be moved outward.

The Seventh Nerve, or Facial. *Origin.* The facial or seventh pair of nerves arises from the floor of the central part of the fourth ventricle, behind and in line with the motor nucleus of the fifth, to the outside of and deeper down than the nucleus of the sixth. The nucleus is narrower in front than behind, and consists of large motor cells with well-marked axis-cylinder proc-

esses, which are gathered up at the dorsal surface of the nucleus to form a root. The root describes a loop around the nucleus of the sixth nerve, running forward for some little distance dorsal to the nucleus, then descending vertically, passing to the outside of its own nucleus, between it and the descending root of the fifth nerve. It emerges at the lower margin of the pons, lateral to the sixth nerve, opposite the front edge of the groove between the olivary and restiform bodies. There are two roots; the lower and smaller is called the *pars intermedia*, and the upper, *pars dura*.

Functions. The seventh nerve is the motor nerve of all the muscles of the face, including the platysma, but not including the muscles of mastication, already enumerated; it supplies, also, the parotid gland, and, through the connection of its trunk with the Vidian nerve, some of the muscles of the soft palate. It supplies the stapedius, the lingualis and some other muscles of the tongue,

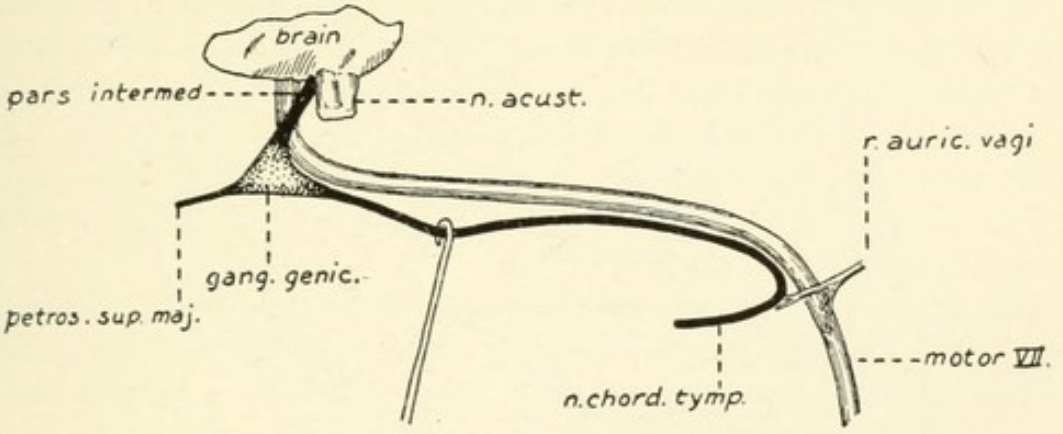


FIG. 388.—Dissection of the Sensory and Motor Divisions of the Facial in a 20-cm. Embryo (Pig). (Streeter.)

and the posterior part of the digastric and stylo-hyoid. Its branches supply the muscles of the external ear.

Fibers from the chorda tympani are distributed to the submaxillary gland and produce secretion when stimulated.

When the facial nerve is divided or in any other way paralyzed, the loss of function in the muscles which it supplies interferes with the perfect exercise of the organs of the special senses. Thus, in paralysis of the facial nerve the orbicularis palpebrarum being powerless, the eye remains open through the unbalanced action of the levator palpebræ. The conjunctiva is thus continually exposed to the air and dust and is liable to repeated inflammation, which may end in thickening and opacity of the cornea.

The sense of taste may be weakened or wholly lost in paralysis of the facial nerve, which involves the chorda tympani. This result, which has been observed in many instances of disease of the facial nerve in man, appears explicable on the supposition that the chorda tympani is the nerve of taste to the anterior two-thirds of the tongue, its fibers being distributed with the so-called

gustatory or lingual branch of the fifth. Streeter has just published a study of the development of the seventh and eighth nerves in which he traces the chorda tympani through the pars intermedia, as shown in figure 388, thus settling this oft-disputed question.

The Eighth Nerve, or Auditory. The eighth nerve consists of two divisions, anatomically distinct and functionally independent. These are the *vestibular* and the *cochlear* divisions of the auditory nerve.

The *cochlear* division arises in the spiral ganglion and passes to the medulla to establish immediate connections with the ventral cochlear nucleus and the tuberculum acusticum. The central relations of these nuclei are established by the striæ acusticæ, the trapezoideus, and the lateral fillet with the internal corpus geniculatum and the inferior corpus quadrigeminum of the opposite side, as told by figure 389. These latter nuclei send tracts to the auditory center in the superior temporal gyrus.

The *vestibular* division arises in the vestibular ganglion, which is entirely distinct from the cochlear ganglion, and enters the medulla, passing to the lateral or chief auditory nucleus. From this point the relations are not fully established, but apparently fibers pass to the nucleus fastigii of the opposite side and to the vermis, where they are brought into relations with motor descending paths.

Functions. The cochlear branch is the auditory nerve proper, and the vestibular is the nerve of equilibrium.

The Ninth Nerve, or Glosso-pharyngeal. *Origin.* The glosso-pharyngeal nerves, figure 364, *IX*, arise by nuclei intimately associated with those of the vagus and spinal accessory nerves. The union of the nuclei is indeed so intimate that it will be as well to consider the origins of the ninth, tenth, and eleventh nerves together.

These three nerves emerge from the bulb and spinal cord in their numerical order from above downward, the *bulbar portion* from the lateral aspect of the bulb in a line between the olivary and restiform bodies; and the *spinal portion* from a line intermediate between the anterior and posterior nerve roots as far down as the sixth or seventh cervical spinal nerves.

The combined glosso-pharyngeal-accessory-vagus nucleus appears to consist of two parts, viz., one *median* or *common origin*, having conspicuous nerve cells of moderate size, and three *lateral origins*, having but few cells of small size. These are: 1, the *nucleus ambiguus*, which lies on the lateral side of the reticular formation and is the motor origin of the glosso-pharyngeal, the vagus, and the spinal accessory; 2, the *fasciculus solitarius*, situated in the bulb, ventral and a little lateral to the combined nucleus, is also called the ascending root of the glosso-pharyngeal nerve or the respiratory bundle; and 3, the *spinal portion*, which takes origin from a group of cells lying in the extreme lateral margin of the anterior cornu. This is the origin of the spinal accessory; it corresponds to the antero-lateral nucleus of the bulb, and the lateral part of the gray matter of the spinal cord.

The fibers of the spinal origin of the nerve pass from these cells through the lateral column to the surface of the cord. The fibers from the median part pass in a ventral and lateral direction through the reticular formation, then ventral to or through the gelatinous substance and strand of fibers connected with the fifth nerve, to the surface of the bulb.

The fibers from the *nucleus ambiguus* join the combined nerve, chiefly the vagus and glosso-pharyngeal.

The bundles of fibers of the *fasciculus solitarius* start in the lateral gray

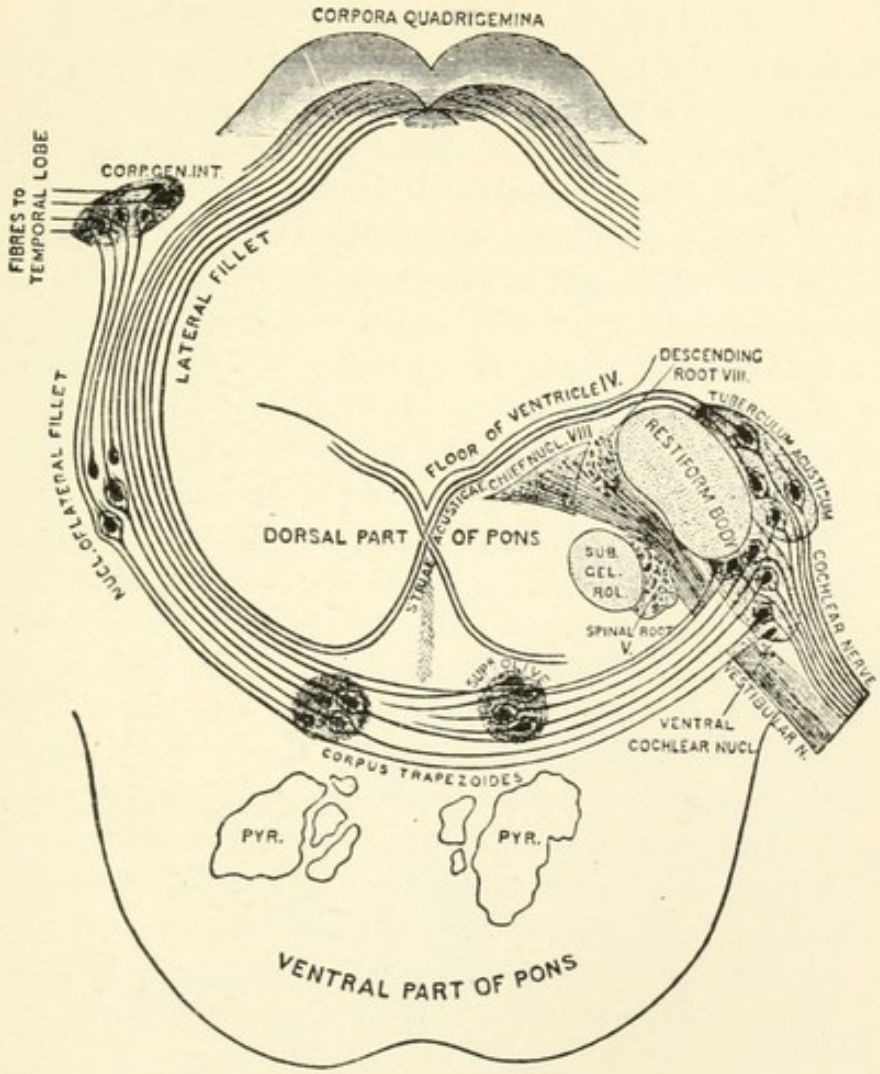


FIG. 389.—The Nuclei of Origin and Central Connections of the Auditory and Vestibular Nerve. (Cunningham.)

matter of the cervical cord and higher in the reticular formation of the bulb, run longitudinally forward, to pass into the roots of the ninth nerve. It is composed of sensory fibers, chiefly of the glosso-pharyngeal.

The glosso-pharyngeal nerve gives filaments through its tympanic branch (Jacobson's nerve), to the fenestra ovalis and fenestra rotunda, and the Eustachian tube; also to the carotid plexus, and through the petrosal nerve, to

the spheno-palatine ganglion. After communicating with the vagus and, soon after it leaves the cranium, with the sympathetic, with the digastric branch of the facial, and the accessory nerve, the glosso-pharyngeal divides into the two principal divisions indicated by its name, which supply the mucous membrane of the posterior and lateral walls of the upper part of the pharynx, the Eustachian tube, the arches of the palate, the tonsils and their mucous membrane, and the tongue as far forward as the foramen cecum in the middle line, and to near the tip at the sides and inferior part.

Functions. The glosso-pharyngeal nerve contains some motor fibers, together with fibers of common sensation and the sense of taste.

Motor fibers are distributed to the palato-pharyngeus, the stylo-pharyngeus, palato-glossus, and constrictors of the pharynx.

Sensory fibers of touch and of common sensation are distributed to the pharynx, the tonsils, and posterior palate. Nerves of taste are supplied to the taste buds on the posterior third of the tongue and to the fauces.

The Tenth Nerve, Vagus or Pneumogastric Nerve. The origin of the vagus nerve is, as we have just seen, situated in the lower half of the floor of the fourth ventricle, figure 374. Its nucleus is said to represent the cells of Clarke's column of the spinal cord. In origin it is closely connected with the ninth, eleventh, and the twelfth. The combined glosso-pharyngeal-vago-accessory nuclei lie outside of, close to, and parallel with the nucleus of the twelfth. There are two main vagal nuclei: one motor, the other sensory.

Distribution. It has, of all the nerves, the most varied distribution and functions, either through its own filaments, or through those which, derived from other nerves, are mingled in its branches. The vagus supplies sensory branches, which accompany the sympathetic on the middle meningeal artery, and others which supply the back part of the meatus and the adjoining part of the external ear. It is connected with the petrous ganglion of the glosso-pharyngeal, by means of fibers to its jugular ganglion, with the spinal accessory, which supplies it with its motor fibers for the larger and upper portion of the esophagus, and with its inhibitory fibers for the heart; also with the twelfth; with the superior cervical ganglion of the sympathetic; and with the cervical plexus. The parts supplied by the branches of the vagus are as follows:

1. A large portion of the mucous membrane and probably all the muscles of the pharynx are supplied by its *pharyngeal* branches.

2. The mucous membrane of the under surface of the epiglottis, and of the greater part of the larynx, and the crico-thyroid muscle, by the *superior laryngeal* nerve.

3. The mucous membrane and muscular fibers of the trachea, the lower part of the pharynx and larynx, and all the muscles of the larynx except the crico-thyroid are supplied by the *inferior laryngeal* nerve. It also supplies the first segment of the esophagus.

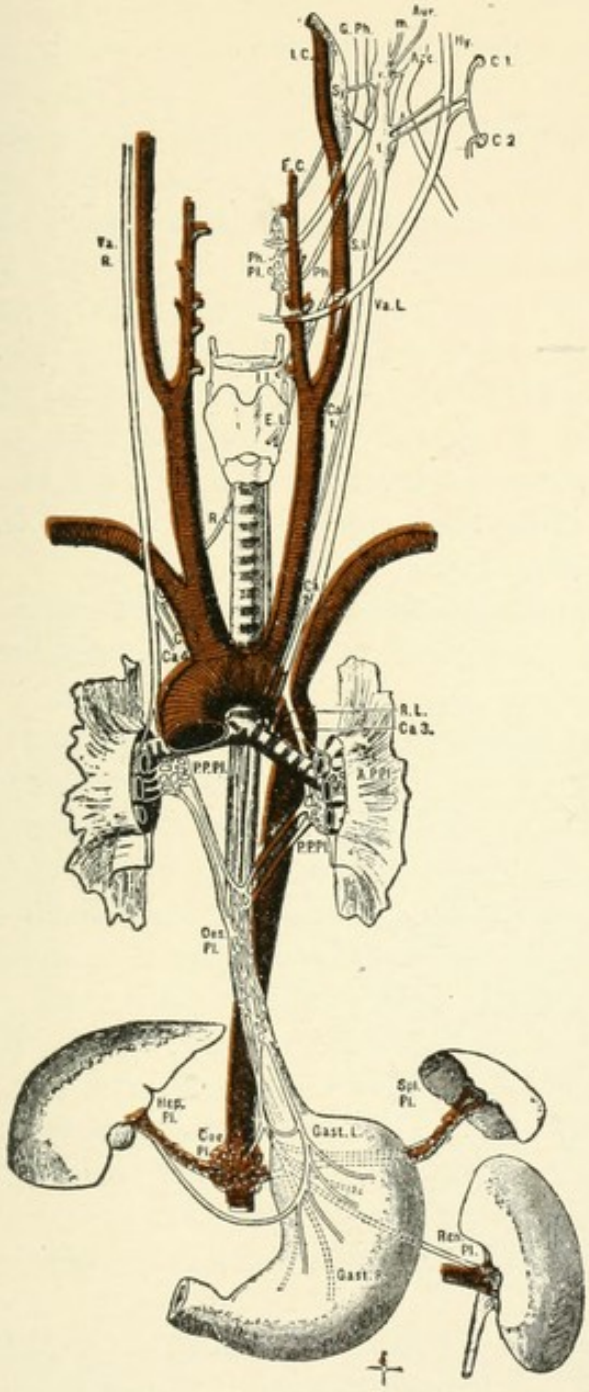


FIG. 390.

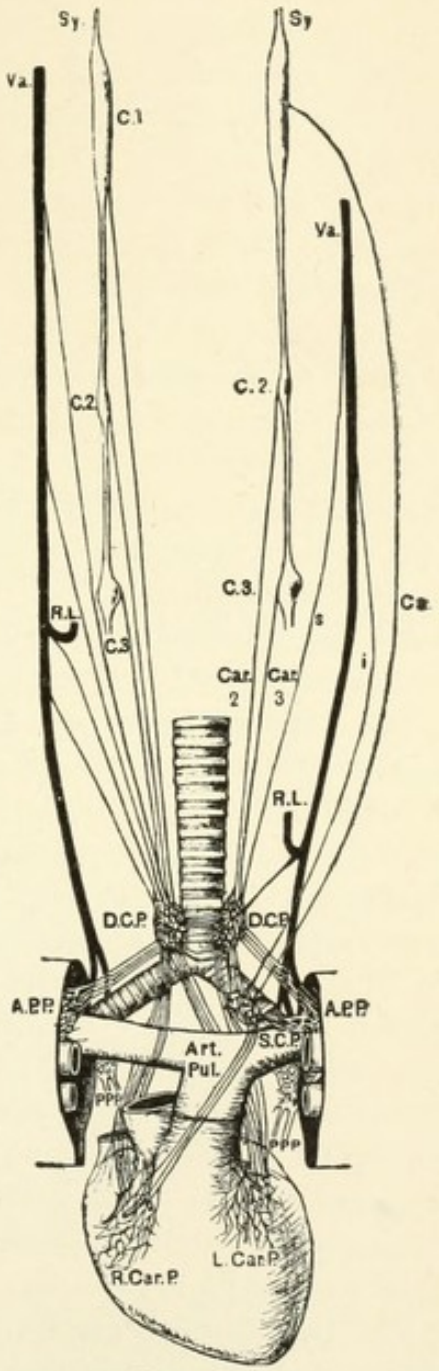


FIG. 391.

FIG. 390.—The Distribution of the Tenth or Vagus Nerve. *Va.R, Va.L.*, Right and left vagi; *r*, ganglion of the root and connections with *Sy.*, sympathetic, superior cervical ganglion; *g.Ph.*, glossopharyngeal; *Acc.*, spinal accessory nerve; *m*, meningeal branch; *Aur.*, auricular branch; *t*, ganglion of the trunk and connections with *Hy.*, hypoglossal nerve; *C1, C2*, loop between the first two cervical nerves—*Sy.*, sympathetic, *Acc.*, spinal accessory nerve; *Ph.*, pharyngeal branch; *Ph.Pl.*, pharyngeal plexus; *S.L.*, superior laryngeal nerve; *I.L.*, internal laryngeal branch; *E.L.*, external laryngeal branch; *I.C.*, internal, and *E.C.*, external carotid arteries; *Ca1*, superior cervical cardiac branch; *Ca2*, inferior cervical cardiac branch; *R.L.*, recurrent laryngeal nerve; *Ca3*, cardiac branches of recurrent laryngeal nerve; *Ca4*, thoracic cardiac branch (right vagus); *A.P.Pl.*, anterior, and *P.P.Pl.*, posterior pulmonary plexuses; *Oes.Pl.*, esophageal plexus; *Gast.R.* and *Gast.L.*, gastric branches of vagus (right and left); *Coe.Pl.*, celiac plexus; *Hep.Pl.*, hepatic plexus; *Pl.*, splenic plexus; *Ren.Pl.*, renal plexus. (Cunningham.)

FIG. 391.—The Constitution of the Cardiac Plexus. *Sy.*, Cervical sympathetic cord; *C.1*, superior, *C.2*, middle, and *C.3*, inferior cervical ganglia; *Car.1*, superior, *Car.2*, middle, and *Car.3*, inferior cervical cardiac sympathetic branches; *Va.*, vagus nerve; *R.L.*, recurrent laryngeal nerve; *s*, superior, and *i*, inferior cervical cardiac branches of vagus; *D.C.P.*, deep cardiac plexus; *S.C.P.*, superficial cardiac plexus; *A.P.P.*, anterior pulmonary plexus; *P.P.P.*, posterior pulmonary plexus; *R.Car.P.*, right, and *L.Car.P.*, left coronary plexuses; *Art.Pul.*, pulmonary artery. (Cunningham.)

4. The mucous membrane and muscular coats of the esophagus receive fibers from the *esophageal* branches.

5. The branches of the vagus form the supply of *inhibitory* nerves to the heart and the great arteries.

6. The lungs are supplied through the anterior and posterior *pulmonary* plexuses.

7. The stomach, the intestines, the spleen, and the liver are supplied by the *gastric*, *splenic*, and *hepatic* vagus branches.

Functions. Throughout its whole course the vagus contains both sensory and motor fibers. To summarize the many functions of this nerve, which have been for the most part considered in the preceding chapters, it may be said that it supplies, 1, motor fibers to the pharynx and esophagus, to the stomach and intestines, to the larynx, trachea, bronchi, and lungs; 2, sensory and, in part, 3, vaso-motor fibers to the same regions; 4, inhibitory fibers to the heart; 5, inhibitory afferent fibers to the vaso-motor center.

Division of both vagi or of both their recurrent branches is often quickly fatal in young animals; but in old animals the division of the recurrent nerve is not generally fatal, and that of both the vagi, even, is not always fatal.

The Eleventh Nerve, or Spinal Accessory. This nerve arises by two nuclei, one the nucleus ambiguus from a center in the floor of the fourth ventricle, partly but chiefly in the medulla and continuous with the glosso-pharyngeal-vagus nucleus; the other, from the outer side of the anterior cornu of the spinal cord as low down as the fifth or sixth cervical nerve. The fibers from the two origins come together at the jugular foramen, but separate again into two branches. The inner arises from the medulla and joins the vagus, to which it supplies fibers, consisting of small medullated nerve fibers. The outer consists of large medullated fibers and supplies the trapezius and sterno-mastoid muscles. The muscles of the larynx, all of which are supplied, apparently, by branches of the vagus, are said to derive their motor nerves from the accessory; and Vrolik makes the very significant statement that in the chimpanzee the internal branch of the accessory does not join the vagus at all, but goes direct to the larynx.

The Twelfth Nerve, or Hypoglossal. *Origin and Connections.* The nerve arises from a large-celled and very long nucleus in the bulb, extending from the floor of the fourth ventricle to the level of the olivary bodies close to the mid-line and inside the nucleus ambiguus. Fibers from this nucleus run from the ventral surface through the reticular formation in a series of bundles passing between the olivary nucleus laterally and the pyramid and accessory olive medially, to gain the ventral surface. The nerve emerges from a groove between the pyramid and olivary body. The fibers of origin are continuous with the anterior roots of the spinal nerves.

This nerve is the motor nerve to the muscles connected with the hyoid bone, including those of the tongue. It supplies the sterno-hyoid, sterno-thyroid, and

omo-hyoid through its descending branch, *descendens noni;* the thyro-hyoid through a special branch; and the genio-hyoid, stylo-glossus, hyo-glossus, and genio-hyo-glossus and linguales through its lingual branches.

Functions. The function of the hypoglossal is exclusively motor. In cases of hemiplegia involving the functions of the hypoglossal nerve the tongue when protruded deviates toward the paralyzed side, when withdrawn it turns away from the paralyzed side. Occasionally it is not possible to observe any deviation in the direction of the protruded tongue; probably because the tongue is so compact and firm that the muscles on either side can push it straight forward or turn it for some distance toward either side. In hypoglossal paralysis from cerebral lesions or lesions of the peduncles the paralysis is contralateral.

IV. THE CEREBELLUM.

The cerebellum is a large division of the brain, located just beneath the cerebrum and behind the medulla and pons. It is connected with the rest

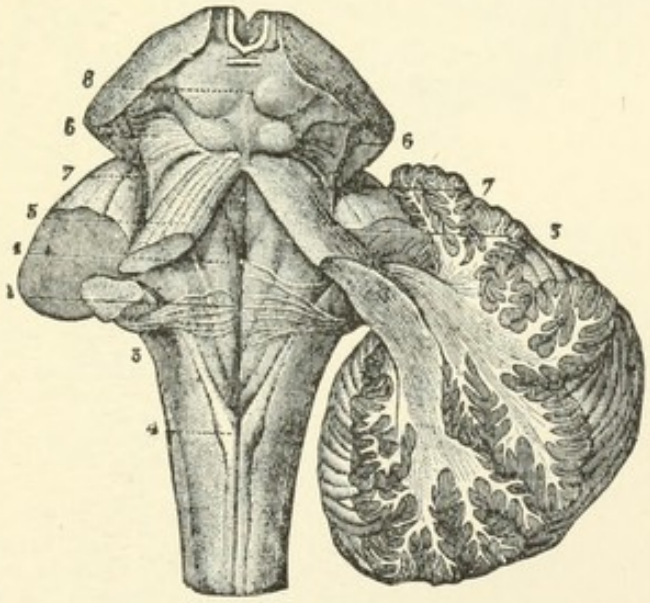


FIG. 392.—Cerebellum in Section and Fourth Ventricle, with the Neighboring Parts. 1, Median groove of fourth ventricle, ending below in the *calamus scriptorius*, with the longitudinal eminences formed by the *fasciculi teretes*, one on each side; 2, the same groove, at the place where the white streaks of the auditory nerve emerge from it to cross the floor of the ventricle; 3, inferior crus or peduncle of the cerebellum, formed by the restiform body; 4, posterior pyramid; above this is the calamus scriptorius; 5, superior crus of cerebellum, or processus e cerebello ad cerebrum (or ad testes); 6, 6, fillet to the side of the crura cerebri; 7, 7, lateral grooves of the crura cerebri; 8, corpora quadrigemina. (From Sappey, after Hirschfeld and Leveillé.)

of the brain by three peduncles on each side: the superior, the middle, and the inferior peduncle, figure 392.

The cerebellum is composed of white and gray matter, the latter being external, as in the cerebrum, and like it infolded, so that a larger area may be contained in a given space. The convolutions of the gray matter, however, are arranged after a different pattern, as shown in figure 393. Besides the

gray substance on the surface, there is, near the center of the white substance of each hemisphere, a small capsule of gray matter called the *corpus dentatum*, figure 393, resembling very closely the *corpus dentatum* of the olivary body of the medulla oblongata.

If a section be taken through the gray matter of the cerebellum, it will be found to be composed of two layers, an outer, or molecular, and an inner, or granular, layer. Each of these layers contains a large number of peculiar-shaped nerve cells and very rich plexuses of nerve fibers. Recent studies of the cortex of the cerebellum by modern methods have revealed a most complex and beautiful arrangement of the parts of the cerebellum.

The General Structure of the Cerebellum. The molecular layer of the cerebellum contains several peculiar types of nerve cells, of which may be

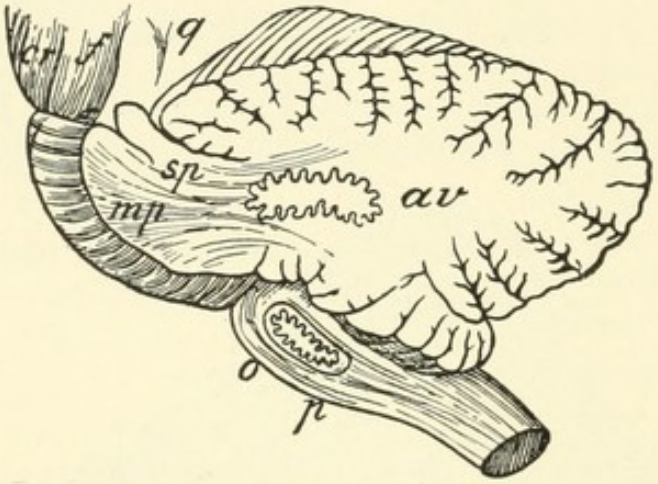


FIG. 393.—Outline Sketch of a Section of the Cerebellum, Showing the Corpus Dentatum. The section has been carried through the left lateral part of the pons, so as to divide the superior peduncle and pass nearly through the middle of the left cerebellar hemisphere. The olivary body has also been divided longitudinally so as to expose in section its *corpus dentatum*. *cr*, Crus cerebri; *f*, fillet; *q*, corpora quadrigemina; *sp*, superior peduncle of the cerebellum, divided; *mp*, middle peduncle or lateral part of the pons Varolii, with fibers passing from it into the white stem; *av*, continuation of the white stem radiating toward the arbor vitæ of the folia; *o*, olivary body with its corpus dentatum; *p*, anterior pyramid. (Allen Thomson.)

specially mentioned Purkinje's cells and the basket cells. The cells of Purkinje lie along the internal margin of the layer, being, in fact, practically at the boundary of the molecular and granular layers. They measure 40 to 60 μ in diameter, and have large, round nuclei. Each cell gives off an enormous number of branching dendrites, which run up toward the surface of the cerebellum in the shape of a bush.

The cells of Purkinje give off at their deeper surface an axone which runs down into the white matter of the cerebellum.

Lying in the molecular layer, somewhat external to the Purkinje cells, are the cells of the type known as basket cells. These cells have a number of dendrites, also send out an axone which runs parallel to the surface of the cortex, which gives off numerous collaterals in its course that form baskets around the cell bodies of the Purkinje cells, figure 394, *ZK*.

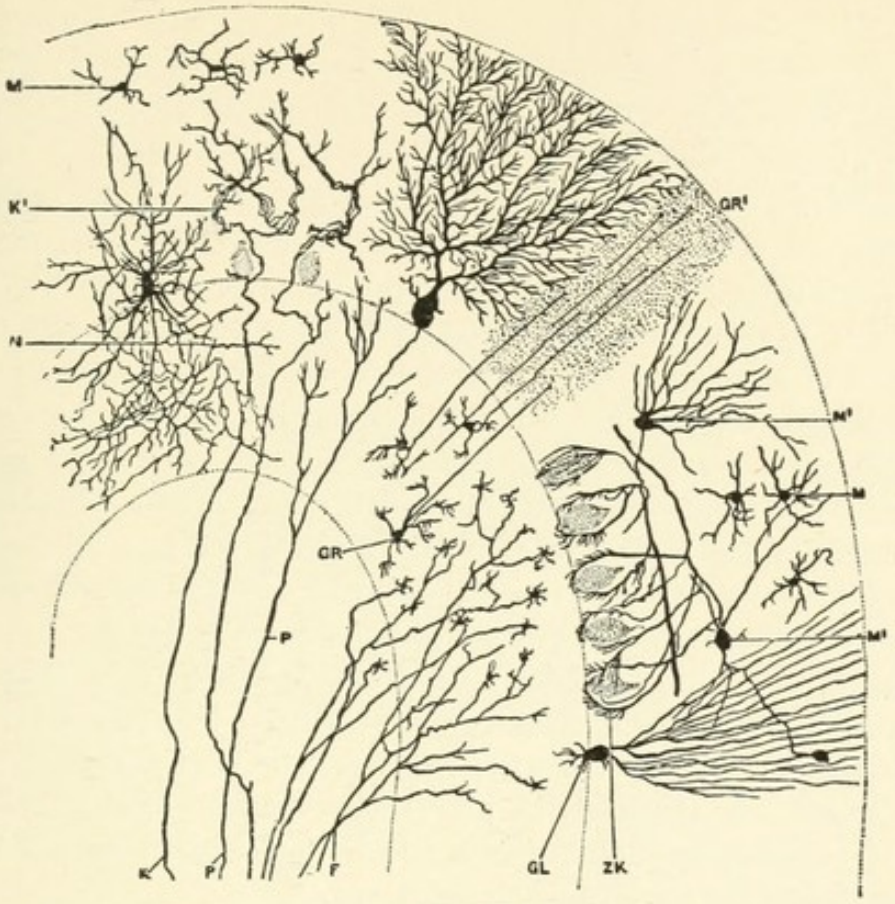


FIG. 394.—Transverse Section Through a Cerebellar Folium (after Kölliker). Treated by the Golgi method. *P*, Axone of cell of Purkinje; *F*, moss fibers; *K* and *K'*, fibers from white core of folium ending in molecular layer in conection with the dendrites of the cells of Purkinje; *M*, simple cell of the molecular layer; *GR*, granule cell; *GR*[1], axones of granule cells in molecular layer cut transversely; *M'*, basket cells; *ZK*, basket work around the cells of Purkinje; *GL*, neuroglia cell; *N*, axone of an association cell.

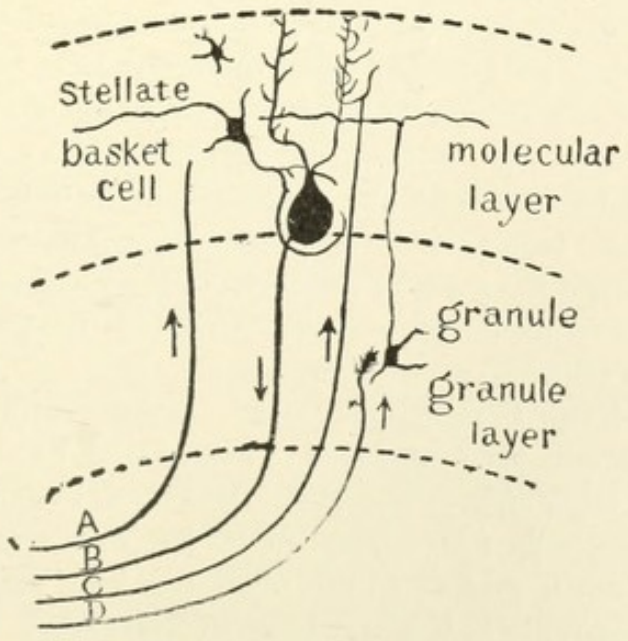


FIG. 395.—*A*, Afferent fiber to basket (stellate) cell; *B*, neuraxone of Purkinje cell; *C*, afferent fiber to Purkinje cell; *D*, afferent (mossy) fiber to granule cell.

The granular layer contains a large number of very small granule-like cells that Golgi was the first to show are really nerve cells. They are only about 5 μ in diameter, and they have a number of short dendrites which end in clubbed extremities. They give off a very slender axis-cylinder process or axone which runs up into the superficial part of the molecular layer and there divides in a T-shaped fashion, the fibers run parallel to the surface of the convolution and pass in between the branches of the cells of Purkinje.

The white substance of the cerebellum consists of nerve fibers, which are of three kinds: 1, Descending fibers, that are made up of the axis-cylinders of the cells of Purkinje, carrying impulses down from the cerebellar cortex. 2, Ascending fibers, which pass into the granular layer, and there end in a number of very short, finely divided brushes of fibers presenting a mossy appearance, so that these are known as the *mossy fibers*. These connect with the granular cells of this layer. 3, Ascending fibers, which pass up through the granular into the molecular layer and there break up into a fine network which interlaces with the dendritic branches of the cells of Purkinje.

Paths through the Cerebellar Cortex. It will be seen that the arrangements for the transmission and diffusion of nerve impulses and for the cooperation of different cells are extremely complicated and delicate. It is not possible to indicate absolutely by any schema the course of fibers and the course of impulses through the cerebellum, but approximately it is somewhat like that in the accompanying figure 396.

Impulses pass up along the ascending fibers to the granular cells by way of the direct cerebellar, the fibers of the gracile and of the cuneatus, from the restiform body, etc. These cells, being stimulated, send the impulses by their axis-cylinders to the molecular layer, and through their T-shaped divisions to the dendrites of the cells of Purkinje. Thence an impulse is sent out by the axis-cylinder process of this cell. Other ascending impulses are brought up by those fibers which pass directly to the molecular layer and send their terminals winding around among the dendrites of the cells of Purkinje. Probably impulses pass up also through the ascending fibers which affect the basket cells, and, through them and their basket-like terminals, the cells of Purkinje. Purkinje cells send cerebellar motor fibers to the nucleus dentatus cerebelli and through the superior peduncles to the nuclei of the oculo-motor nerves, and to the ventro-lateral descending tract of the cord, to end about the anterior-horn cells.

Functions of the Cerebellum. With the exception of its middle lobe, the cerebellum is itself insensible to irritation and may be all cut away without eliciting signs of pain (Longet). Its removal or disorganization by disease is also generally unaccompanied by loss or disorder of sensibility; animals from which it is removed can smell, see, hear, and feel pain, to all appearances, as perfectly as before (Flourens; Magendie). It cannot, therefore, be regarded as a principal organ of sensation. Yet if any of its crura

be touched, pain is indicated; and, if the restiform tracts of the medulla oblongata be stimulated, the most acute suffering appears to be produced.

These phenomena may properly be ascribed to the activity of the cerebral cortex, since the number of collaterals on the fibers that pass to cerebellar tracts is very great, and impulses arising from their stimulation may reach the sensorium by paths other than through the cerebellum.

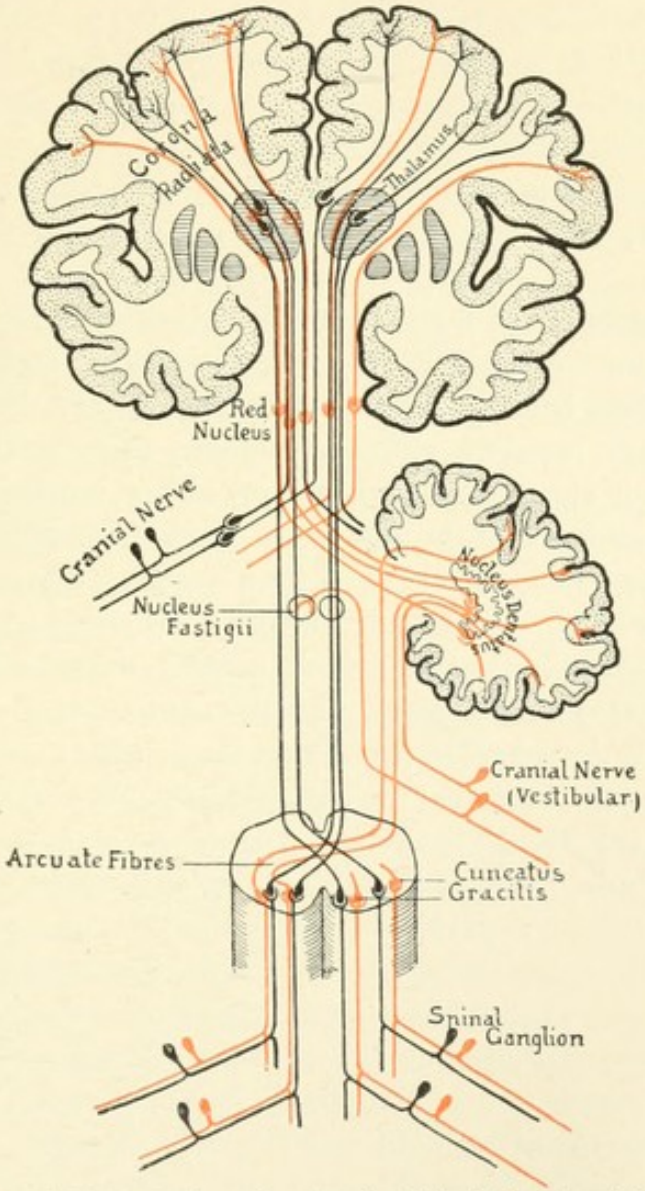


FIG. 396.—Scheme of Principal Ascending Cerebro-Spinal (black) and Cerebellar (red) Conduction Paths. (Modified from Hardesty in Morris' Anatomy.)

The experiments of Longet and many others agree in supporting the view that no stimulation of the cerebellar cortex leads to localized muscular contractions. In other words, there is no localization in the cerebellar cortex as in the cerebrum, the cerebellum apparently acting as a whole. If the cerebellum be removed, as was done by Flourens and numerous later physiologists, a very profound disturbance in motor functions occurs. With the removal

of the superficial layers of the cerebellum, in pigeons particularly, there is increasing feebleness and lack of harmony of the muscles concerned in locomotion. When the entire organ is cut away in pigeons they lose the power of walking, flying, and of standing in the usual erect way. Their power of preserving equilibrium is lost, the most characteristic feature. Birds do not remain in a state of stupor, but attempt to carry out the usual muscular activities. If a pigeon is laid on its back it cannot recover its erect position, though it make motions to do so. If set on its feet it will fall to one side or the other, and is not able to hold its head in the customary position. The endeavors of the animal to maintain its balance are insecure and uncertain, resembling the lack of muscular control of a drunken man.

Such an animal does not lose the power of perceiving sensations, nor of making voluntary efforts, as it will endeavor to avoid the blow that is threatened.

The experiments afford the same results when repeated on all classes of animals; and from them and the others before referred to, Flourens inferred that the cerebellum belongs neither to the sensory nor the intellectual apparatus; and that it is not the source of voluntary movements, although it belongs to the motor apparatus, but is the organ for the coordination of the voluntary movements, or for the excitement of the *combined* action of muscles.

Such evidence as can be obtained from cases of diseases of this organ confirms the view taken by Flourens; and, on the whole, it gains support from comparative anatomy—animals whose natural movements require most frequent and exact combinations of muscular contractions being those whose cerebella are most developed in proportion to the spinal cord.

We must remember, too, that the cerebellum is connected with the posterior columns of the cord through the cuneate and gracile nuclei as well as with the direct cerebellar tract, all of which probably convey to the middle lobe muscular sensations. It is also connected with the auditory nerves and bulb by the internal and external arcuate fibers; and with the tegmentum through the red nuclei. Its connection with the efferent tracts from the different cerebral lobes through the pons is also highly important. Movements of the eyes also occur on direct stimulation of the middle lobe. It seems, therefore, to be connected in some way with all of the chief sensory impulses which have to do with the maintenance of the equilibrium, and is generally included in the nervous apparatus which is supposed to govern this function of our bodies.

Foville supposed that the cerebellum is the organ of *muscular sense, i.e.*, the organ by which the mind acquires that knowledge of the actual state and position of the muscles which is essential to the exercise of the will upon them; and it must be admitted that all the facts just referred to are as well explained on this hypothesis as on that of the cerebellum being the organ for combining movements. A harmonious combination of muscular actions must depend as much on the capability of appreciating the condition of the muscles with regard to their tension, and to the force with which they are contracting, as on the power which any special nerve-center may possess of exciting them to contraction. And

it is because the power of such harmonious movement would be equally lost, whether the injury to the cerebellum involved injury to the seat of muscular sense or to the center for combining muscular actions, that experiments on the subject afford no proof in one direction more than the other.

Forced Movements. The influence of each half of the cerebellum is directed to muscles on the opposite side of the body; and it would appear that, for the right ordering of movements, the actions of its two halves must be always mutually balanced and adjusted. For if one of its crura, or if the pons on either side of the middle line, be divided, so as to cut off from the medulla oblongata and spinal cord the influence of one of the hemispheres of the cerebellum, strangely disordered movements ensue—forced movements. The animals fall down on the side opposite to that on which the crus cerebelli has been divided, and then roll over continuously and repeatedly; the rotation being always round the long axis of their bodies, and generally from the side on which the injury has been inflicted. The rotations sometimes take place with much rapidity; as often, according to Magendie, as sixty times in a minute, and may last for several days. Similar movements have been observed in men; as by Serres in a man in whom there was apoplectic effusion in the right crus cerebelli; and by Belhomme in a woman in whom an exostosis pressed on the left crus. They may, perhaps, be explained by assuming that the division or injury of the crus cerebelli produces paralysis or imperfect and disorderly movements of the opposite side of the body; the animal falls, and then, struggling with the disordered side on the ground, and striving to rise with the other, pushes itself over; and so again and again, with the same act, rotates itself. Such movements cease when the other crus cerebelli is divided; but probably only because the paralysis of the body is thus made almost complete. Other varieties of forced movements have been observed, especially those named "circus movement," when the animal operated upon moves round and round in a circle; and again those in which the animal turns over and over in a series of somersaults. Nearly all these movements may result on section of one or other of the following parts: viz., crura cerebri, medulla, pons, cerebellum, corpora quadrigemina, corpora striata, optic thalami, and even, it is said, of the cerebral hemispheres.

V. THE CEREBRUM.

That portion of the brain which is concerned with all intellectual functions is the cerebrum or, more strictly speaking, the cerebral cortex. The cerebral cortex is the seat of those activities which we describe as intelligence—including states of consciousness, acts of idea formation and volition, and the phenomenon of memory.

The cerebrum includes the cerebral cortex, the mass of fibers connecting it with lower portions of the brain, the basal nuclei represented by the corpora

striata, optic thalami, etc. The structure and function of these basal nuclei have already been given briefly, so we may turn our attention now to the cerebral cortex.

Structure of the Cerebral Cortex. The cerebral cortex forms a large part of the mass of the cerebrum, in fact of the whole brain. Its superficial appearance presents a series of ridges and folds, the gyri and sulci. For general convenience anatomists have divided the cerebral cortex into five lobes: the frontal, that portion in front of the fissure of Rolando extending down to the Sylvian fissure; the parietal, extending from the Sylvian fissure to the parieto-occipital fissure, and bounded below by the Sylvian fissure; the temporal lobe, just ventral to the parietal; the central lobe, or island of Reil; and the occipital lobe, which includes the posterior portion of the cortex behind the

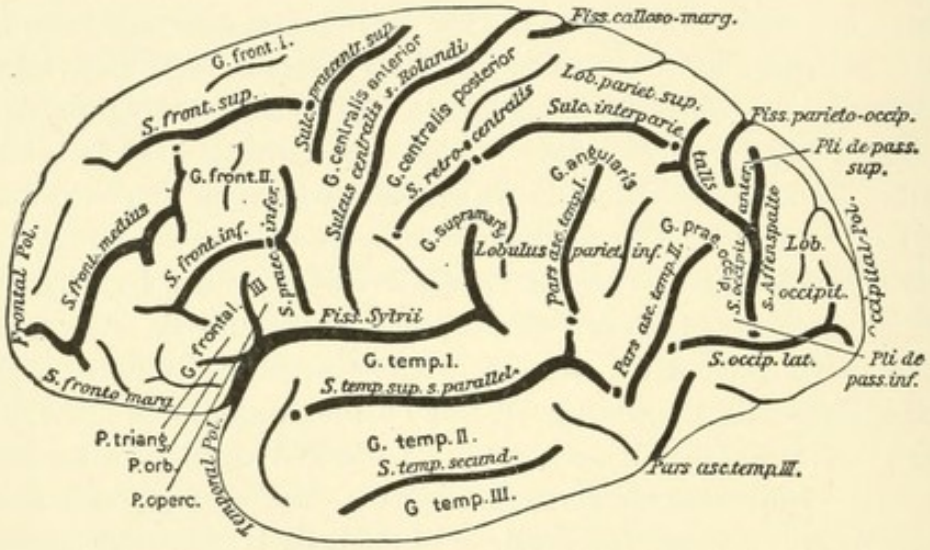


FIG. 397.—Left Hemisphere, from Without. (After Eberstaller.)

parieto-occipital fissure. And, finally, the olfactory and limbic lobes together make up the olfactory division of the brain. For the detailed arrangements of the cortex the reader is referred to text-books of anatomy.

In a transverse section of the cerebral cortex there is shown an external gray layer chiefly composed of nerve cells and an internal white portion of nerve fibers. The folding of the cortex into convolutions increases the total mass of gray matter enormously.

The gray or cellular external part of the cerebral cortex has an average thickness of about 3 mm.; being thin in the occipital and frontal region, 2 mm., and thick in the precentral, 4 mm., and postcentral convolutions.

Several types of nerve cells have been described as present in the cortex, the exact type and relative proportion varying somewhat in different regions. The typical characteristic cell, however, is the pyramidal cell. The pyramidal cell, as its name implies, has a pear-shaped cell body with numerous protoplasmic processes. The apex of the cell is directed toward the surface of the

cortex, and supports numerous branches which extend out into the adjacent territory, bringing it into contact with a relatively large number of nerve cells. These processes are dendritic in character. The base of the pyramidal cell always has a single axis-cylinder process which is directed down into the white matter, and which in some cases ultimately finds its course through the corona radiata into the pyramids below. The axis-cylinder processes give off col-

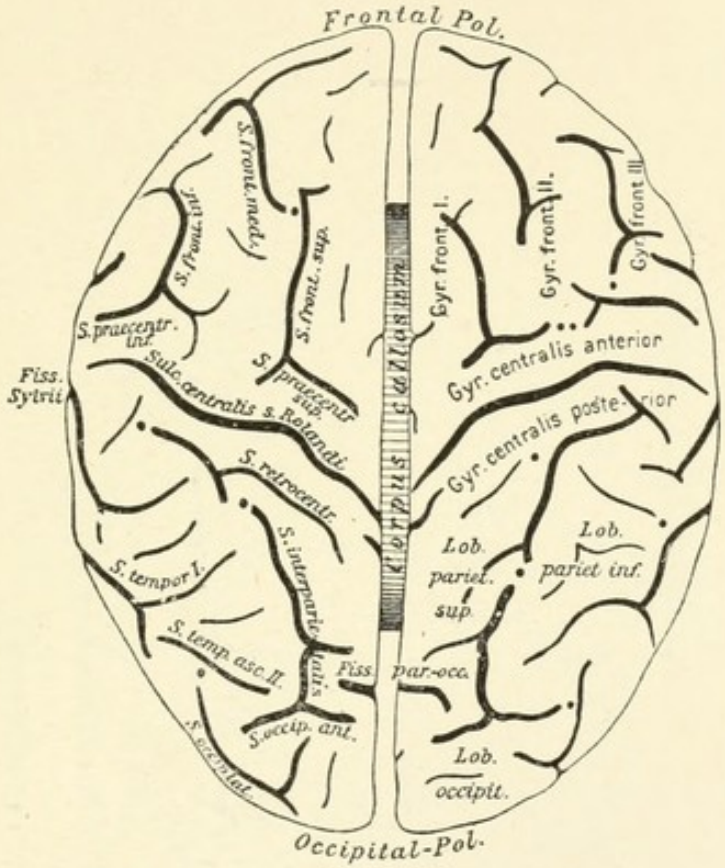


FIG. 398.—The Cerebrum, from Above. (After Eberstaller.)

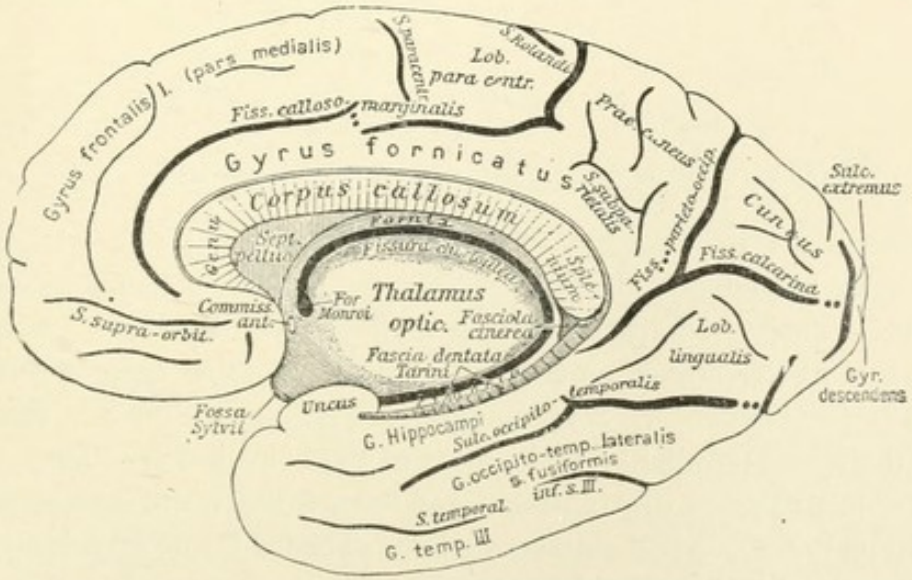


FIG. 399.—Right Hemisphere, from Within. (After Eberstaller.)

laterals both in the immediate neighborhood of the cell and somewhat deeper along its course.

In the superficial layer of the cortex there is a peculiar type of small cell, first described by Cajal. Most of these cells are fusiform in shape, with the long axis parallel to the surface of the convolution. They give off usually two axones which run along parallel to the surface and send down numerous

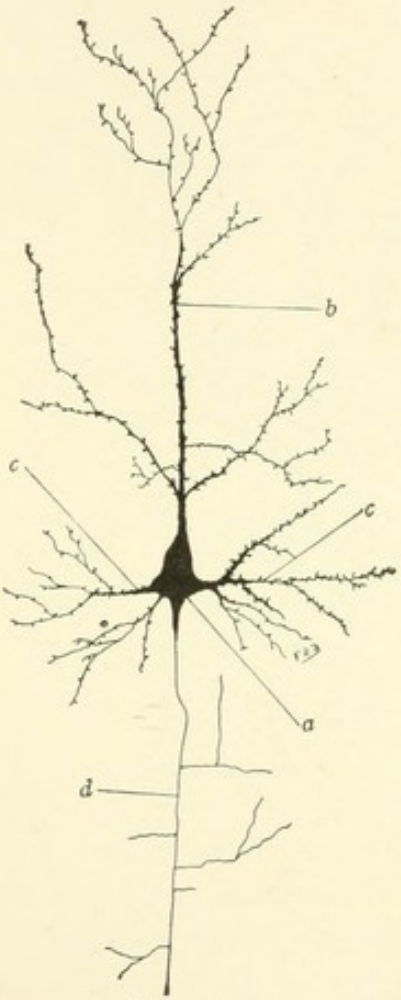


Fig. 400.

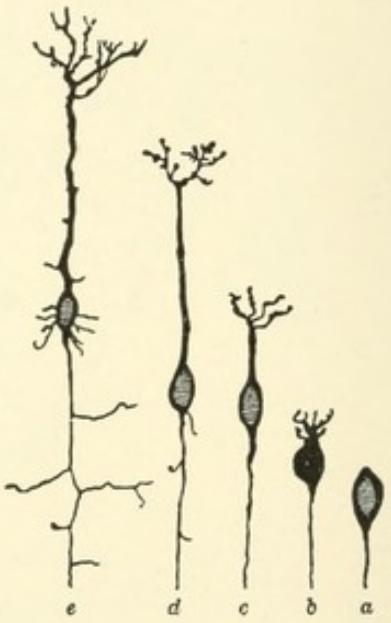


Fig. 401.

Fig. 400.—Typical Pyramidal Cell from the Human Cortex. *a*, Cell body; *b*, main dendrites with gemmules; *c*, lateral dendrites; *d*, axone and collaterals. Only a small part of the axone is shown. (Bailey.)

Fig. 401.—Showing the Stages in the Development of a Pyramidal Cell. (Ramón y Cajal.)

fine collaterals at right angles. Another form of Cajal cell, triangular or quadrangular in shape, is also seen. Both forms have, as a rule, more than one axone. Their collaterals pass in a horizontal direction, forming a fine band of fibers, known as *tangential fibers*. A third type of cell is the *fusiform* or *polymorphous*. Some of these are strictly fusiform in shape and lie with their axes parallel to the surface of the convolution. They give off protoplasmic processes which pass down toward the white matter, some of them turning to run in a horizontal direction. The fusiform and polymorphous cells are grouped in the same layer.

Besides these cells we find scattered through the cortex a considerable number of the neuroglia cells. The character and position of these are shown in figure 402.

The general arrangement of the layers of the cortex is described very differently by the various authors. It is not uniform in the different parts of the

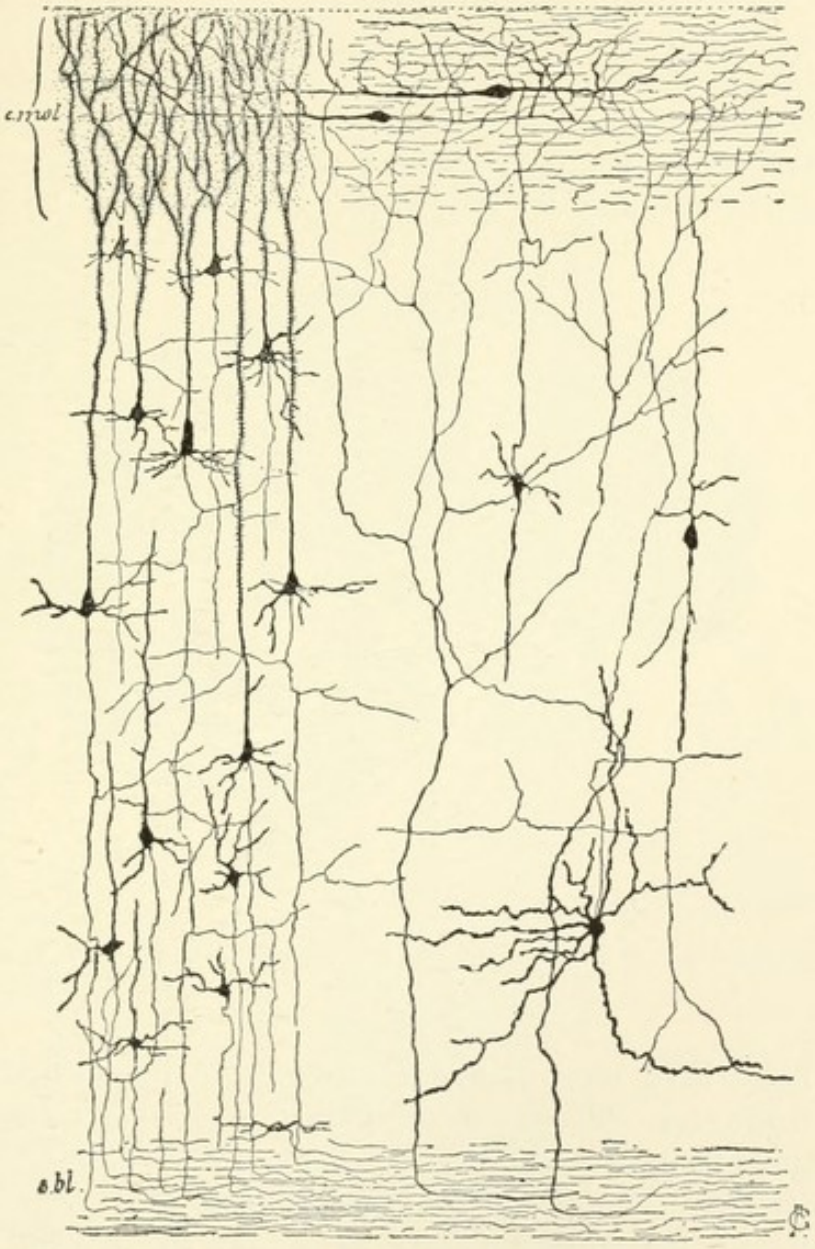


FIG. 402.—The Principal Constituent Elements of the Gray Cortical Layer of the Anterior Cerebrum. (After Ramón y Cajal.)

brain. The simplest and most representative type, however, of the arrangement is that in which the cortex is divided into four layers. The outermost, or superficial, known as the *molecular* layer, contains relatively few cells. It is composed of neuroglia tissue, embedded in which are a number of cells of the Cajal types, which have just been described. There are also in this layer many neuroglia cells. In the superficial part of the layer of some areas of the

cortex are many tangential fibers. The second layer is composed of small pyramidal cells. In parts of the brain there are here interposed what are known as the *vertical fusiform* cells. The third layer is composed of large pyramidal cells, in which, however, one also sees many small pyramidal cells. The fourth layer is composed of the fusiform and polymorphous cells, beneath which is the white substance. This arrangement is shown in the accompanying figures, 404 and 405. The gray matter of the brain contains, however, not only these layers and cells, but an infinitely rich mass of fibers, which can be shown to have a certain definite arrangement. Some of the fibers are vertical, passing directly up to the most superficial layers of cells; others have a horizontal direction, dividing the gray matter into different layers. These

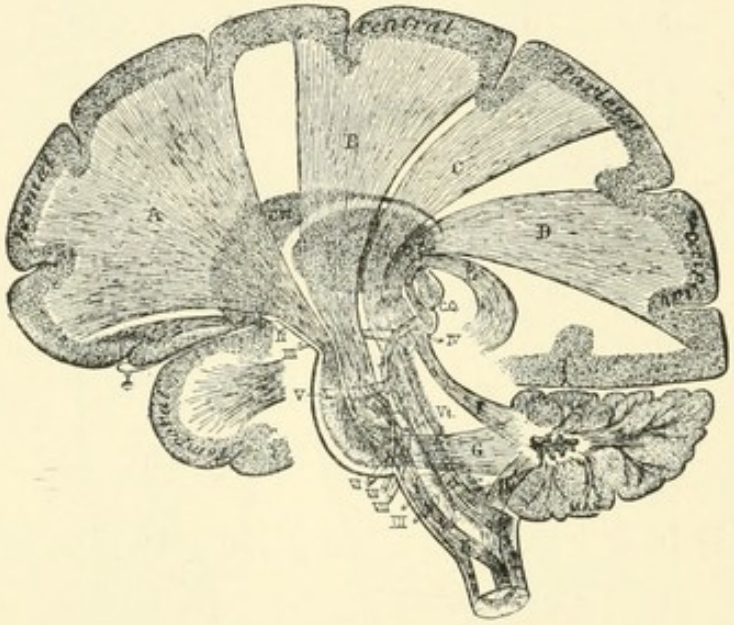


FIG. 403.—Scheme of Descending Conduction Pathways from the Cerebrum to Lower Nerve Centers.

layers of fibers have received different names. A typical arrangement is shown in figure 405. The most conspicuous fibers are those of certain large triangular or pyramidal cells.

The efferent or axone fibers from the cerebral cortex may be divided into three classes: 1, the projection fibers, which descend through the corona radiata and internal capsule, to end in lower centers; 2, the commissural fibers, which cross to the opposite cerebral hemisphere, chiefly through the corpus callosum; 3, the association fibers, which pass in bundles beneath the cortex, to end in other regions of the same hemisphere.

It is by means of projection fibers and collaterals that associations are made with nerve cells in the optic thalamus, tegmentum, and pons, and through the latter region with tracts going to the cerebellum.

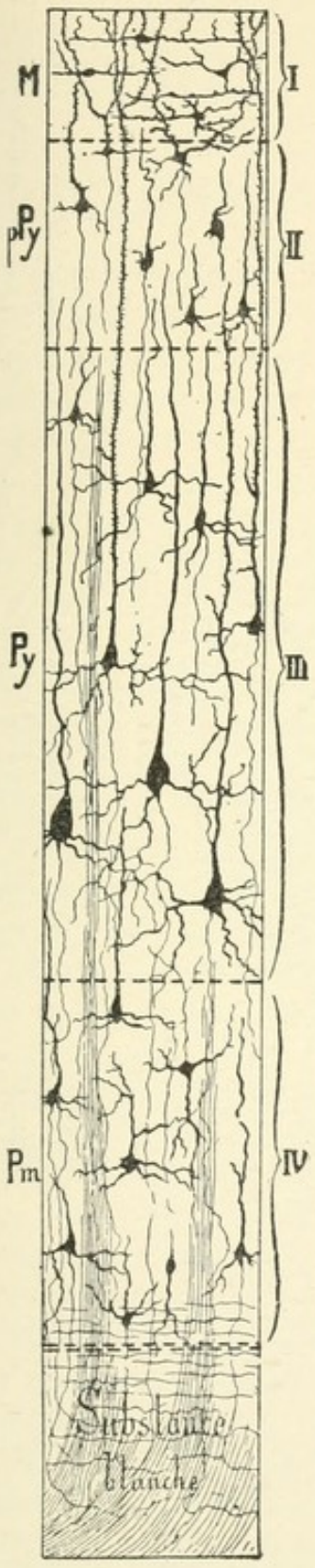


FIG. 404.

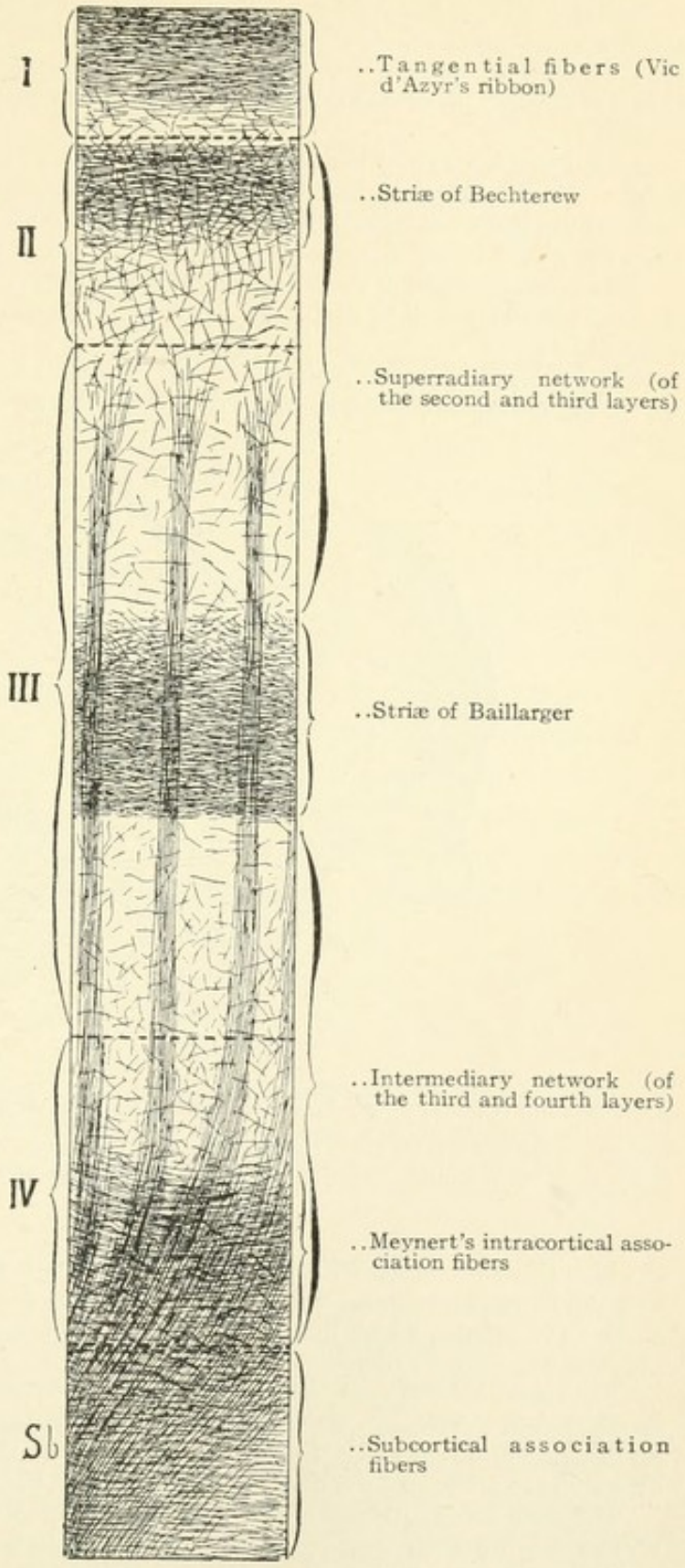


FIG. 405.

FIG. 404.—Schematic Diagram of the Different Layers of the Cerebral Cortex. (After Ramón y Cajal.) I, II, III, and IV, Layers of cortical cells. *M*, Molecular layer; *pPy*, layer of small pyramidal cells; *gPy*, layer of large pyramidal cells; *Pm*, layer of polymorphous cells.

FIG. 405.—Schematic Diagram Showing the Arrangement of the Nerve Fibers in the Cerebral Cortex. The dotted lines separate the four cellular layers of Cajal. *Sb*, White substance.

Weight of the Brain and Cord. The brain of an adult man weighs from 48 to 50 oz., about 1,550 grams, or about 2 per cent of the body weight. It exceeds in absolute weight that of all the lower animals except the elephant and whale. Its weight, *relatively to that of the body*, is exceeded only by that of a few small birds, and some of the smaller monkeys.

In the new-born child the brain (weighing 10 to 14 oz.) is about 10 per cent of the weight. At the age of 7 years the weight of the brain already averages 40 oz., and about 14 years the brain not infrequently reaches the weight of 48 oz. Beyond the age of forty years the weight slowly but steadily declines at the rate of about 1 oz. in 10 years.

The average weight of the female brain is less than the male; and this difference persists from birth throughout life. The difference amounts to about 5 oz. Thus the average weight of an adult woman's brain is about 44 oz.

The brains of idiots are generally much below the average, some weighing less than 16 oz. Still the facts at present collected do not warrant more than a very general statement,

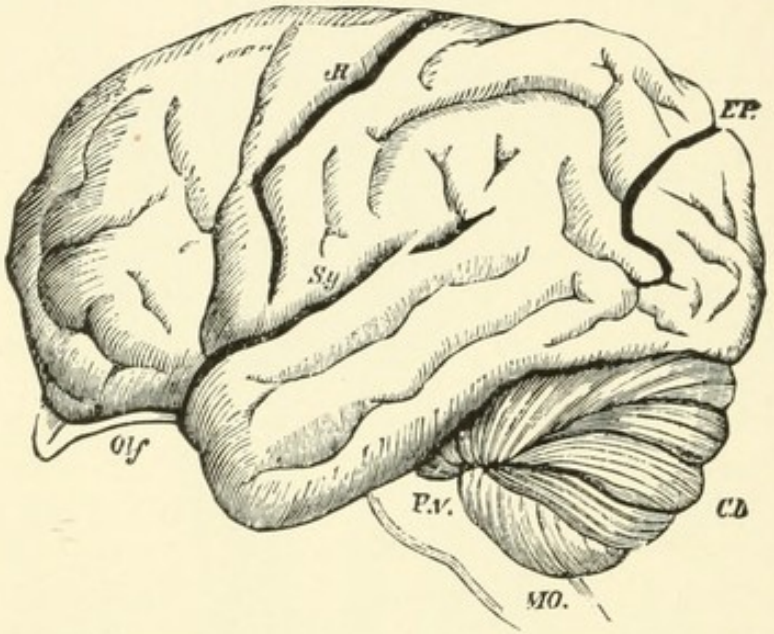


FIG. 406.—Brain of the Orang, $\frac{3}{4}$ Natural Size, Showing the Arrangement of the Convolutions. *Sy*, Fissure of Sylvius; *R*, fissure of Rolando; *EP*, external perpendicular fissure; *Olf*, olfactory lobe; *Cb*, cerebellum; *PV*, pons Varolii; *MO*, medulla oblongata. As contrasted with the human brain, the frontal lobe is short and small relatively, the fissure of Sylvius is oblique, the temporo-sphenoidal lobe very prominent, and the external perpendicular fissure very well marked. (Gratiolet.)

to which there are numerous exceptions, that the brain weight corresponds to some extent with the degree of intelligence. There can be little doubt that the *complexity* and *depth* of the convolutions, which indicate the area of the gray matter of the cortex, correspond with the degree of intelligence.

The spinal cord of man weighs from 1 to $1\frac{1}{2}$ oz.; its weight relatively to the brain is about 1:40 in the adult. As we descend the animal scale, this ratio constantly increases till in the mouse it is 1:4. In cold-blooded animals the relation is reversed, the spinal cord is the heavier. In the newt, 1:05; and in the lamprey, 1:133.

The most distinctive points *in the human brain*, as contrasted with that of apes, are: 1. The much greater size and weight of the whole brain. The brain of a full-grown gorilla weighs only about 15 oz. (450 grms.), which is less than $\frac{1}{3}$ the weight of the human adult male brain, and barely exceeds that of the human infant at birth. 2. The much greater complexity of the convolutions, especially the existence in the human brain of tertiary convolutions in the sides of the fissures. 3. The greater relative size and complexity and the blunted quadrangular contour of the frontal lobes in man, which are relatively broader, longer, and higher than in apes. In apes the frontal lobes project keel-like

(rostrum) between the olfactory bulbs. 4. The much greater prominence of the temporo-sphenoidal lobes in apes. 5. The fissure of Sylvius is nearly horizontal in man, while in apes it slants considerably upward. 6. The distinctness of the fissure of Rolando.

Most of the above points are shown in the accompanying figure of the brain of the orang.

GENERAL FUNCTIONS OF THE CEREBRUM.

Evidence regarding the physiology of the cerebral hemispheres has been obtained, as in the case of other parts of the nervous system, from the study of anatomy, from pathology, and from experiments on the lower animals. The chief evidences regarding the functions of the cerebral hemispheres derived from these various sources are briefly these: 1, Any severe injury of them, such as a general concussion, or sudden pressure as by apoplexy, may instantly deprive a man of all power of manifesting externally any mental faculty. 2, In the same general proportion as the higher mental faculties are developed in the vertebrates and especially in man at different ages, as well as in different individuals, the greater is the development of the cerebral hemispheres in comparison with the rest of the cerebro-spinal system. 3, No other part of the nervous system bears a corresponding proportion to the development of the mental faculties. 4, Congenital and other morbid defects of the cerebral hemisphere are, in general, accompanied by corresponding deficiency in the range or power of the intellectual faculties and the higher instincts. 5, Removal of the cerebral hemispheres in the lower animals produces effects corresponding with what might be anticipated from the foregoing facts.

Effects of the Removal of the Cerebrum. The removal of the cerebrum in the lower animals appears to reduce them to the condition of a mechanism without spontaneity.

In the case of the *frog*, when the cerebral lobes have been removed, the animal appears similarly deprived of all power of spontaneous movement. But it sits up in a natural attitude and breathes quietly. When pricked it jumps away. When thrown into the water it swims. When placed upon a board it remains motionless, although, if the board be gradually tilted over till the frog is on the point of losing his balance, he will crawl up till he regains his equilibrium, and comes to be perched quite on the edge of the board.

If the frog be turned on his back, he regains his normal position. If his back is stroked gently he will utter the usual croaking sound. These activities are carried on by the normal frog. There is one striking difference, however, between the brainless frog and the normal: the former, if placed in a position and left undisturbed, will remain quietly without moving for an indefinite time. It has apparently lost the power to initiate movements. Presumably any memory impressions or effects of former experiences have been lost. Even the more elemental stimuli, which come from tissue hunger and thirst, apparently do not affect the brainless frog. In other words, the oper-

ation has reduced the animal to the condition of an automaton capable of carrying on complex activities, but only after receiving some definite stimulus. This condition contrasts with that resulting from the removal of the entire brain, leaving only the spinal cord. In this case only the simpler reflex actions can take place. The frog does not breathe; he lies flat on the table instead of sitting up; when thrown into a vessel of water he sinks to the bottom; when his legs are pinched he kicks out, but does not leap away.

If the cerebrum of the frog be removed, taking special care not to interfere with the optic nerves or the optic thalami, then he acts somewhat differently. Whereas with the entire cerebrum removed he makes no effort to take food, now he will attempt to catch flies or other insects, and will show other signs of spontaneous activity. He will avoid an object and shows signs of responding to visual sensations, such as the attempt to feed just mentioned.

The cerebral lobes of the frog, however, are very low in the scale of development as compared with other vertebrates. The cortex is a single layer of rather small cells, and the total volume of the cortex as compared with other portions of the brain is small.

The case of the pigeon, which represents a higher animal in the scale, has been extensively studied by Flourens and others. They have shown that when the cerebrum is carefully removed, leaving the basal nuclei undisturbed, and the animal has recovered from the immediate effects of the shock, it is able to carry on many coordinate activities. In the first place it can stand or perch without difficulty; if placed on its back it immediately regains its equilibrium; if tossed in the air it flies until it comes in contact with a firm support. If disturbed on its perch it will walk away, showing the power to coordinate not only wing muscles, but the leg muscles. If left undisturbed, such a pigeon will occasionally make motions, *i.e.*, open its eyes, move its head, preen its feathers, or even take a step or two. It spends most of its time, however, sitting quietly as though asleep. If aroused, the animal shows little or no signs of excitement or fright.

After several months such pigeons are said usually to increase the motions of spontaneity or take short flights, avoiding obstacles in the way and alighting definitely on the perch. They will pick around among food for definite articles, apparently intending to select the food. Early after the operation the pigeon will pick at objects indiscriminately, but does not take food unless it is placed in the mouth.

Apparently the main effect produced here is to diminish the complexity and efficiency of those activities which we call spontaneous. The surprising thing is that there is as little disturbance among the motor functions as is found.

In mammals it is difficult to remove the cerebral hemispheres, but in those animals in which the operation has been carried out, as for example in the rabbit and rat, a result very similar to those observed in the case of the frog and pigeon has been obtained. The animal is able to maintain its equilibrium,

to run or jump, and in fact successfully carry out the most complicated coordinated movements, but it is unable to originate them without stimulation. In the case of the dog, it has been found impossible to remove the whole brain at one operation. However, Goltz has succeeded in removing both the cerebral hemispheres of the dog by doing the operation in successive stages and taking extraordinary precautions to protect his animal against the great fall of temperature and the immediate shock of the operation. He kept his dog alive for some eighteen months and secured a complete recovery from the series of operations. Goltz's dog was able to walk about, it responded to a bright light by closing its eyes, and could be aroused by a sharp, loud sound. It spent its time lying down in the cage, sleeping rolled up dog-fashion. When aroused by stimulation of the skin, it would move away from the stimulating object and would sometimes growl and snap at the object. If it snapped at the object it would do so without going toward it or making the usual effort to seize the object which we are accustomed to expect of a normal vicious dog. This dog did not spontaneously feed itself, but had to have food placed in its mouth before it would swallow. But the animal finally learned to take food, as in the case of the pigeon. This animal gave very definite responses to its condition of nourishment; it slept quietly and was peaceful when fully fed, but was restless and irritable when hungry.

Goltz's dog showed complete absence of those activities which we would call psychic. That is to say, it showed no memory signs, it was unable to learn the signal for feeding, it did not manifest any fondness or signs of pleasure at the presence of its caretaker. In short, there was a complete loss of memory and intelligence, and the animal, although performing some activities, was in fact reduced to a mere automaton. It would be difficult to imagine a more crucial experiment to elucidate the function of the cerebral cortex.

It is quite evident that the apparatus for carrying out coordinated movements is in these animals not localized either in the cerebrum or in the spinal cord. It must therefore be connected in some way with the parts of the brain below the cerebrum and above the cord. There is no reason why such an arrangement may not be supposed to exist in the human brain, although we must look upon the cerebrum as the originator of voluntary movements.

LOCALIZATION OF THE MOTOR FUNCTION OF THE CEREBRAL CORTEX.

The experiments upon the brains of various animals by means of electrical stimulation have demonstrated that there are definite regions of the cerebral cortex the stimulation of which produces definite movements of coordinated groups of muscles of the opposite side of the body. Fritsch and Hitzig were the first to show that the cerebral cortex responds to electric irritation. They

employed a weak constant current in their experiments, applying a pair of fine electrodes not more than one-twelfth inch apart to different parts of the cerebral cortex. The results thus obtained have been confirmed and extended by Ferrier and many others, stimulating chiefly with induction currents.

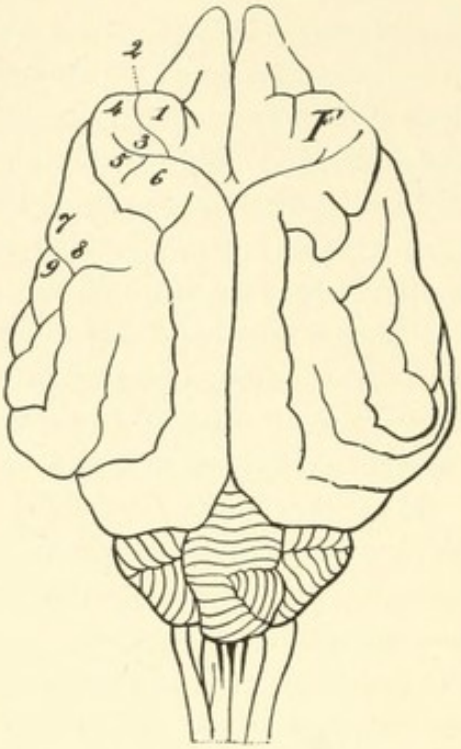


FIG. 407.

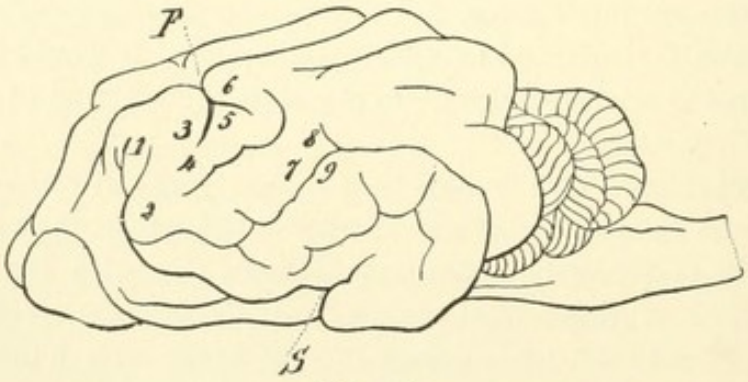


FIG. 408.

FIGS. 407 and 408.—Brain of Dog, Viewed from Above and in Profile. *F*, Frontal fissure sometimes termed crucial sulcus, corresponding to the fissure of Rolando in man; *S*, fissure of Sylvius, around which the four longitudinal convolutions are concentrically arranged; 1, flexion of head on the neck, in the median line; 2, flexion of head on the neck, with rotation toward the side of the stimulus; 3, 4, flexion and extension of anterior limb; 5, 6, flexion and extension of posterior limb; 7, 8, 9, contraction of orbicularis oculi and the facial muscles in general. The unshaded part is that exposed by opening the skull. (Dalton.)

The fundamental phenomena observed in all these cases may be thus epitomized:

1. Excitation of the same spot on the cortex is always followed by the same movement in the same animal. 2. The area of excitability for any given

movement is extremely small, and admits of very accurate definition. 3. In different animals excitations of anatomically corresponding spots produce contractions in similar or corresponding muscles.

The various definite movements resulting from the electric stimulation of circumscribed areas of the cerebral cortex are enumerated in the description of the accompanying figures of the dog's and monkey's brains.

In the case of the dog the results obtained are summed up as follows by Hitzig: 1, One portion, anterior, of the convexity of the cerebrum is motor; another portion, posterior, is non-motor. 2, Electric stimulation of the motor portion produces coordinated muscular contraction on the opposite side of the body. 3, With very weak currents, the contractions produced are distinctly limited to particular groups of muscles; with stronger currents the stimulus is communicated to other muscles of the same or neighboring parts. 4, The portions of the brain intervening between these motor centers are inexcitable.

Following strong stimulation of cortical motor centers other groups of muscles than those innervated by the centers stimulated may also take part in the contractions.

According to the observations of Ferrier, confirmed and extended by later experimenters, stimulation of various parts of the monkey's brain, as indicated by the numbers in figures 409, 410, produces movements of definite muscles, thus: Stimulation of the district marked 1 causes movement of hind foot; of 2, chiefly adduction of the foot; of 3, movements of hind foot and tail; of 4, of latissimus dorsi; of 5, extension forward of arm; *a*, *b*, *c*, *d*, movements of hand and wrist; of 6, supination and flexion of forearm; of 7, elevation of the upper lip; of 8, conjoint action of elevation of upper lip and depression of lower; of 9, opening of mouth and protrusion of tongue; of 10, retraction of tongue; of 11, action of platysma; of 12, elevation of eyebrows and eyelids, dilatation of pupils, and turning head to opposite side; of 13, eyes directed to opposite side and upward, with usually contraction of the pupils; of 13′, similar action, but eyes usually directed downward; of 14, retraction of opposite ear, head turns to the opposite side, the eyes widely opened and pupils dilated; of 15, stimulation of this region, which corresponds to the tip of the uncinate convolution, causes torsion of the lip and nostril of the same side.

It is thus seen that the motor areas chiefly correspond with the ascending frontal and ascending parietal convolutions, and that the movements of the leg are represented at the upper part of these convolutions, then follow from above downward the centers for the arms, the face, the lips, and the tongue.

According to the further researches of Schäfer and Horsley, electrical stimulation of the marginal convolution internally at the parts corresponding with the ascending frontal and parietal convolutions, from the front backward, produces movements of the arm, of the trunk, and of the leg.

A good deal of doubt was thrown upon the experiments of Ferrier by Goltz and other observers, from the results of excising the so-called motor areas of

the dog's brain. It was found that the part might be sliced away or washed away with a stream of water, but that no permanent paralysis ensued.

More extensive observations, however, have confirmed Ferrier's original statement, at any rate with regard to the monkey's brain. Destruction of the

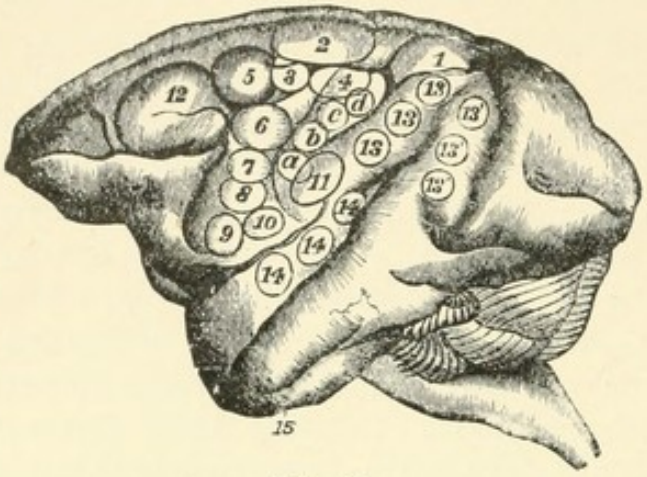


Fig. 409.

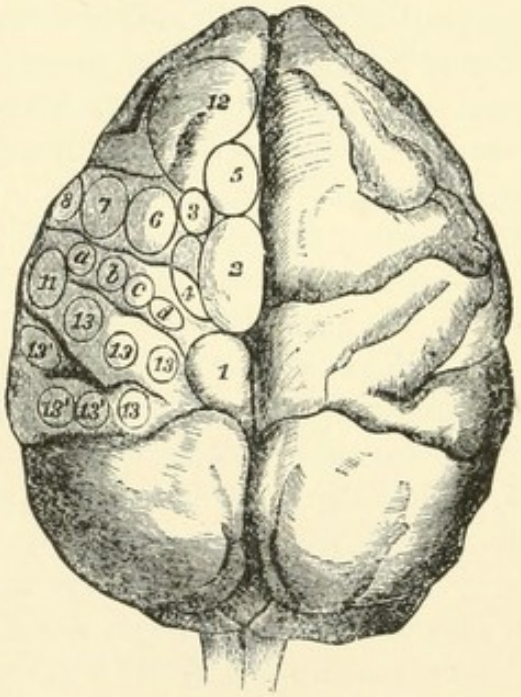


Fig. 410.

Figs. 409 and 410.—Diagrams of Monkey's Brain to Show the Effects of Electric Stimulation of Certain Spots. (According to Ferrier.)

motor areas for the arm produces some permanent paralysis of the arm of the opposite side, and similarly of that for the leg, paralysis of the opppsite leg. If both areas are destroyed, permanent hemiplegia ensues. Paralysis of so extensive and permanent a character does not, however, appear the rule when the brain of a dog is used instead of that of the monkey. It is suggested that in the animal lower in the scale the functions which in the

monkey are discharged by the cortical centers may be subserved to a greater extent by the basal ganglia.

Motor Areas of the Human Brain. It is naturally of great importance to discover how far the results of experiments upon the dog and monkey

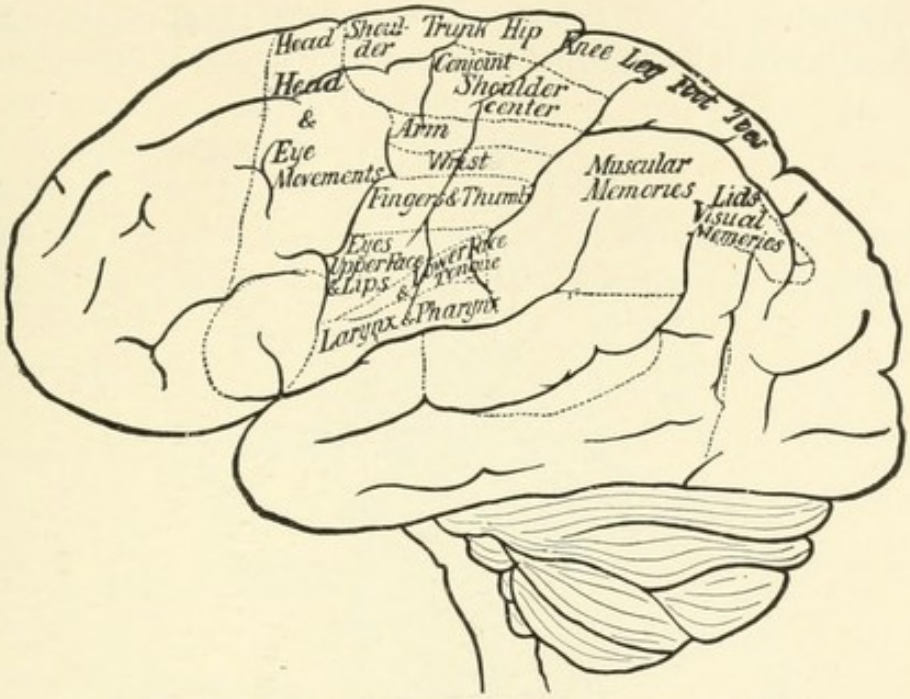


FIG. 411.—Motor Areas of the Human Brain, Lateral View.

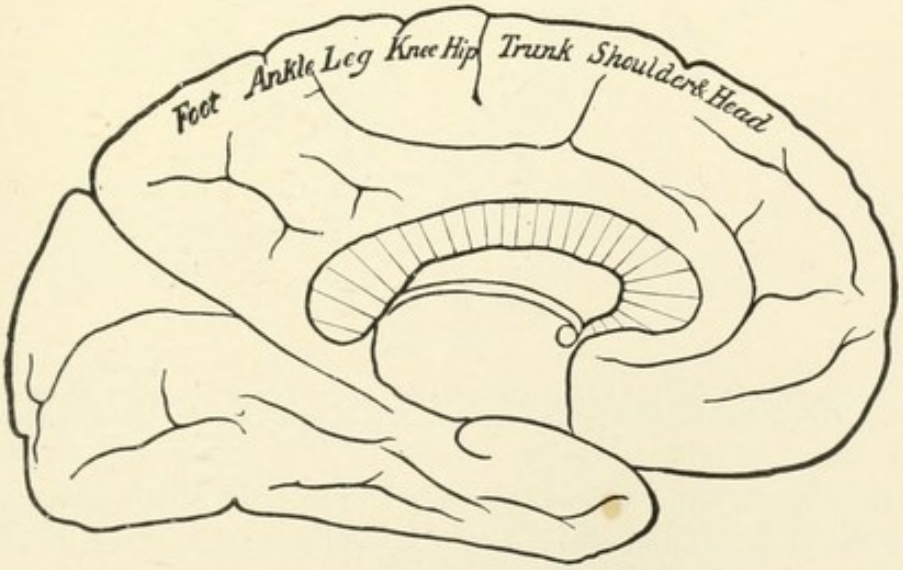


FIG. 412.—Motor Areas of the Human Brain, Median View.

hold good with regard to the human brain. Evidence furnished by diseased conditions is not wanting to support the general idea of the existence of cortical motor centers in the human brain, figure 411.

So far, however, it has been possible to localize motor functions in the precentral and ascending parietal convolutions only; the convolutions which

bound the fissure of Rolando and those on the inner side of the hemispheres which correspond thereto, and possibly the frontal lobe in front of the pre-central convolution.

The position of the centers is probably much the same as in the monkey's brain, those for the leg above, those for the arm, face, lips, and tongue from above downward. Destruction of these parts causes paralysis, corresponding to the district affected, and irritation causes contractions of the muscles of the

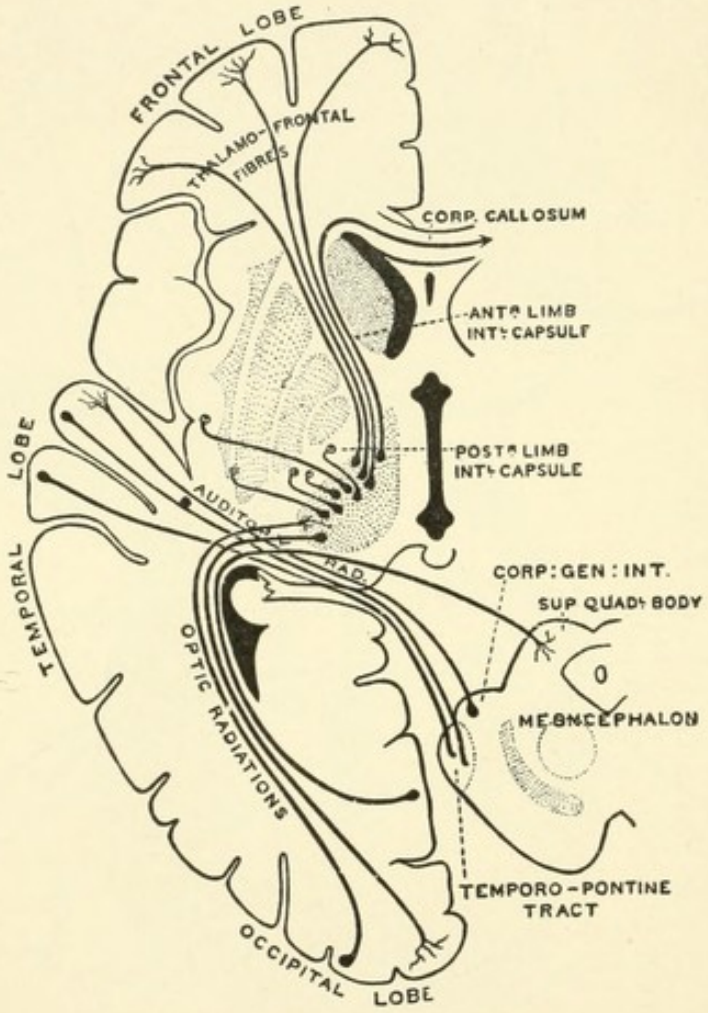


FIG. 413.—Diagram of Certain Connections of the Frontal, Temporal, and Occipital Lobes. Founded on the observations of Flechsig, Ferrier, and Turner. (Cunningham.)

same part. Again, a number of cases are on record in which *aphasia*, or the loss of power of expressing ideas in words, has been associated with disease of the posterior part of the lower or third frontal convolution on the left side. This condition is usually associated with paralysis of the right side, right hemiplegia.

This district of the brain, particularly the convolutions bounding the fissure of Rolando, is now generally known as the *motor area;* and there is no doubt whatever that from this area pass the nerve fibers which proceed to the spinal cord, and are there represented as the pyramidal tracts.

This is the reason that movements are produced on stimulation of the white matter after the superficial gray matter of the animal's brain has been sliced off.

These motor fibers are those which arise from the pyramidal cells of the cortex. From the motor area of the cortex they converge to the *internal capsules*, and pass down to the crus. In the internal capsule the fibers which pass to the pyramidal tracts of the spinal cord occupy that part known as the knee (genu) and the anterior two-thirds of the posterior limb, figure 414. In this district the fibers for the face, arm, and leg are in this relation: those for the face and tongue are just at the knee, and below or behind them come first the fibers for the arm and then those for the leg.

The more accurately known arrangements of these fibers in the monkey's brain, named in order, from above down, are those for the eye, head, tongue,

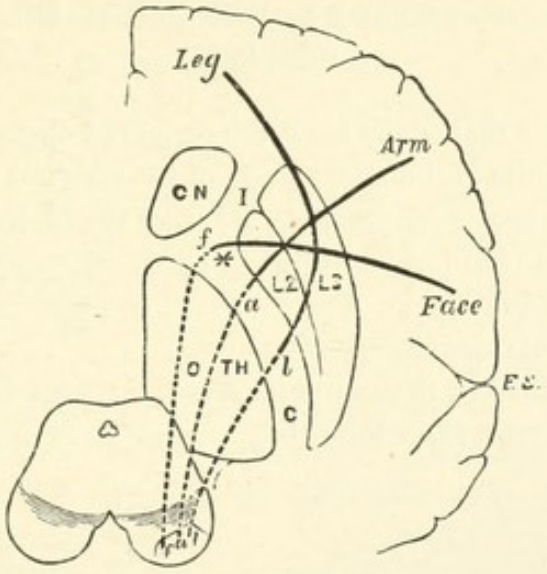


FIG. 414.—Diagram to Show the Relative Positions of the Several Motor Tracts in Their Course from the Cortex to the Crus. The section through the convolution is vertical; that through the internal capsule, *IC*, horizontal; that through the crus again vertical. *CN*, caudate nucleus; *O TH*, optic thalamus; L_2 and L_3, middle and outer part of lenticular nucleus; *f*, *a*, *l*, face, arm, and leg fibers. The words in italics indicate corresponding cortical centers. (Gowers.)

mouth, shoulder, elbow, digits, abdomen, lip, knee, digits. These fibers come for the most part from the portion of the cortex on either side of the fissure of Rolando, but chiefly from the anterior central gyrus, hence called the *Rolandic area*. But the areas for the head and eyes lie more anteriorly in the frontal lobe, to the front of the precentral sulcus—that for the head above that for the eyes, and an area for the trunk (not indicated in the figure 414) is situated more toward the middle line of the hemisphere, internal to that for the leg. Those fibers, passing between the occipital lobe and the optic thalamus and superior corpora quadrigemina, are concerned with vision, and are called fibers of the *optic radiation*. In like manner, from the inferior corpora quadrigemina and the internal geniculate bodies, fibers which make up the auditory radiation pass to the auditory center.

It has already been shown that the motor fibers of the internal capsule of one side cross over to the opposite side in the decussation of the pyramids in the medulla. This decussation is not quite complete, as some fibers pass down on the same side in the direct pyramidal tract. A small portion of these direct fibers end around the motor neurones of the same side, but the great majority cross to the opposite side in the anterior commissure at some lower level of the cord. It follows that the motor areas of the cortex on one side control the muscular movements of the opposite side of the body, but to a slight extent those of the same side. Disease in the region of the fissure of Rolando is usually accompanied by a disturbance of the motor function on the opposite side of the body, although there is some slight motor disturbance on the same side.

LOCALIZATION OF SENSORY FUNCTION IN THE CEREBRAL CORTEX.

There is evidence that fibers from the nerves of special sense are specially connected with definite and distinct parts of the cerebral cortex.

The fibers from the sensory nerves, we have found, are connected with the cerebral cortex by a chain of neurones. These sensory paths, although complex, are definite and distinct. Their cortical connections have been mapped out with considerable definiteness.

The Body Sensory or Somesthetic Area. The motor function around the fissure of Rolando for a long time obscured the fact that this region,

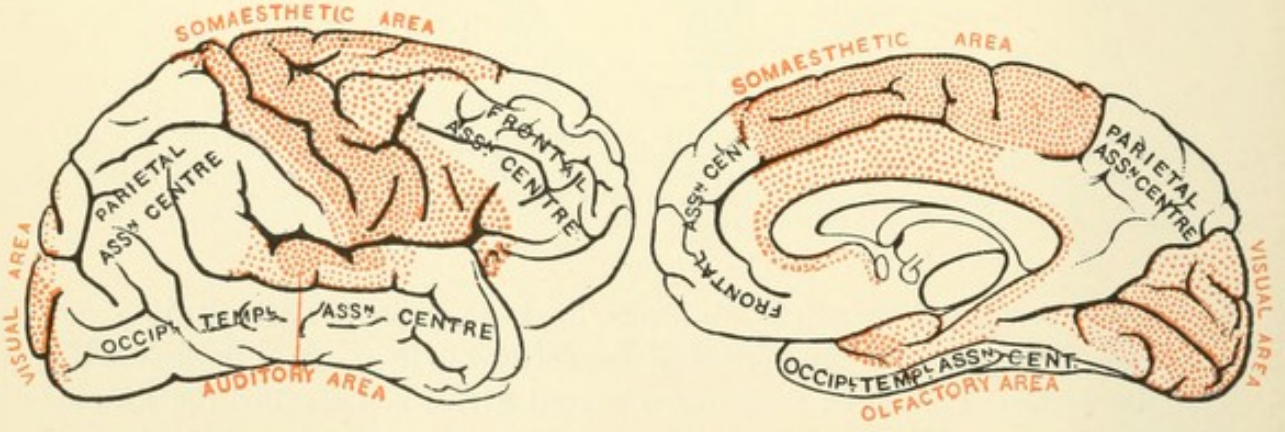


FIG. 415.—Diagrams to Show Flechsig's Sensory and Association Areas on t e Surface of the Cerebral Hemisphere. (From Cunningham, after Flechsig.)

especially the post-central convolution, is intimately connected with the perception of general body sensations. Physiological and pathological observations supported this view, and recently Flechsig has much strengthened the view by his method of studying the progressive development of the brain. In figure 415 we produce Flechsig's diagram showing the body sensory (somesthetic) area. The borders of the area are more or less indefinite and less

distinct than the main portion. This is indicated by the lighter shading. Lesions of this area in the cortex lead to loss of sensibility in definite regions of the opposite side of the body.

Visual or Optic Center. The termination of the optic nerve in each eye, the retina, to the structure of which we shall return when treating of the eye, is so arranged that when we look at an object with both eyes, symmetrical parts of each retina are used. For example, if we look at an object to the left, an image of that object is focussed upon the right half of both retinæ, viz., upon the temporal side of the right retina, and upon the nasal side of the left retina. The optic nerve fibers of these symmetrical parts of the retina are gathered together behind where the optic nerves decussate, viz., in the optic chiasma. The fibers which come from the right side of both eyes are contained in the optic tract of the same side, viz., the right, those from the right eye being outside of the others. In the same way the left optic tract contains internally fibers from the left side of the right eye and externally those from the left side of the left eye. The optic tract thus formed then passes backward and terminates in three distinct nuclei, viz., the pulvinar of the optic thalamus, the anterior corpus quadrigeminum, and the lateral corpus geniculatum. These nuclei atrophy if the eyes are removed from an adult animal; and if the eyes are removed from a newly born animal, they do not fully develop. Through the superior corpora quadrigemina the optic tract establishes synapses that bring it into relation with the nucleus of the third nerve, and which form the basis of the eye reflexes to light stimulation.

It appears that some of the fibers of the optic tract pass directly into the cerebral cortex without joining with the optic thalamus, corpus quadrigeminum, or corpus geniculatum.

It was shown above that the fibers of the cerebral cortex, known as the optic radiation, pass from the occipital region to the three nuclei about which we are speaking, viz., into the pulvinar of the optic thalamus, the anterior corpus quadrigeminum, and lateral corpus geniculatum, and it is known that when the occipital cortex is removed, these three atrophy. It has been further shown that in a newly born animal the removal of such a region is followed by imperfect development of the parts in question.

If one optic nerve be divided, blindness of the corresponding eye results; but if one optic tract be divided there is a half blindness in both eyes, which is called *hemianopsia*, or *hemiopia*, right or left, according as the right or left field of vision is cut off. It is evident that the occipital lobe, figures 412, 413, and particularly the cuneus, is concerned as a visual center, since not only is it connected with the optic nerves, as we have seen, but also because the removal of the right occipital lobe in an animal (monkey) is followed by left hemiopia, removal of the left by right hemiopia, and removal of both occipital lobes by total blindness.

Olfactory Center in the Cortex. The olfactory nerve differs from

the other cranial nerves. In reality it is a representative of the olfactory lobes of other animals, which are part of the cerebrum. The olfactory lobe originates as an offshoot from the cerebral vesicle, the front part of which is developed into the bulb of the olfactory nerve, while the back part forms its peduncle. The nerve, the cavity of which in man is filled up in the fully developed condition with neurogliar substance, lies upon the cribriform plate of the ethmoid bone, and is contained in a groove on the under surface

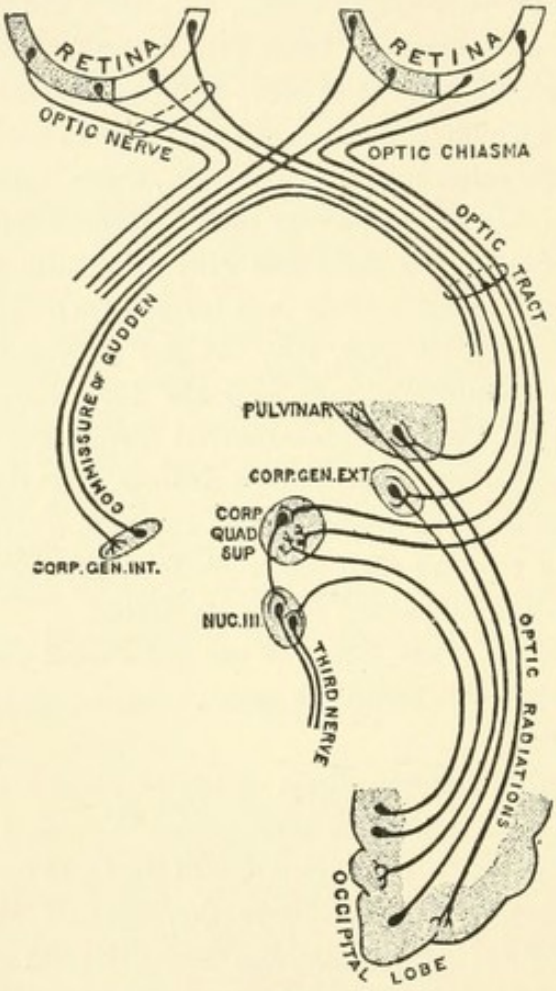


FIG. 416.—Scheme of the Central Connections of the Optic Fibers. (Cunningham.)

of the frontal lobe. On examination of the bulb it is found to be thus made up: Beneath the neurogliar layer is a layer of longitudinal fibers and a few nerve cells next to this is a layer of small cells, nuclear layer, fibers from the layer of nerve fibers passing through it.

The nuclear layer is also separated into groups of cells by an interlacing of the fibers. The next layer is thick and is composed of neuroglia and nerve fibers, some of which are medullated, as well as of cells more or less pyramidal in shape. Below this layer is the layer of *olfactory glomeruli*. These glomeruli are small synapses of olfactory fibers. The larger also includes small

cells and granular matter. A full description of the anatomy of these parts is given later.

Fibers of the olfactory nerve proper are found below this layer, and pass through the cribriform plate to be distributed to the olfactory mucous membrane. They arise from cells in the olfactory mucous membrane, and end in the glomeruli. The peduncle of the nerve or the *olfactory tract*, as it is sometimes called, is made up of longitudinal fibers originating in the bulb, with neuroglia and some nerve cells.

The fibers of the olfactory tract have been traced into the nucleus amygdalæ and its junction with the hippocampal gyrus in the temporal lobe, figure 399. The hippocampus must be in some way connected with smell, since a lesion of it, leaving the olfactory tract uninjured, seriously interferes with that sense.

Taste Center of the Cortex. It is very uncertain where the taste center is situated, if such exist. It has been placed in the anterior portion of the inferior temporal convolution, not far from that of smell, figure 399.

Auditory Center in the Cortex. This center has been localized in the superior temporal convolution. Experiments have been made which connect auditory impulses on either side with the inferior corpus quadrigeminum and the median corpus geniculatum, for when the internal ear is destroyed there results atrophy of these bodies as well as of the lateral fillet of the opposite side. On the other hand, destruction of the part of the temporal lobe above indicated is similarly followed by atrophy of the nuclei of the same side. These nuclei bear much the same relation to the sense of hearing as do the anterior corpora quadrigemina and the lateral corpora geniculata to the sense of sight, figures 389 and 416.

ASSOCIATION CENTERS OF THE CEREBRAL CORTEX.

The theory of localization of the function of different parts of the cerebral cortex has received substantial support from the study of the motor and the sensory areas in man and the mammals. But when the exploration of the cortex is complete and the motor and sensory areas are bounded as definitely as may be, there still remain great areas in which stimulation is apparently non-effective so far as our present means of interpretation reveal. Traumatic and pathological lesions produce no sensory or motor disturbances. The areas of this class which are most extensive, *i.e.*, which cover the greatest amount of cortex, are three in number—the frontal lobe, the parietal lobe, and a large part of the temporal lobe below the superior temporal convolution.

Flechsig has made a study of the development of the human brain, paying especial attention to the progressive development of the great tracts of fibers. He has shown that the tracts appear in a certain order of sequence, also that the myelinization takes place progressively. On the assumption that effective functionization is acquired with the myelin sheath, he showed a close

correspondence in time between the development of the tracts and the manifestation of functions known to involve the tracts in question. The great somesthetic area and its tracts are first to develop; then tracts to the occipital or visual center, to the auditory and other sensory centers, and, finally, to these great areas whose functions remain obscure.

Basing his deductions on the facts of development, on the isolated cases of lesion and disease, and on the careful comparative studies of the brains of certain men of unusual intellectual powers, whose personal characteristics and

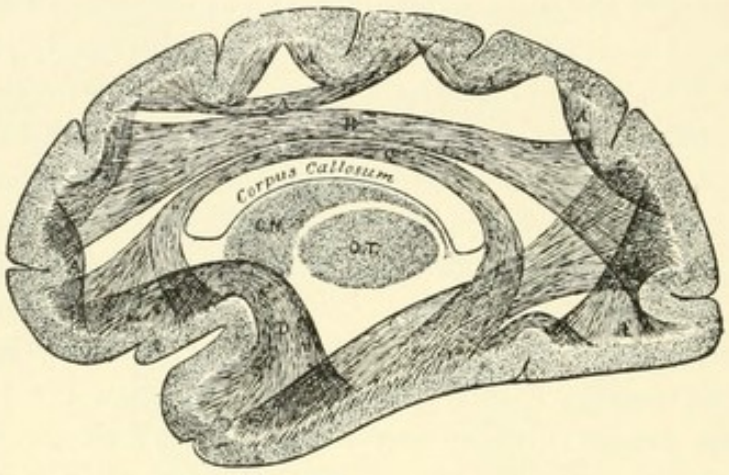


FIG. 417.—The Association Fibers in the Centrum Ovale. *A*, Between adjacent convolutions; *B*, between frontal and occipital lobes; *C*, between frontal and temporal lobes, the cingulum; *D*, between temporal and frontal lobes—lesion of this tract causes paraphasia; *E*, between occipital and temporal lobes—lesion of this tract causes word-blindness; *C.N*, caudate nucleus; *O.T*, optic thalamus.

intellectual genius are known, Flechsig has advanced the hypothesis that the areas of the cortex not concerned directly with motor or sensory functions are association areas.

The Association Centers of Flechsig. The great association centers are the frontal, parietal, and temporal, figure 415. These regions of the cortex are apparently not directly connected with tracts of the brain stem and cord, but they are richly connected with the areas that do have connection with the cord. Short association fibers connect neighboring convolutions within the centers, fibers which are chiefly the axones of the polymorphous cells of the fourth layer of the cortex. Long association fibers run from one center to another, such as the cingulum, superior and inferior longitudinal fasciculi, etc. The longer connectives run from association to association centers, and from association to sensory and motor centers. Flechsig believes that the sensory centers are not connected directly with each other, but only indirectly through the association areas.

Cases of injury and of disease of the human brain in the association areas are not numerous, but such as there are tend to confirm Flechsig's hypothesis that the function of these areas is that of the higher psychic activity.

The Anterior or Frontal Association Center. The frontal area is more closely connected with the motor areas and the centers for the somesthetic sense. With injury to this area the individual shows weakness in attention, in reflection, and in control over the expressions of anger, self-appreciation, and other activities that are expressive of personal volitions and emotions.

The American crowbar case is a classical instance of lesion of the frontal lobe. A young man of twenty-five had an iron bar, an inch and a quarter in diameter and over three feet long, driven through his skull and brain by the premature explosion of a blast of powder. He not only recovered, but lived for twelve years afterward. At the post-mortem examination the puncture was found to be through the prefrontal lobe, anterior to the coronal suture.

This man was considered a most efficient workman and foreman before the injury. After his recovery he was fitful, impatient of restraint, capricious, obstinate; was most inconsiderate of his associates, profane, passionate; from a shrewd business man he was changed to the intellectual level of a child and was regarded by his associates as mentally unbalanced.

A summary of fifty cases of pathological lesions of the prefrontal areas of the human brain is given by Williamson. The mental traits of thirty-two are summarized in the following terms: "A condition of mental decadence; a dull mental state; loss of power of attention; loss of memory; loss of spontaneity; the patient takes no heed of his surroundings; sleeping during the greater part of the day, or remaining semi-comatose." Yet these patients are able to walk about and execute well coordinated muscular activities of all kinds that do not involve complex intellectual activity.

The Parietal Association Centers. Special mention is made of this association area because there is increasing evidence that it is the parietal region of the brain, rather than the frontal, as popularly believed, that is most intimately concerned with acts and powers of imagination, idealization, and reasoning. It is the region through which the individual maintains his interests and relations with the external world as against his own body. The parietal association center is more closely related to the visual, auditory, and speech centers of the cortex. The great musician Bach had an exceptionally well developed parietal region.

On the Cortical Centers in General. For purposes of clearness in presentation, the cortical centers have been discussed one by one, but the reader is guarded against the thought that their activities are in any sense isolated. A motor area does not usually act in the absence of sensory or afferent stimulation in the actual living body, whether it may do so on occasion or not. Neither do sensory impressions arising in the peripheral sense organ make their way over definite tracts to the brain and cortex and arouse sensations alone. Sensations do not occur independent of motor activities on the one hand, and of intellectual acts through the association centers on the other.

The association centers are the highest coordinating regions of the nervous system. They are to the sensory and motor centers what these latter are to the reflex centers of the cord, the difference being one of degree and not of kind. Further, they are probably set into activity by the complex of inflowing or afferent impulses in just the same sense that the spinal reflex centers are set in activity by sensory or afferent stimuli; the condition is, of course, a thousand times more complex.

THE PHYSIOLOGY OF SLEEP.

All parts of the body which are the seat of active change require periods of rest. The alternation of work and rest is a necessary condition of their maintenance and of the healthy performance of their functions. These alternating periods, however, differ much in duration in different cases; but, for any individual instance, they preserve a general and rather close uniformity. Thus, the periods of rest and work mentioned, in the case of the heart, occupy, each of them, about half a second; in the case of the ordinary respiratory muscles the periods are about four or five times as long. In many cases (as of the voluntary muscles during violent exercise), while the periods during active exertion alternate very frequently, yet the expenditure goes far ahead of the repair, and, to compensate for this, an after-repose of some hours becomes necessary, the rhythm being less perfect as to *time* than in the case of the muscles concerned in circulation and respiration.

Obviously, it would be impossible that, in the case of the brain, there should be short periods of activity and repose, or, in other words, of consciousness and unconsciousness. The repose must occur at long intervals and must be proportionately long. Hence the necessity for that condition which we call *Sleep;* a condition which, seeming at first sight exceptional, is only an unusually perfect example of what occurs, at varying intervals, in every actively working portion of our bodies.

By exposing, at a circumscribed spot, the surface of the brain of a living animal, and protecting the exposed part by a watch-glass, Durham was able to prove that the brain becomes visibly paler, anemic, during sleep; and the anemia of the optic disc during sleep, observed by Hughlings Jackson, may be taken as a strong confirmation, by analogy, of the same fact.

The Circulation During Sleep. Blood is supplied to the brain in four distinct but anastomosing arteries. This efficient anatomical arrangement is obviously all the more important when it is remembered that the circulation in the brain has no local device for regulating the blood-flow, but that it must depend on the variations in general blood pressure. Any variation in the flow of blood in the brain depends on changes in general blood pressure; changes which are themselves dependent on variations in the activity of the heart, the caliber of the blood-vessels, etc., discussed on page 186.

Howell and others have studied the circulation by the plethysmographic method during sleep. The results show that with the loss of consciousness, and immediately following, there is a sharp dilatation of the blood-vessels of the arm, probably chiefly of the skin, as shown by the increase in volume. The vessels remain dilated until the individual begins to awaken, when there is a rapid constriction with decrease of volume of the organ.

The dilatation of the general blood-vessels draws off the supply of blood from the brain, and the resulting partial anemia contributes to loss of consciousness. The blood supply is ample for growth and repair and rest of the nervous system. How efficient this rest period is for the rejuvenation of the nervous tissue is indicated even by the relatively gross means, figure 356, shown in the histological preparations of nerve cells.

Somnambulism and Dreams. What we term *sleep* occurs often in very different degrees in different parts of the nervous system; and in some parts the expression cannot be used in the ordinary sense.

The phenomena of *dreams* and *somnambulism* are examples of differing degrees of sleep in different parts of the cerebro-spinal nervous system. In the former case the cerebrum is still partially active; but the activity is no longer corrected by the reception, on the part of the sleeping *sensorium*, of impressions of objects belonging to the outer world; neither can the cerebrum, in this half-awake condition, act on the centers of reflex action of the voluntary muscles, so as to cause the latter to contract—a fact within the painful experience of all who have suffered from nightmare.

In somnambulism the higher centers are capable of coordinating that train of reflex nervous action which is necessary for progression, while the nerve center of the *muscular equilibrium sense* (in the cerebellum?) is, presumably, fully awake; but the *sensorium* is still asleep, and impressions made on it are not sufficiently *felt* to rouse the cerebrum to a comparison of the difference between mere ideas or memories and sensations derived from external objects.

VI. THE SYMPATHETIC SYSTEM.

The fact has already been emphasized that the sympathetic system of nerves is an organic and constituent part of the nervous system.

Organization and Distribution. The sympathetic system consists of those collections of nerve cells or ganglia lying outside of the brain and cord (exclusive of the root ganglia), and the nerve tracts connecting them with one another and with the cerebro-spinal axis. Its parts that should be mentioned are: 1, a double chain of ganglia and fibers, which extends from the cranium to the pelvis, along each side of and in front of the vertebral column, and from which branches are distributed both to the cerebro-spinal system and to other parts of the sympathetic system. With these may be included the small ganglia in connection with those branches of the fifth cerebral nerve which are distributed in the neighborhood of the organs of special sense, namely, the *ophthalmic*, *otic*, *spheno-palatine*, and *submaxillary* ganglia. 2, Various ganglia and plexuses of nerve fibers which give off branches to the thoracic and abdominal viscera, the chief of such plexuses being the *cardiac*,

solar, and *hypogastric;* but in intimate connection with these are many secondary plexuses, as the *aortic*, *spermatic*, and *renal*. Fibers pass from the prevertebral chain of ganglia and from the cerebro-spinal nerves to these plexuses. 3, Various ganglia and plexuses in the substance of many of the viscera, as in the stomach, intestines, and urinary bladder. These, which

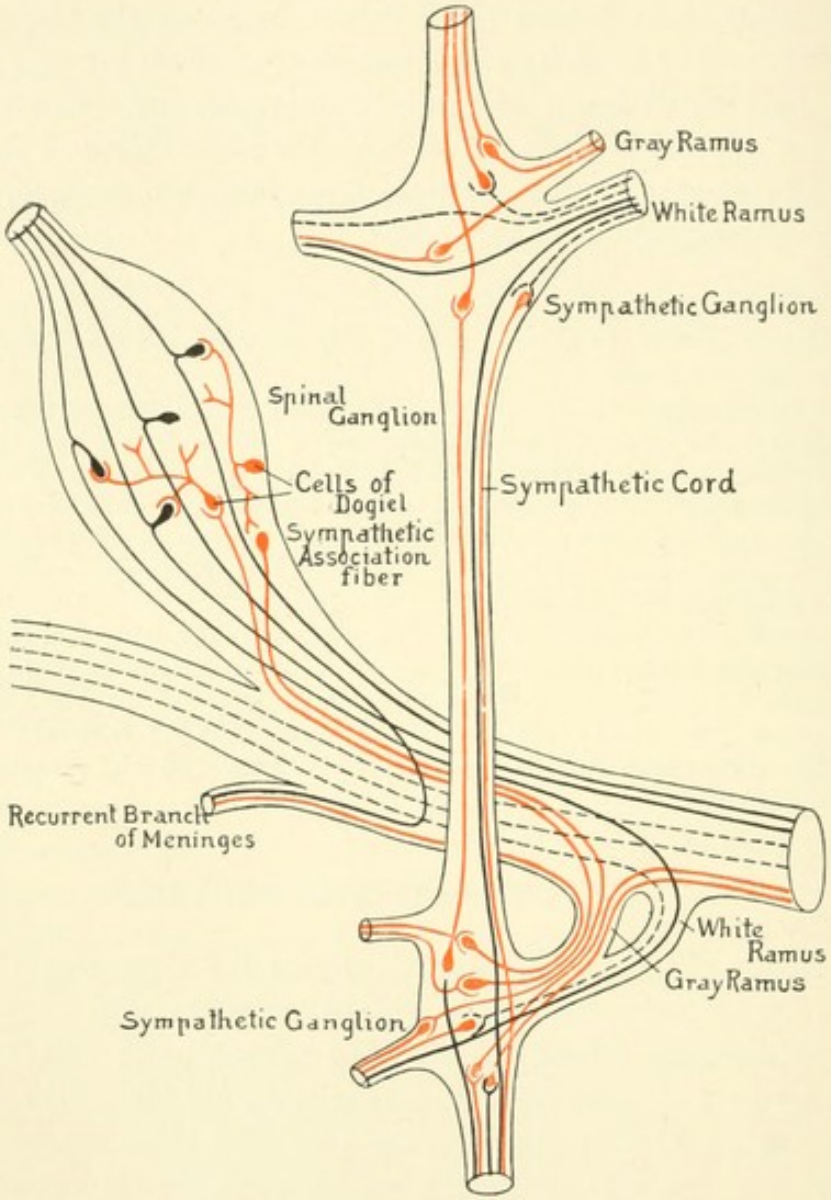


FIG. 418.—Schematic Representation of the Relation of the Constituents of the Sympathetic Chain and the Spinal Nerve. (Modified from Hardesty, in Morris' Anatomy.)

are for the most part microscopic, also freely communicate with other parts of the system, as well as with the cerebro-spinal axis.

The connections between these parts are as follows: 1, The visceral branch or *white ramus*, of certain spinal nerves, which passes into the lateral chain. 2, The *gray rami* consist of bundles of fibers, usually non-medullated, which pass from the chain ganglia back into the spinal or cranial nerves, the

fibers of which they accompany to the periphery. 3, From this chain the *rami efferentes* pass into the collateral ganglia, and from these again other branches pass off into the organs, to end in the terminal ganglia.

The white rami are absent in all the spinal nerves in the regions above the second (occasionally the first) thoracic nerve root, and below the second

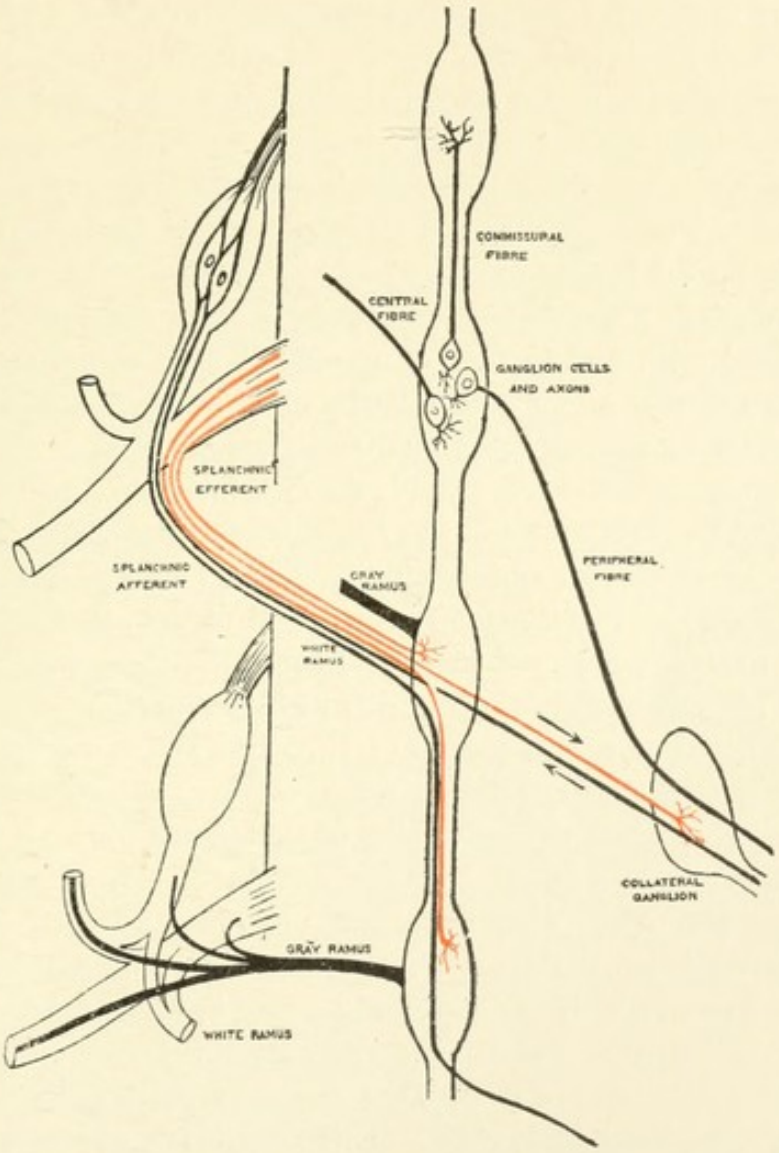


FIG. 419.—Scheme of the Constitution and Connections of Gangliated Cord of the Sympathetic. The gangliated cord is indicated on the right, with the arrangement of the fibers arising from ganglion cells. On the left, the roots and trunks of the spinal nerves are shown, with the arrangement of the white ramus communicans above and the gray ramus below. The cells of origin in the ventral cord of the fibers constituting the white ramus are not shown. (Cunningham.)

lumbar nerve root, with the occasional exception of the roots of the third and fourth lumbar nerves. This is a rather restricted field of origin for the preganglionic fibers which compose the white rami. These fibers end in adjacent ganglia of the chain, or pass to higher or lower levels or to more peripheral ganglia.

A peculiarity in the structure of these white medullated visceral nerves is the

fineness of their fibers. They are a third or a fourth of the diameter of ordinary medullated fibers, measuring 1.8 μ to 2.7 μ instead of 14 μ to 19 μ. Such fibers are a peculiarity of the spinal nerve roots chiefly in the thoracic region, but also found in the second and third sacral nerves, and constitute there the *nervi erigentes* which pass directly to the hypogastric plexus. From the hypogastric plexus branches pass upward into the inferior mesenteric ganglia and downward to the bladder, rectum, and generative organs. These nerves, called by Gaskell *pelvic splanchnic* nerves, differ from the rami viscerales of the thoracic region only in not communicating with the lateral ganglia; the branches which pass upward from the thoracic region to the neck, he calls *cervical splanchnics*, and the splanchnics proper *abdominal splanchnics*.

Functions. The researches of Gaskell and of Langley have done much to clear up the former confusion as to the distribution and functions of the sympathetic. The sympathetic nerve fibers are distributed to smooth muscle, to gland cells, and to cardiac muscle. These are all organs which carry on their activities either automatically or reflexly. There is no voluntary control of the function of these organs.

The efferent sympathetic fibers supply the muscles of the vascular system, to which they send the vaso-motor fibers, *i.e.*, vaso-constrictor and cardiac augmentor or accelerator; and vaso-inhibitory fibers, *i.e.*, vaso-dilators. They supply the muscles of the alimentary canal and of the urinogenital system. The details of arrangement and functional control of these complex systems have already been discussed in connection with the function of the organ or part concerned. They supply the salivary, gastric, and pancreatic glands.

According to Gaskell the functions of the main sympathetic ganglia are the following: 1, They effect the conversion of medullated into non-medullated fibers. 2, They possess a nutritive influence over the nerves which pass from them to the periphery. 3, They increase the number of fibers.

The sympathetic ganglia are not nerve centers in the usual sense. It is better to regard them merely as distributing organs in which reflexes of central origin and comparatively simple type are distributed over relatively large areas. These ganglia do not possess the power of reflex function. A type of pseudo-reflex has been described depending on the law of neurone reaction. But it is not supposed that such reflexes occur in the normal animal.

Afferent or sensory fibers of the ordinary spinal-root ganglion cells are present in the sympathetic nerves of the splanchnic region, being distributed merely to the visceral region. True afferent sympathetic fibers have been demonstrated. These arise from cells located in the sympathetic ganglia, and pass through the rami communicantes, to end by terminal arborizations in the spinal ganglia, chiefly around cells of the Dogiel type. The number and significance of these afferent neurones are yet uncertain.

CHAPTER XV

THE SENSES

THROUGH the medium of the nervous system man obtains a knowledge of the existence both of the various parts of his body and of the external world. This knowledge is based upon *sensations* resulting from the stimulation of certain centers in the brain by nerve impulses conveyed to them by afferent nerves. Under normal circumstances the following structures are necessary for sensation: *a*, A peripheral organ for the reception of the impression; *b*, a nerve for conducting it; *c*, a nerve center for feeling or perceiving it.

Sensations may be conveniently classed as, 1, common, and 2, special sensations.

Common Sensations. Under this head fall all those general sensations which cannot be distinctly localized in any particular part of the body, such as *fatigue*, *discomfort*, *faintness*, *satiety*, *nausea*, together with *hunger* and *thirst*, in which, in addition to a general discomfort, there is in many persons a distinct sensation referred to the stomach or fauces. In this class must also be placed the various stimulations of the mucous membrane of the bronchi, which give rise to coughing, and also the sensations derived from various viscera, such as the desire to defecate, to urinate, and in the female the sensations which precede the expulsion of the fetus. It is impossible to draw a very clear line of demarcation between many of the common sensations above mentioned and the sense of touch, which forms the connecting link between the general and special sensations. Touch is classed with the special senses, and will be considered in the same group with them; yet it differs from them in its wide distribution over the body. Among common sensations some would rank the *muscle sense*, which has been already alluded to. It is by means of this sense that we become aware of the condition of the muscles, and thus obtain the information necessary for their adjustment to various purposes—standing, walking, grasping, etc. This muscular sensibility is shown in our power to estimate the differences between weights by the different muscular efforts necessary to raise them. It must be carefully distinguished from the sense of contact and of pressure, of which the skin is the organ. When standing erect, we can feel the ground contact, and there is a sense of pressure, due to our feet being pressed against the ground by the weight of the body. Both these are derived from the skin of the sole of the foot. If now we raise the body on the toes, we are con-

scious, through the muscular sense, of a muscular effort made by the muscles of the calf. But the muscle sense will be discussed further, page 603.

Special Sensations. The special senses include Touch, Temperature (Heat and Cold), Taste, Smell, Hearing, Sight.

The most important distinction between common and special sensations is that by the former we are made aware of certain conditions of various parts of our bodies, while from the latter is gained a knowledge of the external world. This difference will be clear if we compare the sensations of pain and touch, the former of which is a common, the latter a special, sensation. "If we place the edge of a sharp knife on the skin, we feel the edge by means of our sense of touch; we perceive a sensation, and refer it to the object which has caused it. But as soon as we cut the skin with the knife, we feel pain, a feeling which we no longer refer to the cutting knife, but which we feel within ourselves, and which communicates to us the fact of a change of condition in our own body. By the sensation of pain we are neither able to recognize the object which caused it nor its nature."

It is important in studying the phenomena of sensation clearly to understand that the *sensorium*, or seat of sensation, is in the brain, and not in the particular organ through which the sensory impression is received. In common parlance we are said to see with the eye, hear with the ear, etc., but in reality these organs are only adapted to receive stimuli which produce changes that are, through their respective nerves, conducted to the sensorium, to give rise to sensation.

Hence, if the optic nerve is severed, vision is no longer possible. Although the image falls on the retina as before, the sensory impulse can no longer be conveyed to the sensorium. When any given sensation is felt, all that we can with certainty affirm is that some part of the brain is excited. The exciting cause may be some object of the external world, producing an *objective sensation;* or the condition of the sensorium may be due to some excitement within the brain itself, in which case the sensation is termed *subjective*. The mind habitually refers sensations to external causes; and hence, whenever they are subjective we can hardly divest ourselves of the idea of an external cause, and an illusion is the result.

Sensory Illusions. Numberless examples of such illusions might be quoted. As familiar cases may be mentioned, humming and buzzing in the ears caused by some irritation of the auditory nerve or center. These stimuli may even be interpreted as musical sounds, or voices, sometimes termed auditory spectra. So-called optical illusions in which objects are described as seen, although not present, may be caused by changes going on in some part of the visual apparatus beyond the eye. Such illusions are most strikingly exemplified in cases of delirium tremens or other forms of delirium, and may take the form of animals such as cats, rats, or creeping loathsome forms, etc.

One uniform *internal* cause, which may act on all the nerves of the senses in the same manner, is capillary congestion. This one cause excites in the retina, while the eyes are closed, the sensations of light and luminous flashes; in the auditory nerve, the sensation of humming and ringing sounds; in the olfactory nerve, the sense of odors; and in the nerves of feeling, the sensation of pain. In the same way a chemical substance introduced into the blood may excite in the nerves of each sense peculiar symptoms: In the optic nerves, the appearance of luminous sparks before the eyes; in the auditory nerves, *tinnitus aurium;* and in the common sensory nerves, the sensations of creeping over the surface. So, also, among *external* causes, the stimulus of electricity, or the mechanical influence of a blow, concussion, or pressure, excites in the eye the sensation of light and colors; in the ear, a sense of a loud sound or of ringing; and in the tongue, a saline or acid taste.

Sense Perceptions. The habit of constantly referring our sensations to external causes leads us to interpret the various modifications which external objects produce in our sensations, as *properties* of the external bodies themselves. Thus we speak of certain substances as possessing a disagreeable taste and smell; whereas, the fact is their taste and smell are only disagreeable to *us*. It is evident, however, that on this habit of referring our sensations to causes outside ourselves, perception, depends the reality of the external world to us; and more especially is this the case with the senses of touch and sight. By the cooperation of these two senses, aided by the others, we are enabled gradually to attain a knowledge of external objects which daily experience confirms, until we come to place unbounded confidence in what is termed the evidence of the senses.

We must draw a distinction between mere sensations, and the judgments based, often unconsciously, upon them. Thus, in looking at a near object, we unconsciously estimate its distance and say it seems to be ten or twelve feet off. But the estimate of its distance is in reality a judgment based on many things besides the appearance of the object itself; among which may be mentioned the number of intervening objects, the number of steps which from past experience we know we must take before we could touch it, and many others.

I. THE SENSES OF TOUCH, PAIN, TEMPERATURE, AND THE MUSCLE SENSE.

The Sense of Touch. The sense of touch, like all the special senses, possesses a special end-organ for the initiation of a nerve impulse through contact with external objects. The sense organ of touch is not confined to particular parts of the body of small extent, like the organ of sight, for example, but is found in all parts of the skin and its inversions, the stomodeum and proctodeum. The nerves of sensation are contained in the same

trunks with other sensory nerves. They are found in the posterior or sensory roots of the spinal nerves and in the sensory divisions of the cranial nerves, especially the fifth, seventh, ninth, and tenth.

All parts of the epidermis supplied with sensory nerves are thus, in some degree, organs of touch, yet the sense is exercised in greatest perfection in certain parts, the sensibility of which is extremely delicate, *e.g.*, the skin of the hands, the tongue, and the lips, which are provided with abundant touch papillæ. A peculiar and very acute sense of touch is exercised through the medium of the nails and teeth, and, to a less extent, the hair may be considered an organ of touch, as in the case of the eyelashes.

The sense of touch renders us conscious of the presence of a contact stimulus, from the slightest to the most intense degree of its action. The

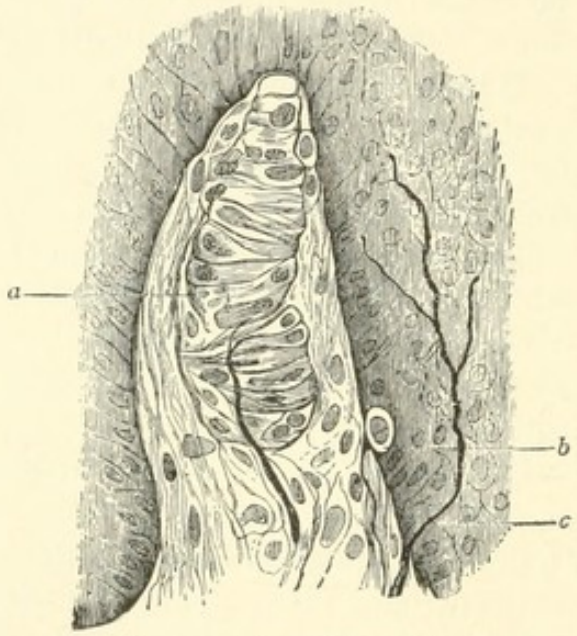


FIG. 420.—Touch Corpuscle.

modifications of this sense often depend on the extent of the parts affected. The sensation of pricking, for example, is produced when the sensitive fibers are intensely affected in a small extent; the sensation of pressure indicates a slighter affection of the parts over a greater extent and depth. It is by the depth to which the parts are affected that the feeling of pressure is distinguished from that of mere contact.

In almost all parts of the body which have delicate tactile sensibility the epidermis, immediately over the dermal papillæ, is moderately thin. When its thickness is much increased, as over the heel, the sense of touch is very much dulled. On the other hand, when it is altogether removed, and the cutis laid bare, the sensation of contact is replaced by one of pain. Further, in all highly sensitive parts, the papillæ are numerous and highly vascular, and the sensory nerves are connected with special *end-organs* which have been described on page 72 *et seq.*

The special endings of the nerves which have to do with touch may, however, be here again mentioned. They are of two kinds, viz., 1, *Touch corpuscles*, which are found chiefly in the hands and feet, particularly on the palmar surface of the hands and fingers, but also on the under surface of the forearm, on the nipple, eyelids, lips, and the genital organs. Touch corpuscles are situated in the cutis vera. 2, *End bulbs* are found in the conjunctiva and other mucous membranes, the lips, genital organs, tongue, rectum, and elsewhere, but not in the skin proper. As regards the Pacinian corpuscles and similar end-organs, which are so widely distributed, and which may be in some way connected with the sensation, when they are found in the skin they are situated very deeply in the cutis vera or in the subcutaneous tissue. They are extremely numerous on the nerves of the palmar surface of the fingers. In addition to these special nerve endings, nerve fibers terminate everywhere in the skin between the cells of the Malpighian stratum of the epidermis.

The acuteness of the sense of touch depends very largely on the cutaneous circulation, which is of course greatly influenced by external temperature. Hence the numbness, familiar to every one, produced by the application of cold to the skin.

Acuteness of the Sense. The perfection of the sense of touch on different parts of the surface is proportioned to the minimal pressure required to stimulate the point, *i.e.*, the threshold stimulus. Or it can be measured by the power which such parts possess of distinguishing and isolating the sensations produced by two points placed close together. This latter is a measure of the power of localization in a degree. This power depends, at least in part, on the number of primitive nerve fibers; for the fewer the primitive fibers which an organ receives, the more likely is it that several impressions on different contiguous points will act on only one nervous fiber, and hence be confounded, and perhaps produce but one sensation. Experiments have been made to determine the tactile properties of different parts of the skin, as measured by this power of distinguishing distances between points of simultaneous contact. These consist in touching the skin with the points of a pair of compasses sheathed with cork, and in ascertaining how close the points of the compasses might be brought to each other and still be felt as two bodies.

TABLE OF VARIATIONS IN THE TACTILE SENSIBILITY OF THE DIFFERENT PARTS OF THE SKIN.

The measurement indicates the least distance at which the two blunted points of a pair of compasses could be separately distinguished. (E. H. Weber.)

Tip of tongue,	1 mm.
Palmar surface of third phalanx of forefinger,	2 "
Palmar surface of second phalanges of fingers,	4 "
Red surface of under-lip,	4 "
Tip of nose,	6 "
Middle of dorsum of tongue,	8 "

Palm of hand,	10 mm.
Center of hard palate,	12 "
Dorsal surface of first phalanges of fingers,	14 "
Back of hand,	25 "
Dorsum of foot near toes,	37 "
Gluteal region,	37 "
Sacral region,	37 "
Upper and lower parts of forearm,	37 "
Back of neck near occiput,	50 "
Upper dorsal and mid-lumbar regions,	50 "
Middle part of forearm,	62 "
Middle of thigh,	62 "
Mid-cervical region,	62 "
Mid-dorsal region,	62 "

In the case of the limbs, before the points are recognized as two, they have to be further separated when the line joining them is in the long axis of the limb than when in the transverse direction.

According to Weber the mind estimates the distance between two points by the number of unexcited nerve endings which intervene between the two points touched. It would appear that a certain number of intervening unexcited nerve endings is necessary before two points touched can be recognized as separate, and the greater this number the more clearly are the points of contact distinguished as separate. The delicacy of the sense of touch may be very much increased by practice. A familiar illustration occurs in the case of the blind, who, by constant practice, can acquire the power of reading raised letters the forms of which are almost, if not quite, undistinguishable by the sense of touch to an ordinary person.

The different degrees of sensitiveness possessed by different parts may give rise to errors of judgment in estimating the distance between two points where the skin is touched. Thus, if blunted points of a pair of compasses (maintained at a constant distance apart) be slowly drawn over the skin of the cheek toward the lips, it is almost impossible to resist the conclusion that the distance between the points is gradually increasing. When they reach the lips they seem to be considerably farther apart than on the cheek. Thus, too, our estimate of the size of a cavity in a tooth is usually exaggerated when based upon sensations derived from the tongue alone. Another curious illusion may here be mentioned. If we close the eyes, and place a small marble or pea between the crossed fore and middle fingers, we seem to be touching two marbles, figure 480. This illusion is due to an error of judgment. The marble is touched by two surfaces which, under ordinary circumstances, could be touched only by two separate marbles, hence the mind, taking no cognizance of the fact that the fingers are crossed, forms the conclusion that two sensations are due to two marbles.

Sense of Temperature. The whole surface of the body is more or less sensitive to differences of temperature. The sensation of heat is distinct

from that of touch, hence it would seem reasonable to suppose that there are special nerves and nerve endings for temperature. At any rate the power of discriminating temperature may remain unimpaired when the sense of touch is temporarily in abeyance. Thus if the ulnar nerve be compressed at the elbow till the sense of touch is very much dulled in the fingers which it supplies, the sense of temperature remains quite unaffected. And in certain diseases of the cord the sense of touch may be impaired in a part, and temperature remain undisturbed, or the converse.

The mapping of the surface of a part of the skin with reference to its sensibility to temperature reveals the fact that there are definite *heat* and

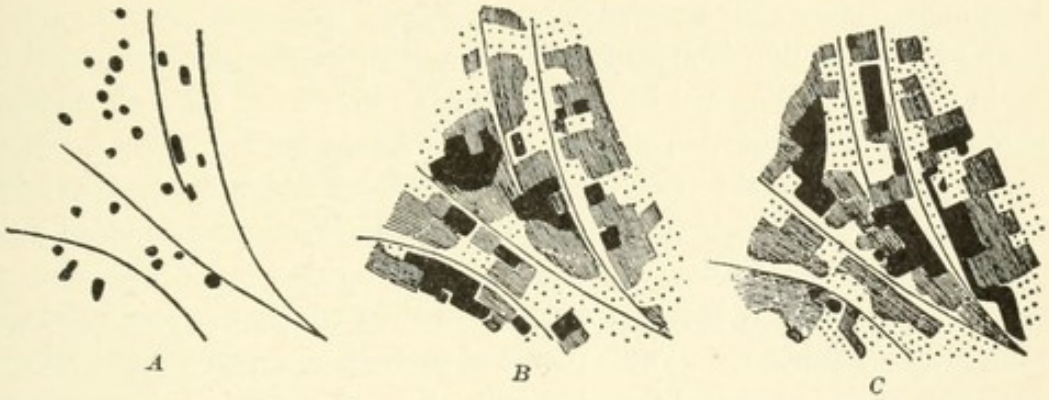


FIG. 421.—Diagram of a Part of the Hand, Showing Distribution of Sense Spots: for touch, *A*; for heat, *B*; and for cold, *C*. In *A* the skin is sensitive except at the parts marked with black; in *B* and *C*, the intensity of the shading represents the relative sensitiveness. (Goldscheider.)

cold spots. Furthermore, the areas do not coincide, leading us to conclude that there are two distinct sense organs concerned, figure 421, *B* and *C*.

The sensations of heat and cold are often exceedingly fallacious, and in many cases are no guide at all to the absolute temperature as indicated by a thermometer. All that we can with safety infer from our sensations of temperature is that a given object is warmer or cooler than the skin. Thus the temperature of our skin is the standard; and as this varies from hour to hour according to the activity of the cutaneous circulation, our estimate of the absolute temperature of any body must necessarily vary too. If we put the left hand into water at 5° C. (40° F.) and the right into water at 45° C. (110° F.), and then immerse both in water at 27° C. (80° F.), it will feel warm to the left hand, but cool to the right. Again, a piece of metal which has really the same temperature as a given piece of wood will feel much colder, since it conducts away the heat much more rapidly. For the same reason air in motion feels very much cooler than air of the same temperature at rest.

In some cases we are able to form a fairly accurate estimate of absolute temperature. Thus, by plunging the elbow into a bath, a practised bath-attendant can tell the temperature sometimes within half a degree centigrade.

The temperatures which can be readily discriminated are between 10° and

45° C. (50° and 115° F.); very low and very high temperatures alike produce a burning sensation. A temperature appears higher according to the extent of cutaneous surface exposed to it. Thus, water of a temperature which can be readily borne by the hand is quite intolerable if the whole body be immersed.

The delicacy of the sense of temperature coincides in the main with that of touch, and appears to depend largely on the thickness of the skin; hence, in the elbow, where the skin is thin, the sense of temperature is delicate, though that of touch is not remarkably so. Weber has further ascertained the following facts: two points so near together on the skin that they produce but a single impression, at once give rise to *two* sensations, when one is hotter than the other. Moreover, of two bodies of equal weight, that which is the colder feels heavier than the other.

As every sensation is attended with a perception and leaves behind it an idea in the mind which can be reproduced at will, we are enabled to compare the idea of a past sensation with another sensation really present. Thus we can compare the weight of one body with another which we had previously felt, of which the idea is retained in our mind. Weber was indeed able to distinguish in this manner between temperatures experienced one after the other, better than between temperatures to which the two hands were simultaneously subjected. This power of comparing present with past sensations diminishes, however, in proportion to the time which has elapsed between them. *After-sensations* left by impressions on nerves of common sensibility or touch are very vivid and durable. As long as the condition into which the stimulus has thrown the organ endures, the sensation also remains, though the exciting cause should have long ceased to act. Both painful and pleasurable sensations afford many examples of this fact.

Sense of Pain. As regards painful sensations, three views can be taken: 1, That it is a special sensation provided with a special conducting apparatus in each part of the body; 2, that it is produced by an over-stimulation of the special nerves concerned with touch or temperature, or of the other nerves of special sense; or 3, that it is an over-stimulation of the nerves of common sensation, which tell us of the condition of our own bodies, both of the surface and also of the internal organs. There seems to be much in favor of all of these views. The weight of evidence is, however, rather against there being any special pain sense with a special end-organ and fibers, though Barker in his own arm experienced the presence of pain sensations while there was absence of sensations of touch and temperature. It is, indeed, certain that, even if any variety of pain be a special sensation, some kind of pain may be produced by stimulation of the bare sensory nerves apart from any special form of nerve termination. It is said that the main difference between the common sensory apparatus which tells us of the condition of all parts of the body of which thirst and hunger are but examples, and the special sense of touch and temperature, is that the latter are provided with

a special local apparatus. By means of this apparatus we are able to localize the sensation. Such a special apparatus is evidently not absolutely essential for the sensation of pain, but this does not exclude the idea that pain may result from over-stimulation of a nerve of special sense or of its termination.

The Muscular Sense. The estimate of a weight is usually based on *two* sensations: 1, of pressure on the skin, and 2, the sense of muscular resistance.

The estimate of weight derived from a combination of these two sensations (as in lifting a weight) is more accurate than that derived from the former alone (as when a weight is laid on the hand); thus Weber found that by the former method he could generally distinguish 19½ oz. from 20 oz., but not 19¾ oz. from 20, while by the latter he could at most distinguish only 14½ oz. from 15 oz.

It is not the absolute, but the relative, amount of the difference of weight which we have thus the faculty of perceiving.

It is not, however, certain, that our idea of the amount of muscular force used is derived solely from the muscular sense. We have the power of estimating very accurately beforehand, and of regulating, the amount of nervous influence necessary for the production of a certain degree of movement. When we lift a vessel, with the contents of which we are not acquainted, the force we employ is determined by the idea we have conceived of its weight. If it should happen to contain some very heavy substance, as quicksilver, we shall probably fail in the attempt; the amount of muscular action, or of nervous energy, which we had exerted being insufficient. It is possible that in the same way the idea of weight and pressure in raising bodies, or in resisting forces, may in part arise from a consciousness of the amount of nervous energy transmitted from the brain rather than from a sensation in the muscles themselves. The mental conviction of the inability longer to support a weight must also be distinguished from the actual sensation of fatigue in the muscles.

So, with regard to the ideas derived from sensations of touch combined with movements, it is doubtful how far the consciousness of the extent of muscular movement is obtained from sensations in the muscles themselves. The sensation of movement attending the motions of the hand is very slight; and persons who do not know that the action of particular muscles is necessary for the production of given movements, do not suspect that the movement of the fingers, for example, depends on an action in the forearm. The mind has, nevertheless, a very definite knowledge of the changes of position produced by movements; and it is on this that the ideas which it conceives of the extension and form of a body are in great measure founded.

There is no marked development of common sensibility to be made out in muscles: they may be cut without the production of pain. On the other hand, there is no doubt that afferent impulses must pass upward from muscles

and tendons acquainting the brain with their condition. This, then, must be a special sense. It has been suggested that the minute end-bulbs of Golgi found in tendons, and that the Pacinian corpuscles in the neighborhood of joints, are the terminal organs of this special sense.

Judgment of the Form and Size of Bodies. By the sense of touch the mind is made acquainted with the size, form, and other external characters of bodies. And in order that these characters may be easily ascertained, the sense of touch is especially developed in those parts which can be readily moved over the surface of bodies. Touch, in its more limited sense, or the act of examining a body by the touch, consists merely in a voluntary employment of this sense combined with movement, and stands in the same relation to the sense of touch, or common sensibility, generally, as the act of seeking, following, or examining odors does to the sense of smell. The hand is the best adapted for it, by reason of its peculiarities of structure—namely, its capability of pronation and supination, which enables it, by the movement of rotation, to examine the whole circumference of a body; the power it possesses of opposing the thumb to the rest of the hand, and the relative mobility of the fingers; and lastly from the abundance of the sensory terminal organs which it possesses. In forming a conception of the figure and extent of a surface, the mind multiplies the size of the hand or fingers used in the inquiry by the number of times which it is contained in the surface traversed; and, by repeating this process with regard to the different dimensions of a solid body, acquires a notion of its cubical extent, but, of course, only an imperfect notion, as other senses, *e.g.*, the sight, are required to make it complete.

It is impossible in this consideration to say how much of our knowledge of the thing touched depends upon pressure and how much upon the muscular sense.

II. TASTE AND SMELL.

The special sense organs for taste and smell are stimulated by chemical substances, the former by chemicals in solution, the latter by volatile materials. They are also closely associated in action and we do not always differentiate between the two.

THE SENSE OF TASTE.

The conditions for the perceptions of taste are: 1, the presence of a sense organ, a nerve, and a nerve center with special endowments; 2, the excitation of the sense organ by the sapid matters, which for this purpose must be *in a state of solution;* 3, a temperature of about 37° to 40° C. (98° to 100° F.).

The Nerves and Organs of Taste. The principal organ of the sense of taste is the tongue. But the soft palate and its arches, the uvula, tonsils,

and probably the upper part of the pharynx, are also endowed with taste. These parts, together with the base and posterior parts of the tongue, are supplied with branches of the glosso-pharyngeal nerve, and evidence has been already adduced that this is the principal nerve of the sense of taste. The anterior parts of the tongue, especially the edges and tip, are innervated

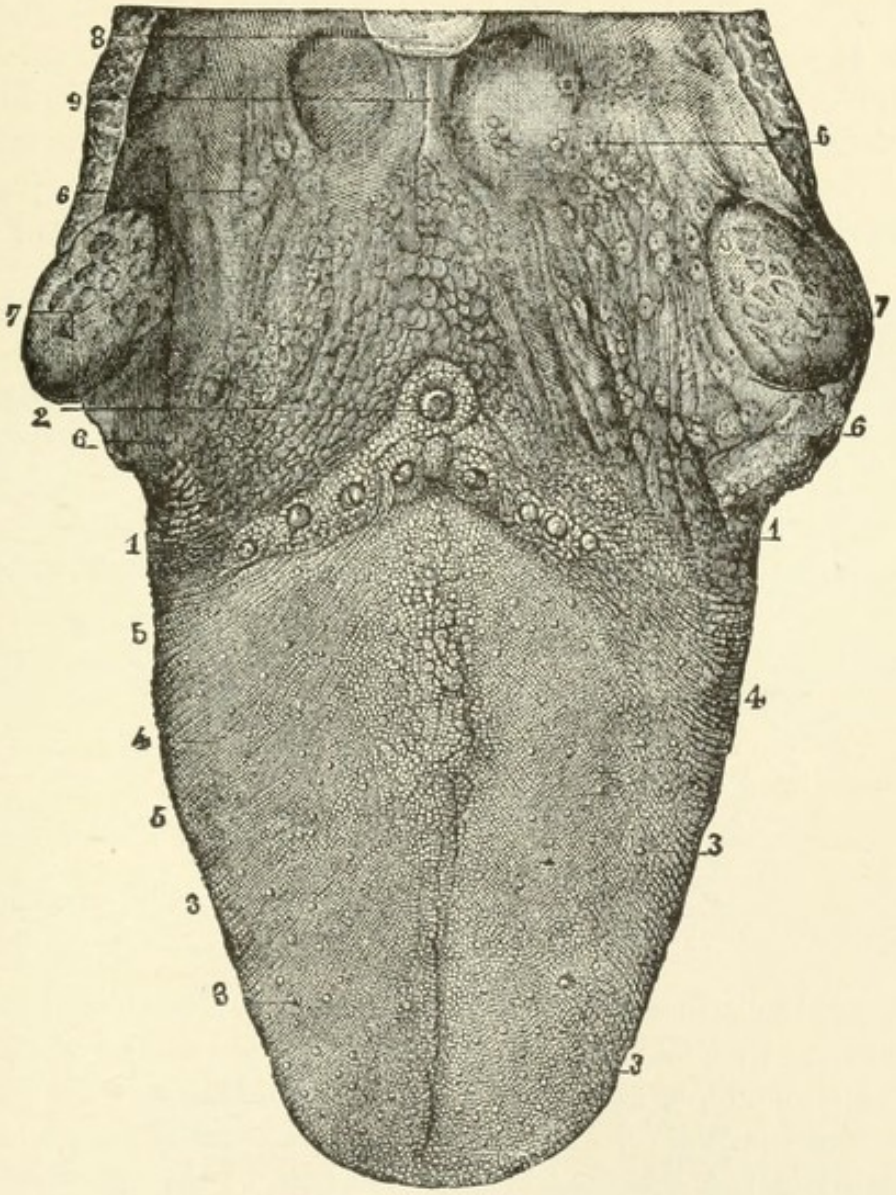


FIG. 422.—Papillar Surface of the Tongue, with the Fauces and Tonsils. 1, Circumvallate papillæ, in front of 2, the foramen cecum; 3, fungiform papillæ; 4, filiform and conical papillæ; 5, transverse and oblique rugæ; 6, mucous glands at the base of the tongue and in the fauces; 7, tonsils; 8, part of the epiglottis; 9, median glosso-epiglottidean fold (frenum epiglottidis). (From Sappey.)

by fibers from the lingual branch of the fifth, but which arise in the ganglion of the pars intermedia and are distributed in the chorda tympani, figures 387 and 388.

The mucous membrane in the regions just mentioned possesses special epithelial structures called taste buds. The taste buds are very abundant

in the side walls of the circumvallate papillæ. They are also present in the fungiform papillæ, in the foliate papillæ, and in the mucous membrane. The taste bud is located at the deeper part of the stratified epithelium, is ovoid in shape, and its free end abuts on the surface or opens to the surface by a short canal. It is composed of two kinds of modified epithelial cells—the supporting cells, which are long, spindle-shaped cells that form a sheath around the special gustatory cells; and the taste cells, which are neuro-epithelial cells that are found in the center of the taste bud. They are very slender cells that project on the surface by a delicate process. A bundle of nerve fibrils enters the base of each taste bud and forms a net about the taste cells.

The *circumvallate*, the *fungiform*, and the *filiform* papillæ, shown in figure 422, are special structures that facilitate the stimulation of the taste

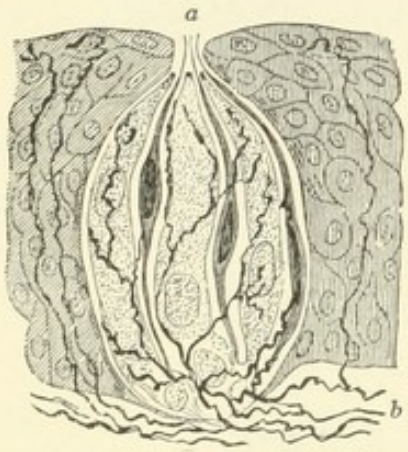


FIG. 423.

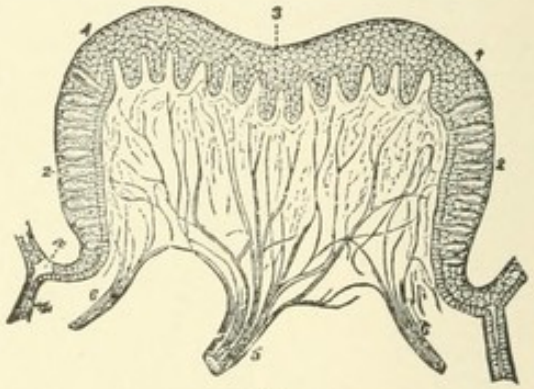


FIG. 424.

FIG. 423.—Taste-Bud from Side Wall of Circumvallate Papillæ. (Merkel-Henle.) *a*, Taste-pore; *b*, nerve fibers, some of which enter the taste bud, intrageminal fibers, while others end freely in the surrounding epithelium, intergeminal fibers.

FIG. 424.—Vertical Section of a Circumvallate Papilla of the Calf. 1 and 3, Epithelial layers covering it; 2, taste goblets; 4, and 4′, duct of serous gland opening out into the pit in which the papilla is situated; 5 and 6, nerves ramifying within the papilla. (Engelmann.)

buds by sapid substances. They are all formed by a projection of the mucous membrane, and contain special branches of blood-vessels and nerves. In details of structure, however, they differ considerably one from another.

Circumvallate Papillæ. These papillæ, figure 424, eight or ten in number, are situated in two V-shaped lines on the base of the tongue. They are circular elevations from 1 to 2 mm. in diameter each, with a central depression, and surrounded by a circular fissure, at the outside of which is a slightly elevated ring. Both the central elevation and the ring are formed of close set simple papillæ.

Fungiform Papillæ. The fungiform papillæ are scattered chiefly over the sides and tip, and sparingly over the middle of the dorsum, of the tongue; the name is deri ed from their being usually narrower at the base than at the summit. They also are supplied with loops of capillary blood-vessels, and nerve fibers.

Conical or Filiform Papillæ. These, which are the most abundant papillæ, are scattered over the whole surface of the tongue, but especially over the middle of the dorsum. They vary in shape somewhat, but for the most part are conical.

Taste Sensations. The occurrence of two kinds of special sensibility, *i.e.*, touch and taste in the same part, makes it sometimes difficult to determine whether the impression produced by a substance is perceived through the ordinary tactile sensitive fibers, or through those of the sense of taste. In many cases, indeed, it is probable that both sets of nerve fibers are concerned, as when irritating acrid substances are introduced into the mouth.

Many of the so-called tastes are due to the sapid substances being also odorous, and exciting the simultaneous action of the sense of smell. This is shown by the insipid tastes of certain substances when their action on the olfactory nerves is prevented by closing the nostrils. Many of the popular drinks lose much of their apparent excellence if the nostrils are held close while they are drunk.

When these accessory sensations are taken into account it is found that the clearly defined tastes are reduced to four: *sweet*, *bitter*, *acid*, and *salt*. These taste sensations are produced by the respective substances when in solution. If dry salt or quinine is placed on the surface of the tongue, no taste appears until solution takes place in the secretions of the tongue. A piece of metal, as a silver coin, gives rise to a seemingly distinct taste sensation, called *metallic*, but it is probably not to be accepted as coordinate with the others. The acid taste may be excited by electricity. If a piece of zinc be placed beneath and a piece of copper above the tongue, and their ends brought into contact, an acid taste (due to the feeble galvanic current) is produced. The delicacy of the sense of taste is sufficient to discern one part of sulphuric acid in 10,000 of water, or one part of quinine in 200,000 of water. But it is far surpassed in acuteness by the sense of smell.

ACUTENESS OF THE SENSE OF TASTE. (HALL.)

The average of 10 individuals.

Sugar	1 part to	520
Quinine	1 " "	444,000
Acetic Acid	1 " "	5,640
Salt	1 " "	469

Exploration of the taste areas reveals the fact that regions of the tongue and mouth are not equally sensitive to the sapid substances. Sweet tastes are especially developed at the tip and sides of the tongue, while bitter tastes are almost absent in the front, but especially developed on the basal region, and in the fauces and pharynx. Salts are more stimulating to the tip of the

tongue, and acids along the sides. Individual tests of the fungiform papillæ by Oehrwall showed that about half the papillæ reacted to sweet, bitter, and acid, but that certain ones reacted only to sweet, or to sweet and bitter, or to acid and bitter. This suggests the specific nature of the taste sensations and tends to prove that there may be a special organ for each kind of stimulus. Experiments have also shown that it is possible to do away with the power of tasting bitters and sweets while the taste for acids and salts remains. This is done by chewing the leaves of an Indian plant, *Gymnema sylvestre*. It has also been shown that the power of tasting sweet substances disappears before that of tasting bitter. Other experiments have shown that the mechanisms for salt and acid tastes are distinct.

After-tastes and Contrasts. Very distinct sensations of taste are

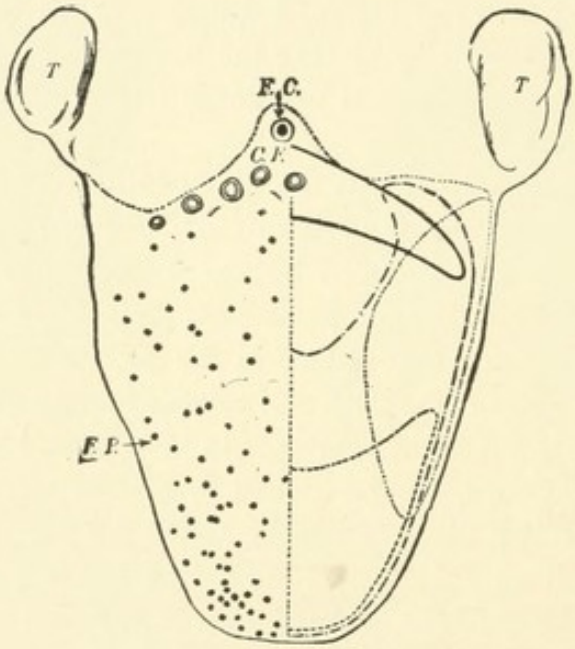


FIG. 425.—Localization of Taste. Bitter ——; acid ....; salt, —·—·—; sweet - - - - -; *T*, tonsils; *FC*, foramen cecum; *CP*, circumvallate papillæ; *FP*, fungiform papillæ. (Hall.)

frequently left after the substances which excited them have ceased to act on the nerve, as the after-taste of metallic bitter, which remains after breaking the stimulating current. Such sensations often endure for a long time, and modify the taste of other substances applied to the tongue. Thus, the taste of sweet substances is intensified after the tasting of common salt. After rinsing the mouth with water containing salt, it is said that sweet solutions are perceived that are too dilute to be detected ordinarily. Many other chemicals produce similar results. The application of a sapid substance, acid for example, to one side of the tongue intensifies the sensation produced by a sapid substance applied to the other side. There is a simultaneous contrast which suggests that the same relation exists between tastes as between colors, of which those that are opposed, *i.e.*, complementary, render each

other more vivid, though no general principles governing this relation have been discovered in the case of tastes. In the art of cooking, however, attention has at all times been paid to the consonance or harmony of flavors in their combination or order of succession, just as in painting and music the fundamental principles of harmony have been employed empirically while the theoretical laws were unknown.

Frequent and continued repetitions of the same taste render the perception of it less and less distinct, in the same way that a color becomes more and more dull and indistinct the longer the eye is fixed upon it. There is fatigue of the taste organ at some point.

THE SENSE OF SMELL.

The sensation of smell is produced by the action of odorous particles on a special end-apparatus, which in turn causes nerve impulses that arouse changes in a special area in the sensorium. The stimulating cause is the direct action of chemical substances as in the sense of taste. In this case, however, the substances must reach the sensory membrane in a gaseous state, or in ex-

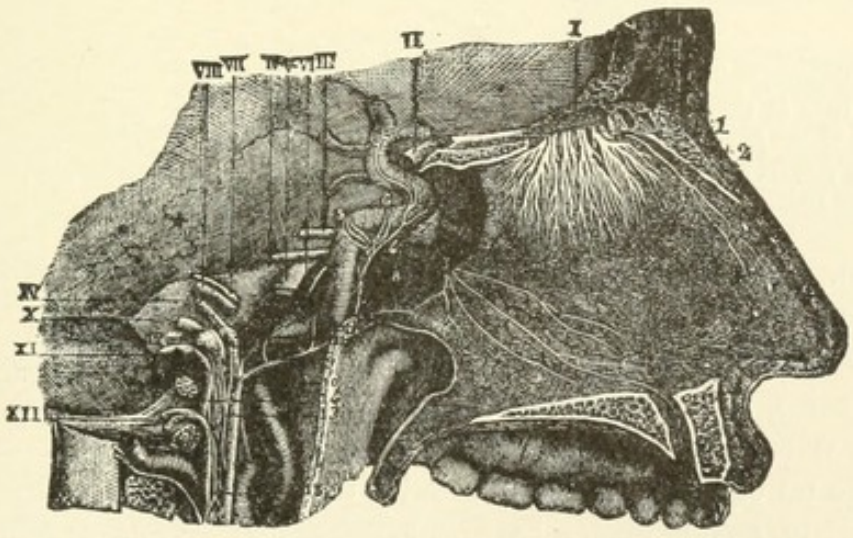


FIG. 426.—Nerves of the Septum Nasi, Seen from the Right Side. ×⅔.—*I*, The olfactory bulb; 1, the olfactory nerves passing through the foramina of the cribriform plate, and descending to be distributed on the septum; 2, the internal or septal twig of the nasal branch of the ophthalmic nerve; 3, naso-palatine nerves. (From Sappey, after Hirschfeld and Leveillé.)

tremely fine division so that it can quickly enter into solution in the moisture on the sensitive mucous surface. The odorous particles are carried to the membrane by inspiratory currents of air.

The Olfactory Apparatus. The essential parts of the olfactory apparatus are the nasal sensory or olfactory membrane to receive the special stimuli, and the nervous apparatus to conduct the olfactory nerve-impulse to the sensory area in the cortex cerebri for its perception.

The nose is not entirely an organ for the seat of smell. In fact the nasal

cavities are divided into three districts called respectively: *Regio vestibŭlaris*, which is the entrance to the cavity. It is lined with a mucous membrane very closely resembling the skin, and guarded by hairs and by sebaceous glands. 2, *Regio respiratoria*, which includes the lower and middle meatus of the nose. It is covered with mucous membrane of stratified columnar ciliated

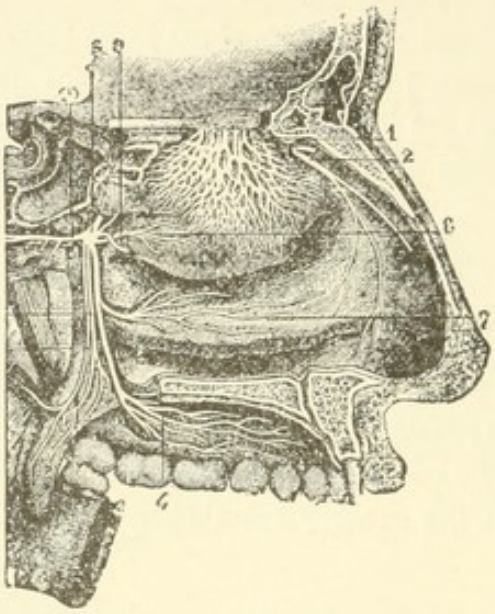


FIG. 427.—Nerves of the Outer Walls of the Nasal Fossæ. 1, Network of the branches of the olfactory nerve, descending upon the region of the superior and middle turbinated bones; 2, external twig of the ethmoidal branch of the nasal nerves; 3, spheno-palatine ganglion; 4, ramification of the anterior palatine nerves; 5, posterior, and 6, middle divisions of the palatine nerves; 7, branch to the region of the inferior turbinated bone; 8, branch to the region of the superior and middle turbinated bones; 9, naso-palatine branch to the septum cut short. (From Sappey, after Hirschfeld and Leveillé.)

epithelium. The mucosa is thick and consists of fibrous connective tissue; it contains a certain number of tubular mucous and serous glands. 3, *Regio olfactoria*. This includes the anterior two-thirds of the superior meatus, the middle meatus, and the upper half of the septum nasi, figures 427 and 428. It is of a yellowish color. It consists of a thicker mucous membrane than in 2, made up of loose, areolar connective tissue covered by epithelium of a special variety, resting upon a basement membrane. The cells of the epithelium are of two principal kinds: *a*, columnar epithelial cells whose function is to support *b*, the bipolar olfactory cells. The epithelial cells are prismatic in shape and have upon their surfaces facets into which the olfactory cells fit themselves, figure 428, *e*. They are thus analogous to the cells of Müller of the retina. The olfactory cells have an oblong or fusiform shape, which is mainly determined by the large nucleus. The thin protoplasmic body has two processes, an external and an internal. The external is large and passes up to the free surface, to end in a small bunch of fibrils that are not vibratile. The internal process is very fine, often varicose, and passes through the cribriform plate to form a glomerular basket with the branches of the mitral cells of the olfactory bulb.

The olfactory bulb must be studied in relation with the nerve fibers and olfactory cells with which it is connected. These parts together form a sensory end-organ which resembles in many respects the retina. The discovery of its true structure has thrown a flood of light on the architecture of the nerve centers as a whole.

The olfactory bulb is not a nerve, but a modification of the brain cortex. A transection shows it to be made up of four layers: 1, Peripheral fibers. 2, Olfactory glomerules. 3, Layer of mitral cells. 4, Layer of granular cells and deep nerve fibers.

The first and external layer is composed of the fine nerve fibrils of the olfactory nerves. They pass through the cribriform plate of the ethmoid, arising from the olfactory cells of which they are processes.

The glomerular layer contains numbers of small round bodies whose structure shows that they are made up of the interlocking expansions of the olfactory fibers, on the one hand, and of the branches of the "mitral" cells, on the other. These are mingled in a close network, but do not anastomose. It was by the study of these bodies in part that the fact of the non-continuity of the neurones was demonstrated, figure 429. This layer also contains small fusiform cells with branching dendrites that extend outward to the glomeruli. Each has an axis-cylinder process which passes inward to join the fibers of the internal olfactory nerves.

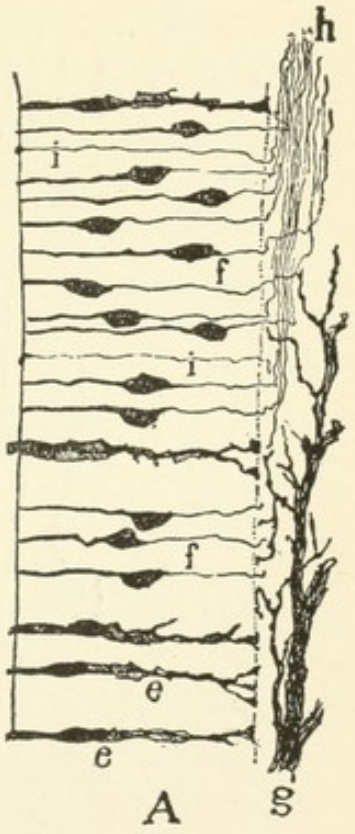


FIG. 428.—Bipolar Olfactory Cells from the Nasal Fossæ of the Rat (Full-term Fetus). *A*, Epithelium of the olfactory mucosa; *e*, epithelial cells; *f*, *f*, nerve cells; *i*, nerve fibers terminating freely on the epithelial surface; *h*, olfactory nerve fibers; *g*, sensory nerve derived from the trigeminus. (Cajal.)

The layer of mitral cells contains large cells, some of them triangular and some in the shape of a miter. They have numerous dendrites, one of which passes into a glomerulus and then breaks up in a fine arborization. An axis-cylinder process passes off from the inner surface and is continued as an internal olfactory nerve fiber in the olfactory tract.

The layer of granules and central fibers contains a large number of very small nerve cells, which are peculiar in that they have no axis-cylinder. Their dendrites extend chiefly into the layer of mitral cells. They resemble the spongioblasts of the retina and probably have commissural functions. This layer has also some small star-shaped cells whose dendrites end in the mitral-cell layer. Among these cells run numerous fibers, chiefly from the mitral cells and the fusiform cells of the glomerular layer. The general arrangement is shown in figure 429.

The Stimulation of the Olfactory Membrane. The extent of the nasal mucous surfaces, and of the frontal and antral sinuses connected with them, might suggest that the sensory olfactory surface is widely distributed, but such is not the case. Air impregnated with vapor of camphor has been injected into the frontal sinus through a fistulous opening, and odorous substances have been injected into the antrum of Highmore; but in neither case was any odor perceived by the patient. All parts of the nasal cavities are endowed with cutaneous sensibility by the nasal branches of the first and

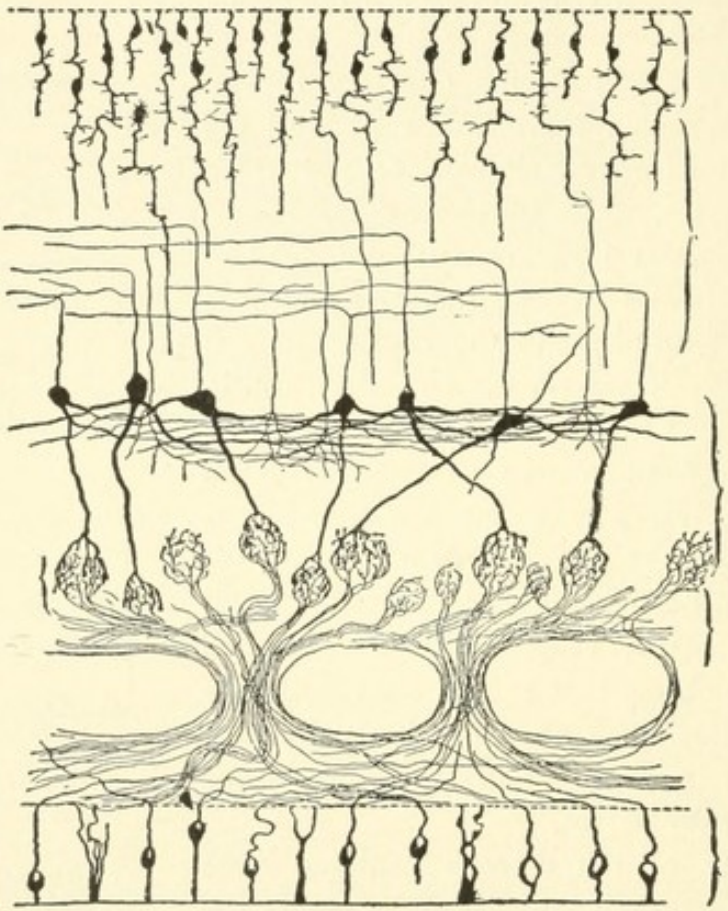


FIG. 429.—Principal Constituent Elements of the Olfactory Bulb of a Mammal. (Van Gehuchten.)

second divisions of the fifth nerve, hence the sensations of cold, heat, itching, tickling, and pain, and the sensation of tension or pressure in the nostrils. That these nerves cannot perform the functions of the olfactory nerves is proved by cases in which the sense of smell is lost, while the mucous membrane of the nose remains susceptible to the various modifications of the sense of touch. But it is often difficult to distinguish the sensation of smell from that of mere feeling, and to ascertain what belongs to each separately. This is true particularly of the sensations excited by acrid vapors in the nose, as of ammonia, horse-radish, mustard, etc., and the difficulty is the greater when it is remembered that these acrid vapors have nearly the same action upon the mucous membrane of the eyelids.

The true olfactory membrane is limited to the small area on either side of the superior meatus and supplied by the olfactory nerve. It is stimulated by odorous substances when they penetrate the upper chamber of the nose. Currents of air can be drawn over this membrane more certainly and effectively by sniffing the air, as noticed in the acts of a dog following the trail. The odorous particles must come into contact with the olfactory cells when in solution in the moisture over the surface and produce its stimulus by chemical change. Mere presence in solution is not always adequate to a stimulation. It seems that movement over the surface is necessary, at least to effective stimulation. Haycraft has repeated some of the older experiments and finds that eau de Cologne can be introduced into the nasal cavity in warm saline solutions without producing a sensation of smell even when 10 per cent solutions are used. He also showed that Cologne, bergamot, etc., can be slowly diffused into the nasal cavity without producing a stimulus. If, while the vapor is thus in the nasal cavity, the nostril be closed and the person goes into pure air and breathes, then an odorous sensation is at once experienced. This shows that even odorous gases "must be moved over the olfactory surface" in order to produce a stimulus.

The presence of bodies in quantities so minute as to be undiscernible even by spectrum analysis, 0.00000003 of a grain of musk, can be distinctly smelt (Valentin). Opposed to the sensation of an agreeable odor is that of a disagreeable or disgusting odor, which corresponds to the sensations of pain, dazzling and disharmony of colors, and dissonance in the other senses. The cause of this difference in the effect of different odors is unknown; but this much is certain, that odors are pleasant or offensive in a relative sense only, for many animals pass their existence in the midst of odors which to us are highly disagreeable. A great difference in this respect is, indeed, observed among men. Many odors, generally thought agreeable, are to some persons intolerable; and different persons describe differently the sensations that they severally derive from the same odorous substances. There seems also to be in some persons an insensibility to certain odors, comparable with that of the eye to certain colors; and among different persons, as great a difference in the acuteness of the sense of smell as among others in the acuteness of sight. We have no exact proof that a relation of harmony exists between odors as between colors and sounds, though it is probable that such is the case, since it certainly is so with regard to the sense of taste. Such a relation would account in some measure for the different degrees of perceptive power in different persons; for as some have no ear for music, so others have no clear appreciation of the relation of odors, and therefore little pleasure in them.

Most of the substances taken as foods into the mouth give off odorous particles that stimulate the olfactory membrane. In fact, the chief elements in food flavors are not tastes, but smells, or combinations of the two. This

is particularly true of meats. Meats are especially prized for their delicate flavors, and cooking is performed to bring out these flavors. Yet meat has little taste other than salt; the so-called tastes are due to odorous particles entering the nostril and stimulating the olfactory membrane at the same moment the taste buds of the mouth are stimulated.

Subjective sensations occur frequently in connection with the sense of smell. Often a person smells something which is not present, and which other persons cannot smell; this is very frequent with nervous persons but it occasionally happens to every one. In a man who was conscious of a bad odor, the arachnoid was found after death to be beset with deposits of bone, and a lesion in the middle of the cerebral hemispheres was also discovered. Dubois was acquainted with a man who, ever after a fall from his horse, which occurred several years before his death, believed that he smelt a bad odor.

III. HEARING AND EQUILIBRATION.

THE ANATOMY OF THE EAR.

For descriptive purposes, the Ear, or Organ of Hearing, is divided into three parts, 1, the external, 2, the middle, and 3, the internal ear. The first two are only accessory structures to the third, which contains the essential parts of the organ of hearing. The accompanying figure, 430, shows very well the relation of these divisions to each other.

The External Ear. The external ear consists of the *pinna* or *auricle* and the *external auditory canal or meatus*.

The principal parts of the *pinna*, figure 430, are two prominent rims enclosed one within the other, the *helix* and *antihelix*, and inclosing a central hollow named the *concha ;* in front of the concha, a prominence directed backward, the *tragus*, and opposite to this one directed forward, the *antitragus*. From the concha, the auditory canal passes inward and a little forward to the membrana tympani, to which it thus serves to convey the vibrations of the air. It consists of a fibro-cartilage tube lined by skin continuous with that of the pinna, and extending over the outer part of the *membrana tympani*. Fine hairs and sebaceous glands are present toward the outer part of the canal, while deeper in the canal are small glands, resembling the sweat glands in structure, which secrete the *cerumen*.

Regarding the external ear, therefore, as a collector and conductor of sonorous vibrations, all its inequalities, elevations, and depressions become of evident importance; for those elevations and depressions upon which the undulations fall will tend to intensify certain sound waves while not affecting others. It is thought that this forms at least an aid in determining the direction whence a sound comes.

The Middle Ear or Tympanum. The middle ear, or tympanum, 3, figure 430, is separated by the *membrana tympani* from the external auditory canal. It is a cavity in the temporal bone, opening through its anterior and inner wall into the Eustachian tube.

The Eustachian canal establishes communication between the tympanic cavity and pharynx, thus equalizing the air pressure on the sides of the

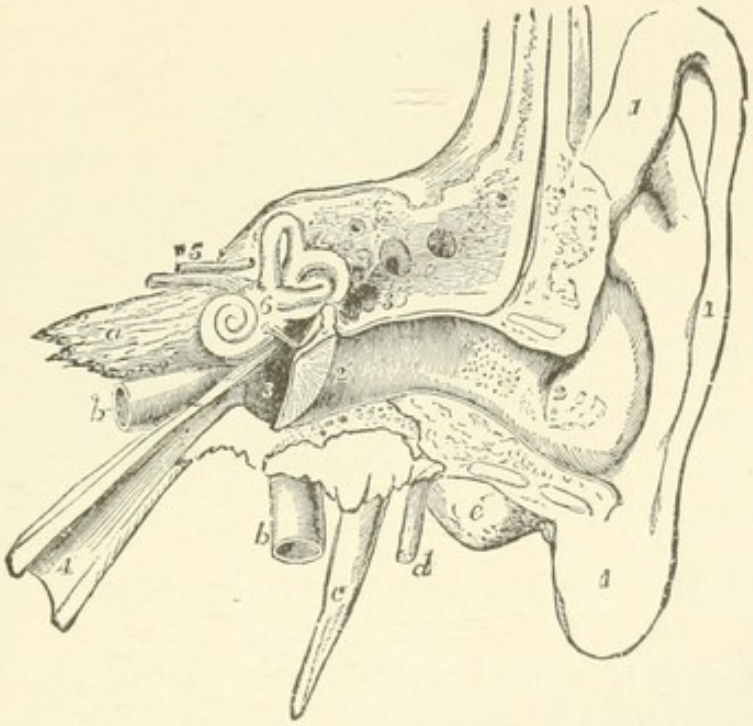


FIG. 430.—Diagrammatic View from Before of the Parts Composing the Organ of Hearing of the Left Side. The temporal bone of the left side, with the accompanying soft parts, has been detached from the head, and a section has been carried through it transversely, so as to remove the front of the meatus externus, half the tympanic membrane, the upper and anterior wall of the tympanum and Eustachian tube. The meatus internus has also been opened, and the bony labyrinth exposed by the removal of the surrounding parts of the petrous bone. 1, The pinna and lobe; 2, 2′, meatus externus; 2′, membrana tympani; 3, cavity of the tympanum; 3′, its opening backward into the mastoid cells; between 3 and 3′, the chain of small bones; 4, Eustachian tube; 5, meatus internus, containing the facial (uppermost) and the auditory nerves; 6, placed on the vestibule of the labyrinth above the fenestra ovalis; *a*, apex of the petrous bone; *b*, internal carotid artery; *c*, styloid process; *d*, facial nerve issuing from the stylo-mastoid foramen; *e*, mastoid process; *f*, squamous part of the bone covered by integument, etc. (Arnold.)

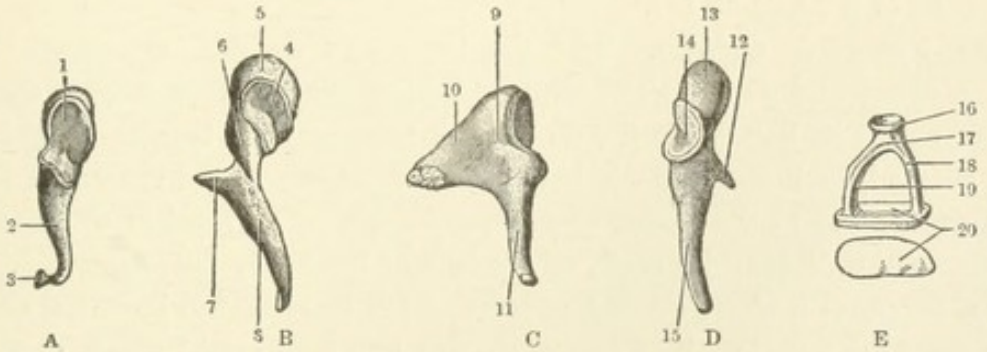


FIG. 431.—Tympanic Ossicles of Left Ear. *A*, Incus seen from the front; *B*, malleus, viewed from behind; *C*, incus, and *D*, malleus, seen from inner aspect; *E*, stapes. 1, Body of incus, with articular surface for head of malleus; 2, processus longus; 3, processus lenticularis; 4, articular surface for incus; 5, head, 6, neck; 7, processus brevis; 8, manubrium; 9, body; 10, short process; 11, long process; 12, processus longus; 13, head; 14, facet for incus; 15, manubrium, 16, head; 17, neck; 18, crus anterius; 19, crus posterius; 20, foot plate.

tympanic membrane, serving the same mechanical purpose as the vent-hole in a snare or bass drum. The cavity of the tympanum communicates posteriorly with air cavities, the *mastoid cells*, in the mastoid process of the temporal bone; but its only opening to the external air is through the Eustachian tube. The cavity of the tympanum is lined with mucous membrane, the

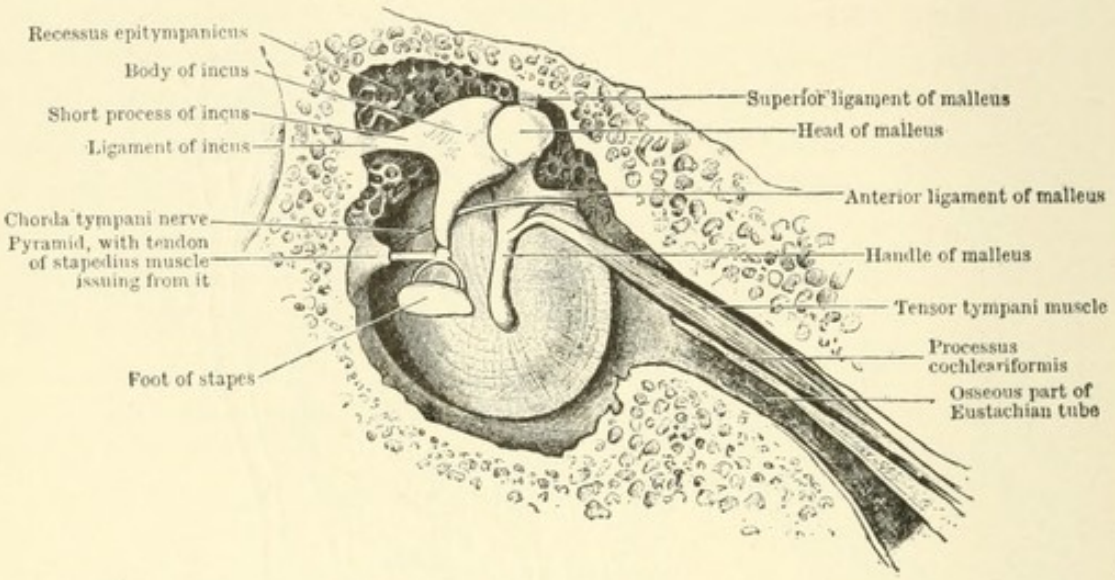


FIG. 432.—Left Membrana Tympani and Chain of Tympanic Ossicles (Seen from Inner Aspect). (Cunningham.)

epithelium of which is ciliated and continuous with that of the pharynx. It contains a chain of small bones, *ossicula auditus*, which extends from the membrana tympani to the fenestra ovalis.

The Membrana Tympani. The tympanic membrane is placed in a slanting direction at the bottom of the external canal, its plane being at an angle of about forty-five degrees with the lower wall of the canal. It is formed chiefly of a tough and tense fibrous membrane, the edges of which are set in a bony groove. Its outer surface is covered by a continuation of the epithelial lining of the auditory canal, its inner surface with part of the mucous membrane of the middle ear.

The Tympanic Ossicles. The ear bones, or ossicles, are named the *malleus*, *incus*, and *stapes*. The malleus is attached by a long slightly curved process, called its handle, to the membrana tympani, the line of attachment being vertical, including the whole length of the handle, and extending from the upper border to the center of the membrane. The head of the malleus is irregularly rounded; its neck, or the line of boundary between it and the handle, supports a short conical process which receives the insertion of the *tensor tympani* muscle. The incus, shaped like a bicuspid molar tooth, is articulated by its broader part to the malleus. Of its two fang-like processes, one directed backward has a free end lodged in a depression in the mastoid bone; the other, curved downward and more pointed, articulates by means

of a roundish tubercle with the stapes. The stapes is a little bone shaped exactly like a stirrup, of which the base or bar fits into the fenestra ovalis. The *stapedius* muscle is attached to the neck of the stapes.

The bones of the ear are covered with mucous membrane reflected over them from the wall of the tympanum. They are movable both altogether and one upon the other. The malleus moves and vibrates with every movement and vibration of the membrana tympani, and its movements are communicated through the incus to the stapes, and through the stapes to the membrane closing the fenestra ovalis. The malleus, also, is movable in its articulation with the incus. The membrana tympani which moves the long process of the malleus is altered in its degree of tension by the degree of contraction of the tensor tympani muscles. The stapes is movable on the process of the incus, the contractions of the stapedius muscle draws it outward. The axis round which the malleus and incus rotate is the line joining the processus gracilis of the malleus and the posterior process of the incus.

The Internal Ear. The internal ear, or labyrinth, constitutes the proper organ of hearing. It contains special epithelial structures to which are distributed the auditory nerve. The organ is located in a cavity in the petrous bone, called the *osseus labyrinth*. The auditory organ within is

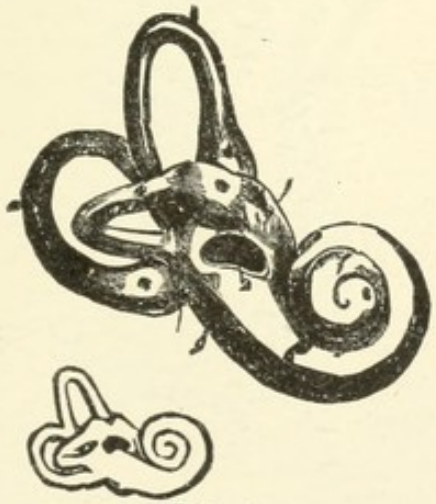


FIG. 433.

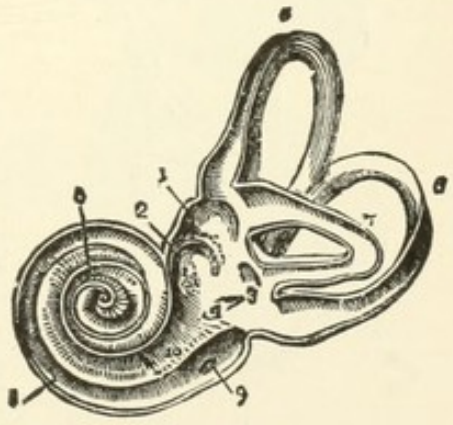


FIG. 434.

FIG. 433.—Right Bony Labyrinth, Viewed from the Outer Side. The specimen here represented is prepared by separating piecemeal the looser substance of the petrous bone from the dense walls which immediately enclose the labyrinth. 1, The vestibule; 2, fenestra ovalis; 3, superior semicircular canal; 4, horizontal or external canal; 5, posterior canal; *, ampullæ of the semicircular canals; 6, first turn of the cochlea; 7, second turn; 8, apex; 9, fenestra rotunda. The smaller figure in outline below shows the natural size. ×2.5. (Sömmering.)

FIG. 434.—View of the Interior of the Left Labyrinth. The bony wall of the labyrinth is removed superiorly and externally. 1, Fovea hemielliptica; 2, fovea hemispherica; 3, common opening of the superior and posterior semicircular canals; 4, opening of the aqueduct of the vestibule; 5, the superior, 6, the posterior, and 7, the external semicircular canals; 8, spiral tube of the cochlea (scala tympani); 9, opening of the aqueduct of the cochlea; 10, placed on the lamina spiralis in the scala vestibuli. ×2.5. (Sömmering.)

called the *membranous labyrinth*. The membranous labyrinth contains a fluid called *endolymph;* while outside it, between it and the osseous labyrinth, is a fluid called *perilymph*. This is not a pure lymph, as it contains mucin.

The osseous labyrinth consists of three principal parts, namely the *vestibule*, the *cochlea*, and the *semicircular canals*, containing the respective divisions of the membranous labyrinth. The osseous labyrinth possesses openings on its inner wall for the entrance of the divisions of the auditory nerve from the cranial cavity, in its outer wall the *fenestra ovalis*, 2, figure 433, an opening filled by the base of the stapes, and the fenestra rotunda. The vestibule also presents an opening, the orifice of the *aqueductus vestibuli*.

The Membranous Labyrinth. The membranous labyrinth cor-

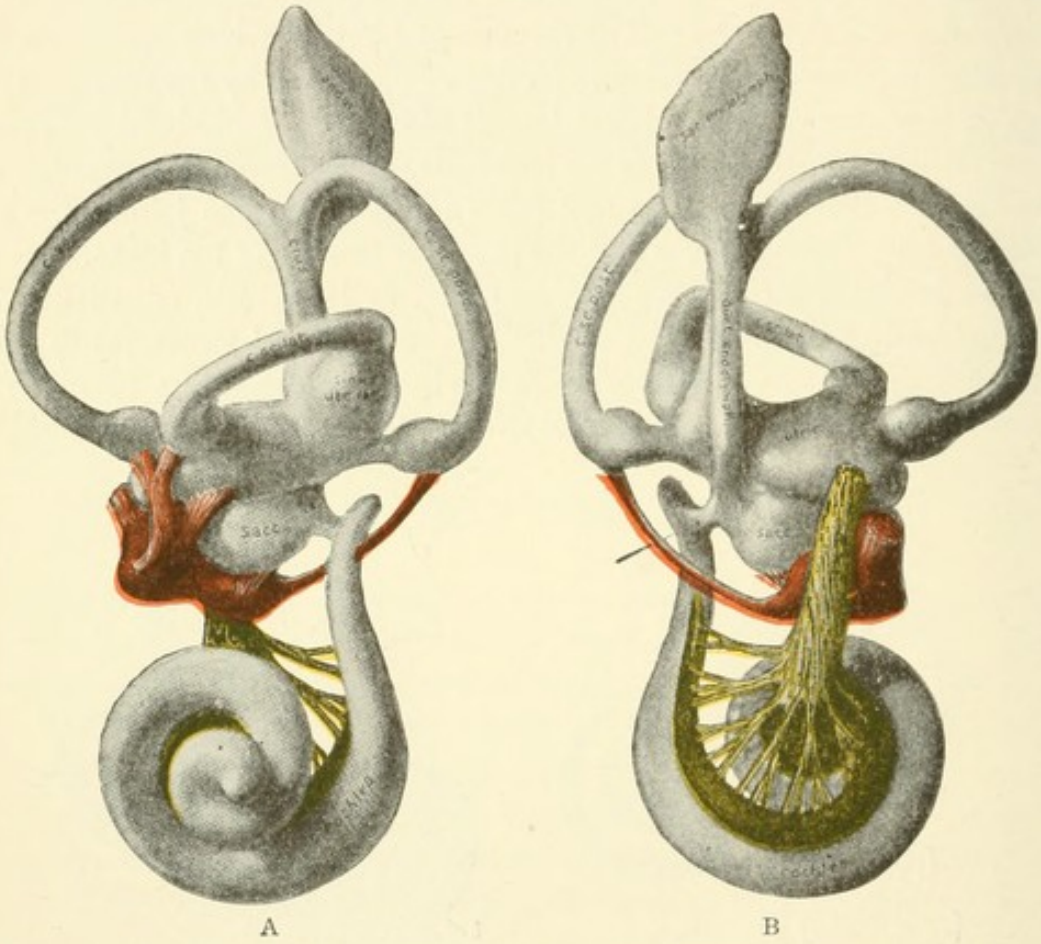


FIG. 435.—Membranous Labyrinth of a 30 mm. Human Fetus. *A*, Viewed from its Lateral Aspect; *B*, viewed from the mesial aspect. (Streeter.)

responds generally with the form of the osseous labyrinth, so far as regards the vestibule and semicircular canals, but is separated from the walls of these parts by perilymph, except where the nerves enter into connection within it. The labyrinth is a closed membrane containing endolymph.

The Utriculus and the Sacculus. The vestibular portion of the inner ear consists of membranous sacs, the upper, the *utriculus*, the lower called the *sacculus*. The former is connected with the semicircular canals, the latter with the cochlea by the *cochlear canal*. The utriculus and the sacculus have on their floors a special patch of sensory epithelium called the *maculæ*. The fibers of the vestibular divisions of the auditory nerve end in the maculæ,

figure 435. In the cavities of the sacculus and utriculus are small masses of calcareous particles called *otoliths*.

The Semicircular Canals. There are three semicircular canals for each ear, one horizontal and two vertical ones placed almost at right angles to each other. The three canals, therefore, occupy the three planes of space. Each has a considerable enlargement or swelling, called an ampulla. The epithelium of the ampulla is modified at the point of entrance of the nerve into a thickened hillock called the *crista acustica*. This epithelium is composed of rod cells or supporting cells which extend the full thickness of the crista, and of hair cells, which occupy the inner or free half of the crista. The hair cells are the sensory cells. They have hair-like processes which project from the free ends of the cells out into the endolymph of the cavity. Nerve fibrils run up into the crista and apparently form terminal arborizations about the hair cells, or, according to some observers, end in the cells.

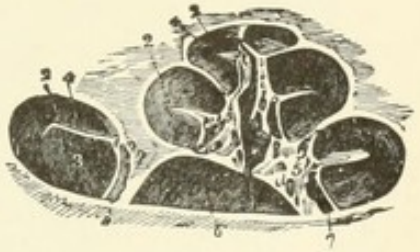


FIG. 436.—View of the Osseous Cochlea Divided through the Middle. 1, Central canal of the modiolus; 2, lamina spiralis ossea; 3, scala tympani; 4, scala vestibuli; 5, porous substance of the modiolus near one of the sections of the canalis spiralis modioli. ×5. (Arnold.)

The Cochlea and the Organ of Corti. The membranous cochlea is located in the spiral canal in the petrous bone, called the cochlear canal. It is attached to the wall of the cavity between the fenestra ovalis and the fenestra rotunda, and to the outer wall of the canal and the free border of the lamina spiralis almost, but not quite, to its summit. A small cavity is thus left around the upper end of the cochlea connecting the *scala vestibuli* above with the *scala tympani* below. A cross-section through the cochlear canal shows the relations of the cochlear canal which was named *scala media* by the earlier anatomists. The free portion of the membranous wall above is called the *membrane of Reisner*, while that below is called the *basilar membrane*. The basilar membrane supports the special sensory apparatus for the reception of stimuli of sound waves.

Organ of Corti. The basilar membrane supports cells of several types. About midway between the outer edge of the lamina spiralis and the outer wall of the cochlea are situated the *rods of Corti*. Viewed sideways, they are seen to consist of an external and internal pillar, each rising from an expanded foot or base on the basilar membrane, figure 438. They slant inward toward each other, and each ends in a swelling termed the head, the head of the inner pillar overlying that of the outer, figure 438. Each pair of pillars forms, as it were, a pointed roof arching over a space, and by a succession of them a little tunnel is formed. It has been estimated that there are about three thousand of these pairs of rods of Corti between the base of the cochlea and its apex. They are found progressively to increase in length, and be-

come more oblique; in other words, the tunnel becomes wider, but diminishes in height as we approach the apex of the cochlea.

Leaning against the rods of Corti and apparently supported by them are sensory cells or hair cells. The hair cells are in two series, the inner and the outer hair cells. The former consist of a single layer, the latter of three or four layers, figure 438. There are two additional types of supporting cells, the cells of Deiters and of Hensen. The whole structure when viewed from above bears a remarkable resemblance to the keyboard of a piano.

The cochlear division of the auditory nerve enters the base of the modiolus and sends a spiral whorl of fibers out under the spiral lamina The gan-

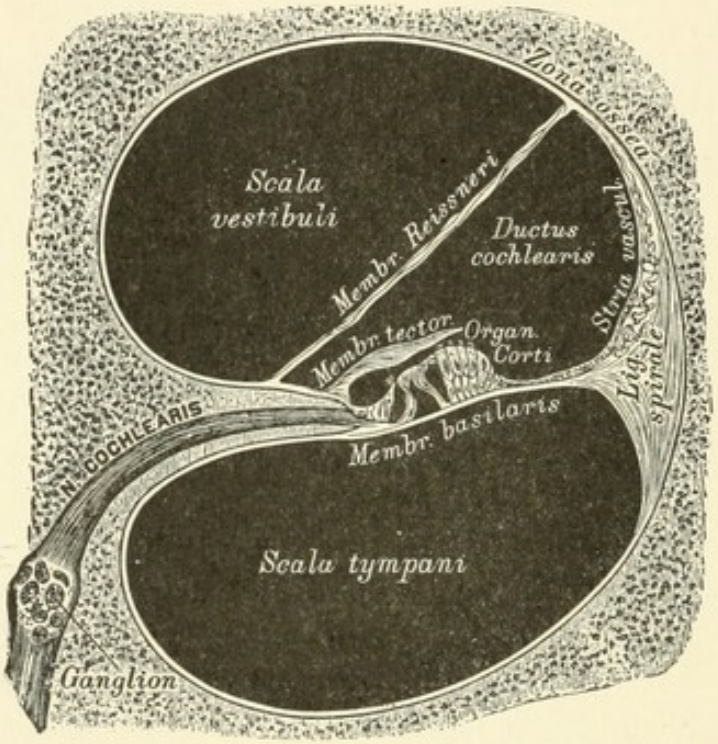


FIG. 437.—Semidiagrammatic Section of a Cochlear Whorl. (After Heitzmann.)

glionic cells of the cochlear division of the auditory nerve are located in the base of the lamina where they form the spiral ganglion. The nerve fibers from the ganglion cells pass out through small holes in the periphery of the spiral plate of bone, to enter the organ of Corti. Here they form small longitudinal bundles that quickly end about the hair cells.

THE PHYSIOLOGY OF HEARING.

All the acoustic contrivances of the organ of hearing are means for conducting sound. Since all matter is capable of propagating sonorous vibrations, the simplest conditions must be sufficient for mere hearing; since all substances surrounding the auditory apparatus would stimulate it. The complex development of the organ of hearing, therefore, must have for its object

the more effective propagation of the sonorous vibrations and their intensification by resonance; and, in fact, the whole of the acoustic apparatus may be shown to have reference to these principles.

The external ear and the auditory passages influence the propagation of sound to the tympanum by collecting from the atmosphere the sonorous undulations that strike against the external ear and by transmitting them by the air in the passage to the membrana tympani.

In animals living in the atmosphere, the sonorous vibrations are conveyed to the auditory epithelium through three different media in series;

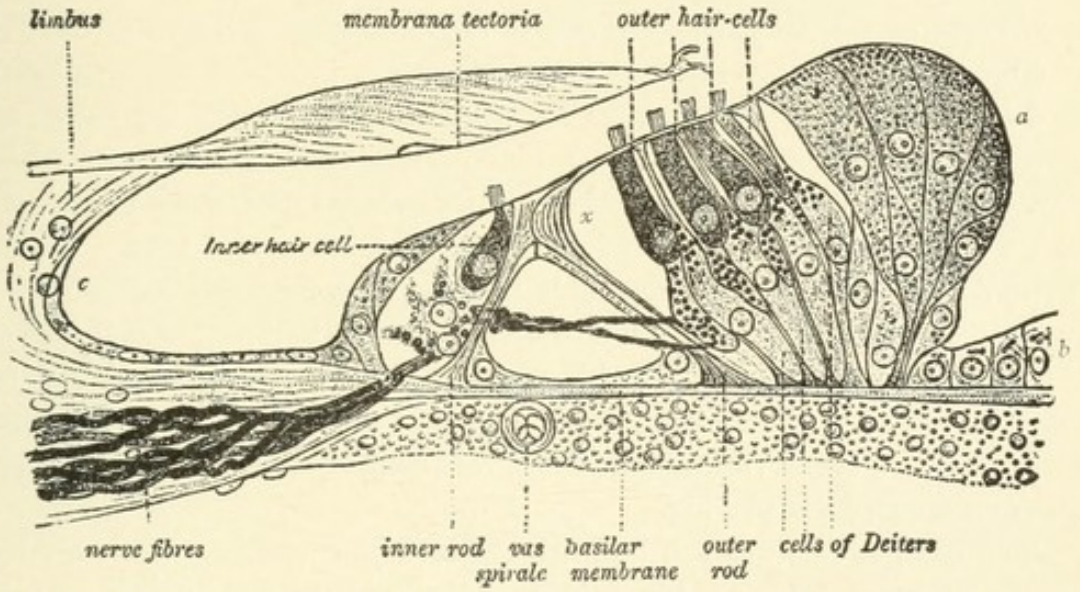


FIG. 438.—Semidiagrammatic Representation of the Organ of Corti and Adjacent Structures. (Merkel-Henle.) *a*, Cells of Hensen; *b*, cells of Claudius; *c*, internal spiral sulcus; *x*, Nuel's space. The nerve fibers (dendrites of cells of the spinal ganglion) are seen passing to Corti's organ through openings (foramina nervosa) in the bony spiral lamina. The black dots represent longitudinally running branches, one bundle lying to the inner side of the inner pillar, a second just to the outer side of the inner pillar within Corti's tunnel, the third beneath the outer hair cells.

namely, the air of the external ear and meatus, which sets in vibration the tympanic membrane, the solid chain of auditory ossicles, and the fluid of the labyrinth. Sonorous vibrations are imparted too imperfectly from air to the solid structures of the body as a whole for the propagation of sound to the internal ear to be adequately effected by that means alone. In passing from air directly into water, sonorous vibrations suffer also a considerable diminution of their strength; but if a tense membrane exists between the air and the water, the sonorous vibrations are communicated from the former to the latter medium with very great intensity. This fact, of which Müller gives experimental proof, furnishes at once an explanation of the use of the fenestra ovalis and of the membrane closing it. It is the means of communicating, in full intensity, the vibrations of the ear bones, or, in their absence, of the air in the tympanum, to the fluid of the labyrinth. The vibration of the fluid, the perilymph and endolymph, of the internal ear, sets the basilar membrane in vibration and in consequence stimulates the sensory apparatus

resting upon it. This last is the essential stimulating act, while all that precedes is more or less accessory or contributory to this act. Just what the accessory apparatus contributes can best be understood by an examination of the stimulus and the sensation which results from its action.

Sound. Any elastic body, *e.g.*, air, a membrane, or a string, performing a certain number of regular vibrations per second, gives rise to what is termed a musical sound or *tone*. We must, however, distinguish between a musical sound and a mere noise; the latter being due to irregular vibrations.

Musical sounds are distinguished from each other by three qualities: 1, *Strength* or *Intensity*, which is due to the amplitude or length of the wave of vibrations. 2, *Rate*, the number of vibrations in a second. 3, *Quality*, or *Timbre*, the peculiar property by which we distinguish the same note sounded on two instruments, *e.g.*, a piano and a flute. It has been proved by Helmholtz to depend on the number of secondary tones, termed *harmonics*, which are present with the predominating or fundamental tone. That is, rhythmic vibrations are either simple in form, like the vibrations of a reed or tuning fork, or compound, like the vibrations of a violin or piano string. If the string of a violin is plucked it not only vibrates as a whole, but in segments in the ratio of one, two, three, etc. The form of air wave that is produced by several such vibrating bodies is very complex indeed, as, for example, when an orchestra is playing.

The compound wave can be analyzed into its constituent elements by a system of resonators, on the principle of sympathetic vibration. If one sounds a series of musical notes before such a system of resonators it will be found that the tones and overtones are selected by the resonators and made more prominent so that they can be identified.

The sensation of sound has in it certain elements that correspond closely with the physical properties of sound, *i.e.*, loudness, pitch, and quality. Loudness is dependent merely on the intensity of the stimulation. A sound wave of great energy, for example, produces a larger movement of the tympanic membrane, and it, through the chain of bones and the fluid of the internal ear, a larger swing of the basilar membrane, hence a more intense stimulus of the organ of Corti.

Function of the External and Middle Ears. It has already been stated that the external ear collects the sound waves and conducts them against the membrana tympani. This membrane vibrates as a whole to the compound waves that impinge upon it, and thus serves for the transmission of sound from the air to the chain of ossicles of the middle ear. It is often compared to the membrane of a drum, but there are fundamental differences.

When a drum is struck, a certain definite fundamental tone is elicited; similarly a drum is thrown into vibration when certain tones are sounded in

its neighborhood, while it is quite unaffected by others. In other words, it can take up and vibrate in response only to those tones whose vibrations nearly correspond in number with those of its own fundamental tone. The tympanic membrane can take up an immense range of tones produced by vibrations ranging from 30 to 4,000 or 5,000 per second. This would be clearly impossible if it were an evenly stretched membrane. The fact is that the membrana tympani is by no means evenly stretched, and this is due partly to its slightly funnel-like form, and partly to its being connected with the chain of auditory ossicles. Further, if the membrane were quite free in its center, it would go on vibrating as a drum does some time after it is struck; each sound would be prolonged, leading to considerable confusion. This

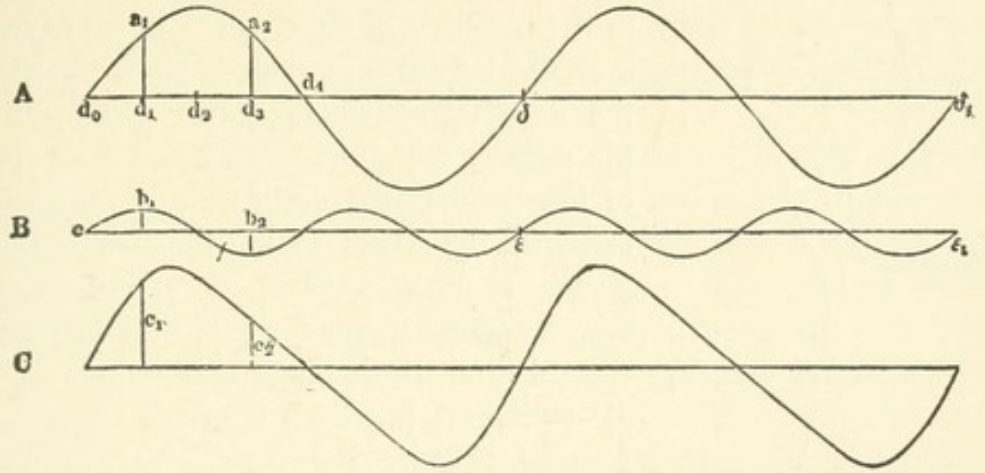


FIG. 439.—Showing *A* and *B*, Simple Pendular Vibrations, Separated by One Octave. *C*, The form of the curve produced by the combination of *A* and *B*.

evil is obviated by the ear bones, which check the continuance of the vibrations like the "dampers" in a piano.

The vibrations of the membrana tympani are transmitted by the chain of ossicles to the fenestra ovalis and fluid of the labyrinth, their dispersion in the tympanum being prevented by the difficulty of the transition of vibrations from solid to gaseous bodies. The necessity of the presence of air on the inner side of the membrana tympani, in order to enable it and the auditory ossicles to fulfil the objects just described, is obvious. Without this provision, neither would the vibrations of the membrane be free nor the chain of bones isolated, so as to propagate the sonorous undulations with concentration of their intensity. But while the oscillations of the membrana tympani are readily communicated to the air in the cavity of the tympanum, those of the solid ossicles will not be conducted away by the air, but will be propagated to the labyrinth without being dispersed in the tympanum.

The propagation of sound through the auditory ossicles to the labyrinth must be effected by oscillations of the bones as a whole.

The existence of the membrane over the fenestra rotunda permits approxi-

mation and removal of the stapes to and from the labyrinth. When the membrane of the fenestra ovalis is pressed toward the labyrinth by the stapes, the membrane of the fenestra rotunda may, by the pressure communicated through the fluid of the labyrinth, be pressed toward the cavity of the tympanum. The long process of the malleus receives the undulations of the membrana tympani, figure 440, *a*, *a*, and of the air in a direction indicated by the arrows, nearly perpendicular to itself. From the long process of the malleus they are propagated to its head, *b;* thence into the incus, *c*, the long process of which is parallel with the long process of the malleus. From the long process of the incus the undulations are communicated to the stapes, *d*, which is united to the incus at right angles. The several changes in the direction of the chain of bones have, however, no influence in changing the character of the undulations, which remain the same as in the meatus externus. From the long process of the malleus the undulations are communicated by the stapes to the fenestra ovalis in a perpendicular direction. Increasing tension of the membrana tympani diminishes the facility of transmission of sonorous undulations from the air to it. It has been inferred, therefore, that hearing is rendered less acute by increasing the tension of the membrana tympani. This is accomplished by the contractions of the tensor tympani muscle. The exact influence of the stapedius muscle in the act of hearing is unknown. It acts upon the stapes in such a manner as to make it rest obliquely in the fenestra ovalis, depressing that side of the stapes on which it is attached and elevating the other side to the same extent. It seems to prevent too great a movement of the bone.

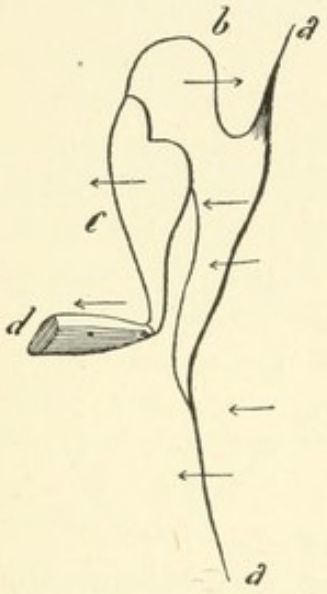


FIG. 440.—Diagram to Illustrate the Action of the Ossicles of the Middle Ear in the Conduction of Sound to the Internal Ear.

The pharyngeal orifice of the Eustachian tube is usually shut. During swallowing, however, it is opened; which may be shown as follows: If the nose and mouth be closed and the cheeks blown out, a sense of pressure is produced in both ears the moment we swallow. This is due, doubtless, to the bulging out of the tympanic membrane by the compressed air, which at that moment enters the Eustachian tube. The principal office of the Eustachian tube has relation to the prevention of the effects of increased tension of the membrana tympani. Its existence and openness will provide for the maintenance of the equilibrium between the air within the tympanum and the external air, so as to prevent the inordinate tension of the membrana tympani which would be produced by too great or too little pressure on either side. While discharging this office it serves as an outlet for mucus. If the

tube were *permanently* open, the sound of one's own voice would probably be greatly intensified, a condition which would of course interfere with the perception of other sounds. At any rate, it is certain that sonorous vibrations can be propagated up the tube to the tympanum by means of a catheter inserted into the pharyngeal orifice of the Eustachian tube.

The Function of the Internal Ear. The fluids of the labyrinth receive the sonorous vibrations at the fenestra ovalis and, we must assume, conduct the same throughout the cavity. In all forms of organs of hearing even to the simplest, liquid is the medium through which the auditory sensory epithelium is stimulated. We have already seen that in the mammalian ear there is a special mechanical arrangement to intensify the vibrations of the fluid in the cochlear canal.

The utriculus, sacculus, and semicircular canals are probably not concerned with auditory function, but with the sense of equilibrium; hence they will be discussed separately a little later.

The cochlea is the special organ of hearing. When it is set in vibrations the movement stimulates the sensory hair cells on the basement membrane, producing a sensory impulse which is transmitted along the paths to the brain and there produces an auditory sensation. If the stimulus results from a disturbance of an explosive or non-harmonic nature, the sensation is interpreted as a noise. If the disturbance is rhythmic or harmonic and repeated in sequence within certain limits of rate, then a tone is perceived.

The intensity of sound, the energy of the disturbance, affects the basilar membrane by producing motion of varying amplitude. This stimulates the hair cells with greater or less intensity, which can be detected by the sensorium as *loudness*. Loudness of the sound sensation is interpreted as intensity of sound wave.

The interpretation of pitch is accomplished by the ear through a wide range of rates of vibration that produce sensations of tone. The average person can perceive musical tones over a range of vibration of from sixty-four double vibrations per second for the lower notes, to four thousand and ninety-six for the higher notes. These limits may be extended to thirty per second and forty thousand per second, respectively, but only a small number of tones can be perceived outside of the narrower limits given above. This extraordinary range of tone is conceivable only on the supposition of localization of the stimulus in some part of the organ. Most physiologists look to the basilar membrane and the organ of Corti for the localization.

Suppose a simple tuning fork to be vibrating with a frequency of sixty-four per second, then these waves will be conducted through the auditory apparatus until they fall on the basilar membrane, and will set it in vibration at the same rate. The exact type of the vibration is at present a matter of inference. The piano theory of Helmholtz is probably the most satisfactory. It assumes that the basilar membrane vibrates as would a number of strings

set in the transverse dimension. In support of this assumption it is asserted that the membrane is taut in the transverse and loose in the longitudinal plane. Retzius has estimated that it contains about 24,000 fibers, and that it measures in width at the base 0.135 mm. and at the apex 0.234 mm. In the above illustration the vibration frequency of sixty-four would supposedly set in sympathetic vibration that part of the apex of the basilar membrane which vibrated in the same frequency, and the sensory cells of the organ of Corti, located over the vibrating fiber, would be stimulated accordingly. In the same way notes of medium and of high frequency stimulate localized areas of sensory cells in the middle and basal parts of the organ of Corti and produce sensations of corresponding pitch.

This idea of localization of auditory sensory stimulation makes it easier to understand the analysis by the ear of compound sonorous waves. Such waves impinge on the membrana tympani and are transmitted through the conducting media unanalyzed, and may be supposed to fall on the basilar membrane as compound waves. The basilar fibers acting like so many resonators, take up the constituent sonorous elements in sympathetic vibration. In short, the basilar membrane is an analyzer in which the compound wave is reduced to its simple components, each of which stimulates its corresponding portion of the organ of Corti. The auditory nerve impulses are conducted through the cochlear nerves to the sensorium where they produce auditory sensations with the same definiteness of pattern as cutaneous or optical stimuli produce sensations that correspond to the patterns of stimulation. The audition is so definite that one can consciously pick out one or the other of the constituent stimulating elements and follow and examine the same to the exclusion of the others, as when one follows a single instrument in an orchestra or a single voice in a group of chattering children.

Bernstein says of this wonderful organ:

"In the cochlea we have to do with a series of apparatus adapted for performing sympathetic vibrations with wonderful exactness. We have here before us a musical instrument which is designed, not to create musical sounds, but to render them perceptible, and which is similar in construction to artificial musical instruments, but which far surpasses them in the delicacy as well as the simplicity of its execution. For, while in a piano every string must have a separate hammer by means of which it is sounded, the ear possesses a single hammer of an ingenious form in its ear bones, which can make every string of the organ of Corti sound separately."

Auditory Judgments. *Direction.* The power of perceiving the direction of sounds is not a faculty of the sense of hearing itself, but is an act of the mind judging on experience previously acquired. From the modifications which the sensation of sound undergoes according to the direction in which the sound reaches us, the mind infers the position of the sounding body. The only true guide for this inference is the more intense action of the

sound upon one than upon the other ear. But even here there is room for much deception, by the influence of reflexion or resonance, and by the propagation of sound from a distance, without loss of intensity, through curved conducting tubes filled with air. By means of such tubes, or of solid conductors, which convey the sonorous vibrations from their source to a distant resonant body, sounds may be made to appear to originate in a new situation. The direction of sound may also be judged of by means of one ear only; the position of the ear and head being varied, so that the sonorous undulations at one moment fall upon the ear in a perpendicular direction, at another moment obliquely. But when neither of these circumstances can guide us in distinguishing the direction of sound, as when it falls equally upon both ears, its source being, for example, either directly in front or behind us, it becomes impossible to determine whence the sound comes.

Distance. The judgment of the distance of the source of sounds is inferred from their intensity. The sound is interpreted as coming from an exterior sonorous body. When the intensity of the voice is modified in imitation of the effect of distance, it excites the idea of its originating at a distance Ventriloquists take advantage of the difficulty with which the direction of sound is recognized, and also the influence of the imagination over our judgment, when they modulate the voices, and at the same time pretend, themselves, to hear sounds as coming from a certain direction.

Duration of the Auditory Stimulus. By removing one or several teeth from the toothed wheel of a vibrator, the fact has been demonstrated that in the case of the auditory organ, as in that of the eye, the sensation continues longer than the impression which causes it; for a removal of the tooth produced no interruption of the sound. The gradual cessation of the sensation of sound renders it difficult to determine its exact duration beyond that of the impression of the sonorous impulses.

Binaural Sensations. Corresponding to the double vision of the same object with the two eyes is the double hearing with the two ears; and analogous to the double vision with one eye, dependent on unequal refraction, is the double hearing of a single sound with one ear, owing to the sound coming to the ear through media of unequal conducting power. The first kind of double hearing is very rare; instances of it, however, have been recorded. The second kind, which depends on the unequal conducting power of two media through which the same sound is transmitted to the ear, may easily be experienced. If a small bell be sounded in water, while the ears are closed by plugs, and a solid conductor be interposed between the water and one ear, two sounds will be heard differing in intensity and tone; one being conveyed to the ear through the medium of the atmosphere, the other through the conducting-rod.

Subjective Sensations. Subjective sounds are the result of a state of irritation or excitement of the auditory nerve produced by other causes than

sonorous impulses. A state of excitement of this nerve, however induced, gives rise to the sensation of sound. Hence the ringing and buzzing in the ears heard by persons of irritable and exhausted nervous system, and by patients with cerebral disease, or disease of the auditory nerve itself; hence also the noise in the ears heard for some time after a long journey in a rattling, noisy vehicle. Ritter found that electric currents also excite sounds in the ears. From the above truly subjective sound we must distinguish those dependent, not on a state of the auditory nerve itself merely, but on sonorous vibrations excited in the auditory apparatus. Such are the buzzing sounds attendant on vascular congestion of the head and ear or on aneurismal dilatation of the vessels. Frequently even the simple pulsatory circulation of the blood in the ear is heard. To the sounds of this class belong also the buzz or hum, heard during the contraction of the palatine muscles in the act of yawning, during the forcing of air into the tympanum so as to make tense the membrana tympani.

Irritation or excitement of the auditory nerve is capable of giving rise to movements in the body and to sensations in other organs of sense. In both cases it is probable that the laws of reflex action, through the medium of the brain, come into play. An intense and sudden noise excites, in every person, closure of the eyelids, and, in nervous individuals, a start of the whole body or an unpleasant sensation throughout the body like that produced by an electric shock.

THE SENSE OF EQUILIBRIUM.

Although the utriculus, sacculus, and semicircular canals form the major part of the labyrinth and are closely associated with the cochlea in development, there is increasing evidence that these structures are not concerned with hearing, but rather with a sense of equilibrium. This view has been strengthened by recent investigations into the anatomical relations of the different elements in the auditory nerve, figure 435.

These structures have each a special modification of the sensory epithelium which receives the vestibular branch of the eighth nerve. These epithelial areas are differentiations of the embryonic ear pit, which is derived from the epiblast. In fishes which have well-developed semicircular canals and vestibule, this sensory epithelium has a common origin from the embryonic anlage which gives rise to the ear, the branchial sense organ, and the lateral line organs, all of which probably have static functions.

The Semicircular Canals. The semicircular canals are connected with the utriculus, are three in number on each side, and have been already shown to lie in space practically at right angles to one another. Each is filled with endolymph, and each has a special organ, the crista acustica, which receives a division of the vestibular branch of the eighth nerve.

The function of the semicircular canals is believed to be to give rise to sensations by which we determine the motion of the body in space. It was shown long ago that if one closes his eyes and turns rapidly around the vertical axis, then suddenly stops and opens the eyes, surrounding objects seem to be rotating around this same vertical axis. If the head be inclined so that the face is in the horizontal plane and the rotation around the vertical axis be repeated, then, upon suddenly raising the head into the ordinary position and opening the eyes, objects seem to be moving about the head around the horizontal axis. In both these cases the direction of the apparent motion of objects depends upon the actual motion of the body that preceded it and is in the opposite direction. In the first case the rotation is in the plane of the horizontal circular canal. It is assumed here that, at the beginning of such a movement, the endolymph, being fluid and inert, tends to remain still for a moment and the canal to move over it so as to produce pressure in the funnel of the ampulla. That is, it has the same effect as though the endolymph moved in the canal. This relative motion bends the hairs of the hair cells of the crista acustica, thus stimulating the hair cells and giving rise to sensory nerve impulses. When the head suddenly stops rotating the situation is just reversed and there will be a second stimulation, but in the opposite direction. When one considers the position of the three semicircular canals, it will be seen that movement of the head in any direction will stimulate one or more of the cristæ, giving rise to either simple or complex sensory impulses.

This theory is borne out by the effects of operation on the semicircular canals. By the observations of Flourens, injury to the semicircular canals causes disturbances in muscular coordination, especially in movements that take place in the plane of the injured canal. If a horizontal canal in a pigeon be sectioned, the animal supports its head in the vertical position very well, but is unable to coordinate its horizontal movements. It tends to produce rotary motions around the vertical axis. If a vertical canal is sectioned, the head falls to one or the other side according to the canal, and the animal shows instability of position in that plane. It has been shown that stimulation of a sectioned canal produced reflex movements in that plane.

Muscular coordination is a complex phenomenon and involves operation of numerous sensory impulses from other organs of the body, especially from the eye and general skin. Some confusion has arisen from the fact that there are associated with the disturbance in the semicircular canals movements of the eyes and head in higher animals, and of the eyes, head, and fins in such animals as fishes—the so-called compensatory movements. Without going into details, it is sufficient to state that the sense organs of the semicircular canals probably form only one of the series of sensory structures concerned in the coordination of movements.

The Utriculus and Sacculus. The utriculus and sacculus each have a sensory area, the maculæ, over which there rests in the human ear

and in most animals small particles of calcareous matter, otoliths. These otoliths, therefore, lie among the projecting hairs of the sensory cells. This is characteristic of these sensory areas and differentiates them from the arrangement present in the cristæ. There would seem to be close agreement in function between the maculæ and cristæ, and we naturally look to the influence of the otoliths on the processes which result in the stimulation of the maculæ. Attempts have been made to remove the otoliths, with the result that in such animals there is apparent inability to maintain a constant position in space. The experiments have been performed which have suggested the theory that the otoliths take an active part in stimulating the sensory cells, probably by their mere pressure. If the head is inclined in one or the other direction, the pressure of the otoliths will shift on the hair cells, and that is sufficient to stimulate them. If this view is correct, then we may regard these structures as static in function as compared with the semicircular canals, which are dynamic. The anatomical separation of the nerves for the cochlea from the division for the utriculus, sacculus, and semicircular canals itself suggests isolation in function, figures 389 and 435. It is conceivable that loud noises of an explosive nature may cause sufficient vibration of the endolymph to affect the otoliths and thus stimulate the cristæ. Yet, if such stimulation takes place it is probably only of secondary importance.

IV. THE SENSE OF SIGHT.

THE EYE.

The eye, the organ of vision, is the most complex and most highly developed of the organs of special sense. It consists not only of a special sensory epithelium, the retina, sensitive to light stimulation, but of a series of special structures which intensify and localize the stimulus. There are also accessory organs for the protection of the eye.

The Eyelids and Lachrymal Apparatus. The eyeball is kept moist over its free surface and protected from external injury by the eyelids, by the glands that secrete the lachrymal fluid to moisten the surface of the cornea, and by the oil glands that secrete oil on the margins of the lids.

The conjunctiva, or lining membrane of the lids, which is reflected on to the free surface of the eyeball, protects the eye from injury by its extraordinary sensitiveness to irritation by dust or other external substance. Its stimulation produces reflex secretion of the lachrymal fluid that flows over the surface of the eye, and tends to wash away the stimulating substance.

The Eyeball and its Parts. The detail of the structure of the eyeball is too complex to be given here except in so far as seems necessary for a clearer presentation of the physiological facts. A gross dissection reveals

the tough, white, *sclerotic* coat; the intermediate thin, vascular, pigmented *choroid* coat; and the inner nervous coat, the *retina*.

The section also shows that the eyeball is specialized in structure in its anterior region and that its contained cavity is divided into two parts, viz.,

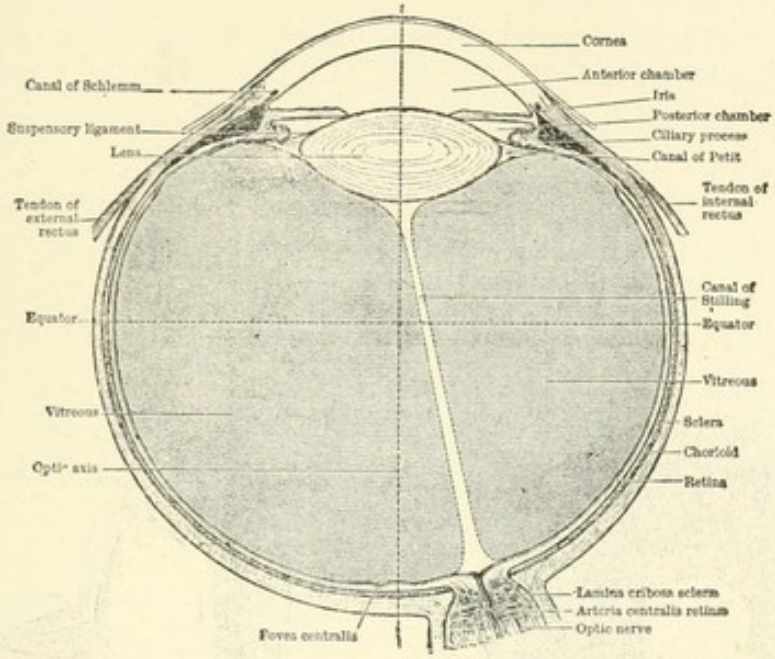


FIG. 441.—Section of the Eyeball.

the *anterior* and *posterior chambers* are filled with the transparent *aqueous fluid*. This fluid is like lymph in its composition. The *vitreous chamber* between the lens and the retina is filled with the clear jelly-like *vitreous substance*.

The Cornea. The sclerotic coat is continuous with the *cornea* in front of the eyeball, but the cornea is transparent and its radius of curvature

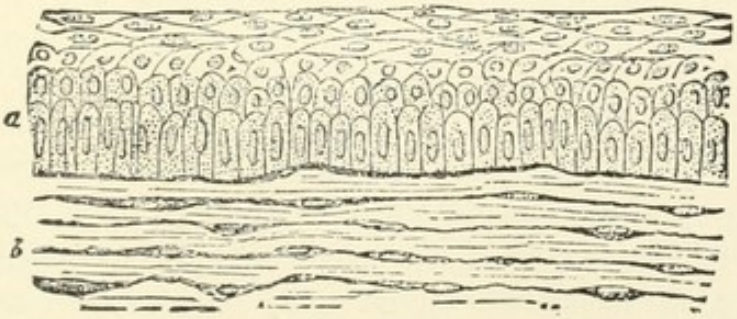


FIG. 442.—Vertical Section of Rabbit's Cornea. *a*, Anterior epithelium, showing the different shapes of the cells at various depths from the free surface; *b*, portion of the substance of cornea. (Klein.)

is less than that of the main portion of the eye. It is composed of stratified epithelial cells, and is richly supplied with sensory nerves that form an intra-epithelial plexus of delicate varicose fibrils. The cornea has no blood-vessels, but has a rich network of lymphatic spaces.

The Lens. The lens is a special modification composed of highly refractive material, situated just behind the iris. It is enclosed in a capsule and supported in its place by the suspensory ligament, which is fused into the capsule around its equator. The lens is a biconvex structure composed of transparent fibers which are arranged in concentric layers. Its posterior curvature is greater than the anterior, the radii being 6 and 10 mm. respectively.

The Ciliary Apparatus and the Iris. These structures are a continuation and modification of the choroid coat in the anterior portion of the eye. Around the circumference of the cornea the choroid coat is considerably thickened and folded in the modification known as the ciliary apparatus. A radial layer of muscle, figure 445, is knitted into the base of the cornea, on the one hand, and extends back into the choroid, on the other. Thick bundles of the circular fibers are also present in this mass of muscle. From the ciliary

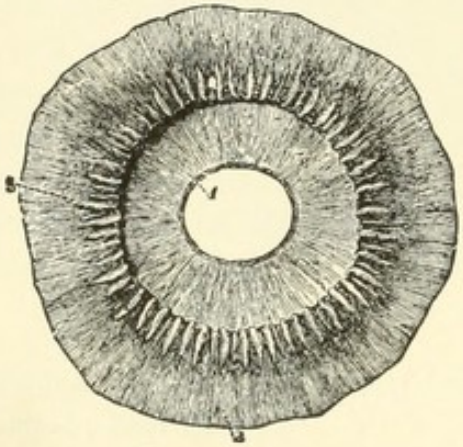


FIG. 443.

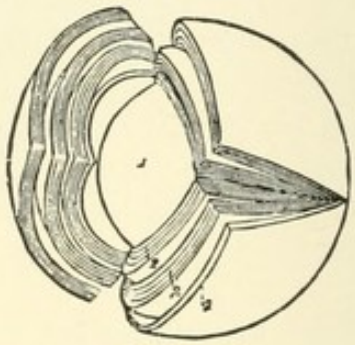


FIG. 444.

FIG. 443.—Ciliary Processes, as Seen from Behind. 1, Posterior surface of the iris, with the sphincter muscle of the pupil; 2, anterior part of the choroid coat; 3, one of the ciliary processes, of which about seventy are represented. ×½.

FIG. 444.—Laminated Structure of the Crystalline Lens. The laminæ are split up after hardening in alcohol. 1, The denser central part or nucleus; 2, the successive external layers. ×4. (Arnold.)

processes, extending over the lens, is the iris. It is a sheet of connective tissue and muscle lined with epithelium and highly pigmented.

In the middle anterior portion is a round aperture, the pupil. The muscle fibers are arranged circularly and radially and are of the unstriated muscle type. Contractions of the circular muscles of the iris produce constriction of the pupil, while contractions of the radial fibers produce dilatation. Both the ciliary apparatus and the iris are supplied with motor nerves.

Fibers of the third cranial nerve are distributed to the ciliary muscles, apparently to both radial and circular muscles, and when these nerves are stimulating the resulting contractions of the muscles tend to remove the tension from the capsule of the lens. These nerve fibers pass through the ciliary ganglion where they form a synapsis with ganglionic cells. Motor fibers from the third cranial nerve also supply the circular muscles of the iris, which produce constriction of the pupil through the motor nerves by way of the

cervical sympathetic and superior cervical ganglion, and the ophthalmic branch of the fifth cranial nerve.

Structure of the Retina. The retina occupies the deeper half of the cup of the eyeball. It extends forward as far as the ora serrata, where its complex structure changes the form to a simple epithelial layer, which lines the anterior portion of the eyeball and the ciliary processes. In the center of the retina is a round yellowish spot having a minute depression in its center, called the *yellow spot of Sömmering*. The depression in its center is the

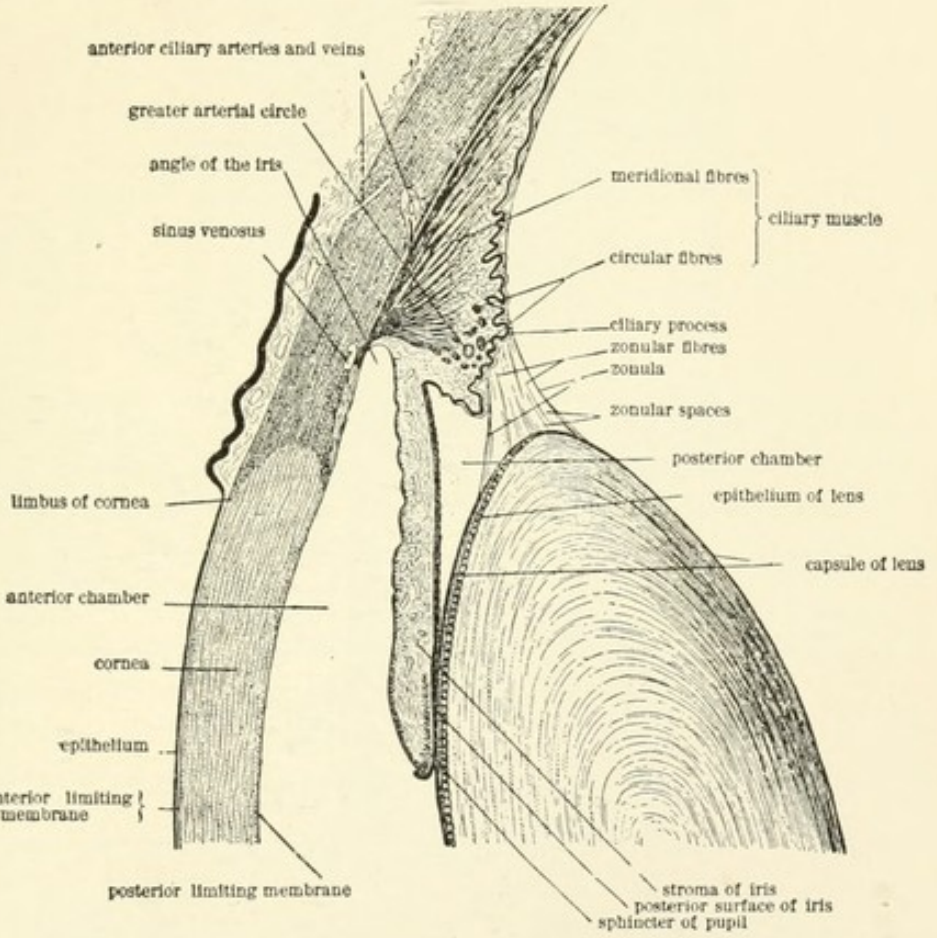


FIG. 445.—Meridional Section of a Portion of the Anterior Part of the Eyeball. (Toldt.)

fovea centralis. About 2.5 mm. to the inner side of the yellow spot is the point at which the optic nerve enters and spreads out its fibers into the retina.

The optic nerve arises from the base of the brain and passes forward toward the orbit, being covered by the membranes which cover the brain. The fibers of the optic nerve are exceedingly fine, and are surrounded by the myelin sheath, but do not possess the ordinary external nerve sheath. As they pass into the retina they lose their myelin sheaths and proceed as axis-cylinders (the cells of origin of these fibers are in the retina). Neuroglia supports the nerve fibers in the optic nerve trunk. In the center of the nerve is a small artery, the *arteria centralis retinæ*. The number of fibers in the

optic nerve is said to be upward of 500,000. The fibers of the optic nerve spread out over the inner surface of the retina as far as the ora serrata.

The retina itself consists of layers of nerve elements supported by delicate connective tissue. The older descriptions recognize some eight or ten layers in the retina, but the newer investigations of Cajal, Golgi, Retzius, and others have shown that the retina is a much simpler structure than heretofore described. The retina is formed of essentially three layers of nerve cells.

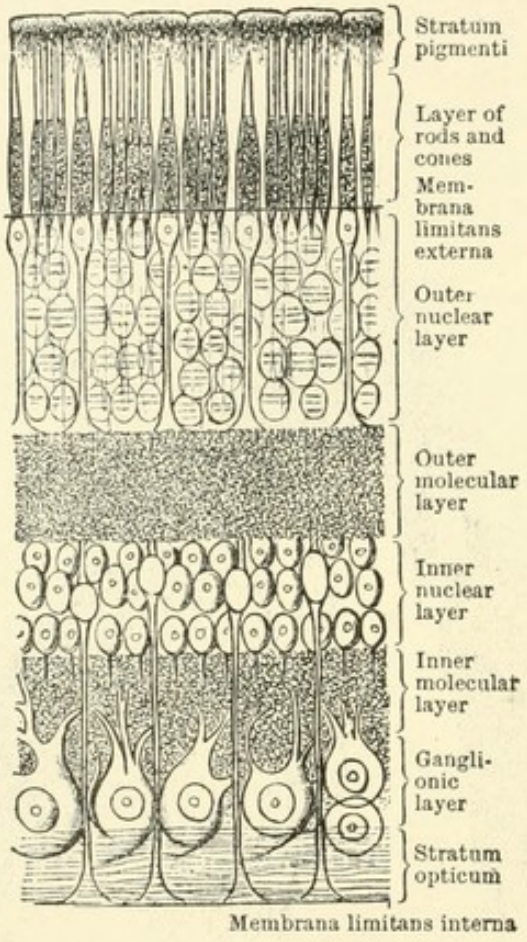


FIG. 446.—Section of Human Retina. (Cunningham, modified from Schulze.)

Naming from the center of the eye outward, they are: The ganglionic layer; the layer of bipolar cells; and the layer of rods and cones, figure 447. The cells of these layers have numerous fibrous processes which interlock in such a way that they seem to form different areas when studied in cross-section. If we recognize the strata of interlacing fibers, then the following may be made out:

The layer of ganglion cells. . .	1. Ganglionic layer, with the fibers of the optic nerve. 2. Internal molecular layer.
The layer of bipolar cells	3. Internal granular layer. 4. The external molecular layer.
The layer of visual cells.	5. The external granular layer. 6. The layer of rods and cones.

The Nerve Fiber and Nerve Cell Layers. The inside of the retina is formed of a layer of nerve fibers which have their origin in the adjacent large nerve cells and run toward the exit of the optic nerve. Externally the gan-

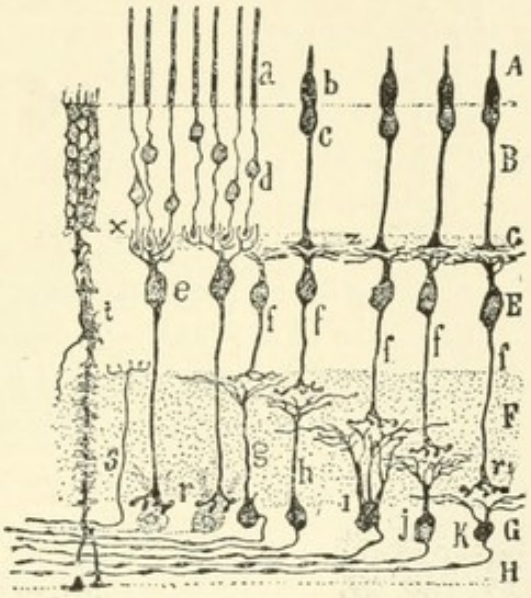


FIG. 447.—Transverse Section of a Mammalian Retina. *A*, Layer of rods and cones; *B*, bodies of visual cells (external granular); *C*, external molecular layer; *E*, layer of bipolar cells (internal granular); *F*, internal molecular layer; *G*, layer of ganglionic cells; *H*, layer of optic-nerve fibers; *a*, rod; *b*, cone; *c*, body of the cone cell; *d*, body of the rod cell; *e*, bipolar rod cells: *f*, bipolar cone cells; *g*, *h*, *i*, *j*, *k*, ganglionic cells ramifying in the various strata of the internal molecular zone; *r*, inferior arborization of the bipolar rod cells, connecting with the ganglionic cells; *r*, inferior arborization of the bipolar cone cells; *t*, epithelial or Müller cells; *x*, point of contact between the rods and their bipolar cells; *z*, point of contact between the cones and their bipolar cells; *s*, centrifugal nerve fiber. (Cajal.)

glionic cells send up numerous processes, or dendrites, which interlace with the fibers of the bipolar cells of the second layer.

The Middle Layer. The middle layer consists of bipolar cells which send one process toward the ganglionic layer to interlace with the dendrites of the

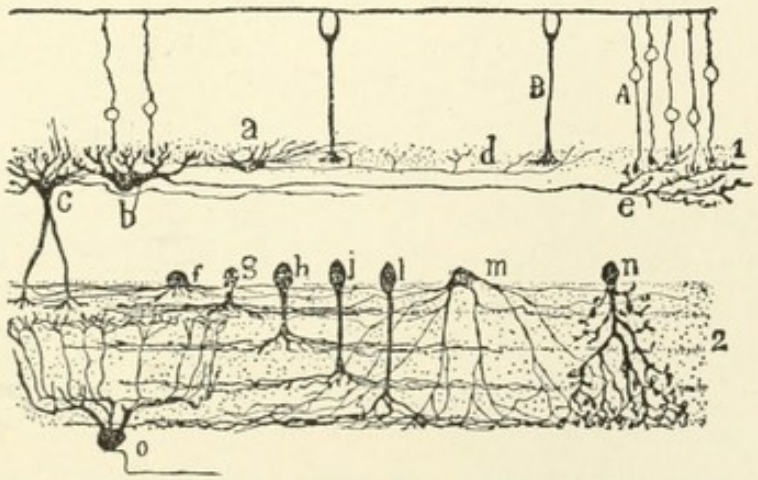


FIG. 448.—Perpendicular Section of the Retina of a Mammal. *A*, External grains or bodies of rods; *B*, bodies of cones; *a*, horizontal external or small cell; *b*, horizontal internal or large cell; *c*, horizontal internal cell with descending protoplasmic appendages; *e*, flattened arborization of one of the large cells; *f*, *g*, *h*, *j*, *l*, spongioblasts ramifying in the various strata of the internal molecular zone; *m*, *n*, diffuse spongioblasts; *o*, ganglionic cell; 1, external molecular zone; 2, internal molecular zone. (Cajal.)

ganglionic cells, and one process externally. This process is often divided into many branches, which separate out into a horizontal brush, interlacing with the processes of the rods and cones. Special cells have been described for this layer of the retina, as, for example, the spongioblasts of Cajal.

The External Layer of Rods and Cones. The rod cells are composed of two parts quite different in structure, known as the outer and inner limbs. The outer limb is a cylindrical rod about 30 μ long by 2 μ in diameter. It is transparent and composed of doubly refractive material. The inner limb of the cell is about the same length as the outer, is similar, and is longitudinally striated, and contains a nucleus on its course, figure 447, *d*.

The cone cells are also made up of two limbs, the outer of which is conical instead of cylindrical as in the case of the rods. In other respects they are similar to the rods in structure, with the exception that the inner limb ends in a brush of fibrils which interlace with the bipolar cells of the middle layer.

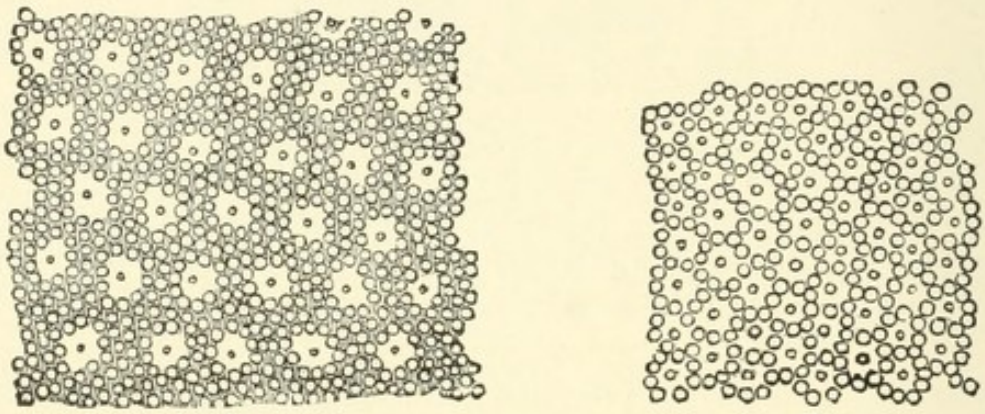


FIG. 449.—Distribution of the Rods and Cones. *A*, In the peripheral part of the retina; *B*, from the region of the macula lutea.

In man and mammals the number of rod cells are much greater than the cones, but it is said that in birds cones predominate. Even in man the center of the fovea centralis is devoid of rods and consists of cones only, figure 450.

All the elements of the retina are sustained and isolated by large cells lying vertically which are known as the *fibers of Müller*. The nucleus of the fiber of Müller is found at the level of the internal granular layer, and the two extremities of the protoplasm or cell body are condensed in two homogeneous layers, known as the *external* and the *internal limiting layer*. The external limiting layer is placed just between the two segments of the rod and cone cells. The internal limiting layer is situated upon the internal surface of the retina.

At the ora serrata the layers are not perfect and disappear in this order: nerve fibers and ganglion cells, then the rods, leaving only the inner limbs of the cones, these cease, then the inner molecular layer. The Müllerian fibers persist.

At the pars ciliaris retinæ, the retina is represented by a layer of columnar cells, derived from the fusion of the nuclear layers which are in contact with the pigment layers of the retina and continued over the ciliary processes.

Pigment Layer. This layer, which was formerly considered part of the choroid, consists of cells which cover and entirely surround the outer limbs of the rods and cones.

Blood-vessels of the Eyeball. The eye is very richly supplied with blood-vessels. In addition to the conjunctival vessels, which are derived from the palpebral and lachrymal arteries, there are at least two other distinct sets of vessels supplying the tunics of the eyeball. 1, The vessels of the sclerotic, choroid, and iris, and 2, the vessels of the retina. The first are the short and long *posterior* ciliary arteries which pierce the sclerotic in the posterior half of the eyeball, and the *anterior* ciliary which enter near the insertions of the recti. These vessels anastomose and form a very rich choroidal plexus; they also supply the iris and ciliary processes, forming a very highly vascular circle round the outer margin of the iris and adjoining portion of the sclerotic. The distinctness of these vessels from those of the conjunctiva is well seen in the difference between the bright red of blood-shot eyes (conjunctival congestion), and the pink zone surrounding the cornea which indicates deep-seated ciliary congestion.

The central artery of the optic nerve enters the retina from the center of the optic disc and sends out branches over the retinal cup lying in the nerve

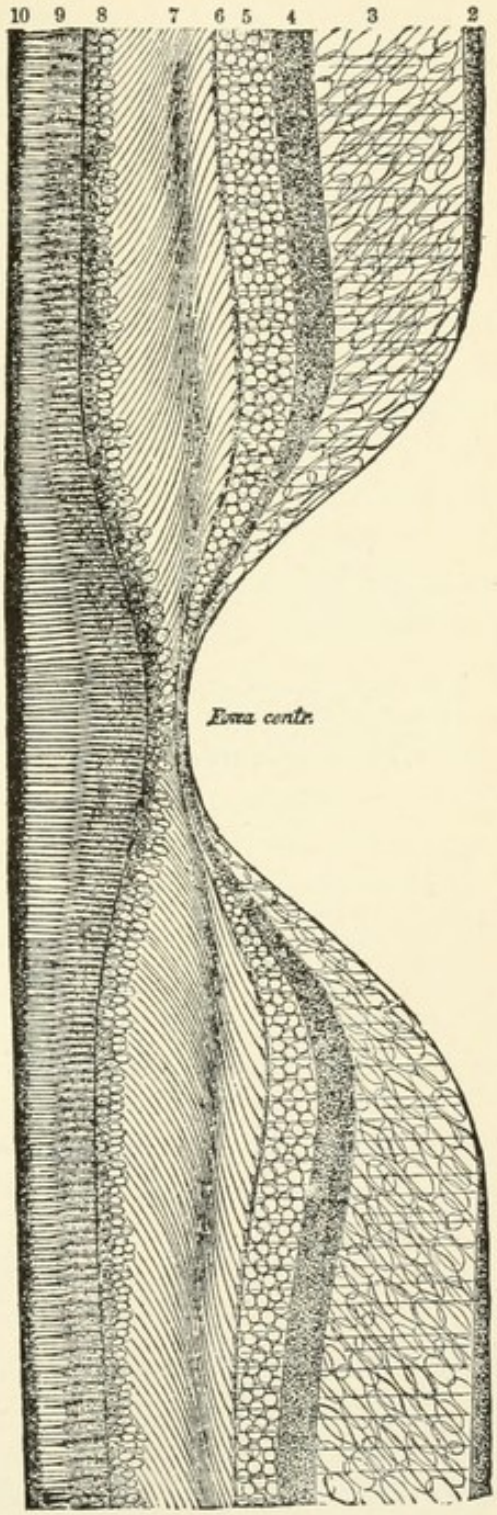


FIG. 450.—Diagrammatic Section of the Macula Lutea and Fovea Centralis. 2, Layer of nerve fibers; 3, layer of multipolar cells; 4, internal molecular layer, composed of intertwining arborescent processes; 5, layer of bipolar cells, or internal granular layer; 6, external molecular layer, composed of intertwining arborescent processes; 7, nuclei of epithelial cells, or external granular layer; 8, frillwork formed by processes from fibers of Müller, often called the "external limiting membrane"; 9, layer of rods and cones; 10, layer of pigment epithelium.

fiber layer, figure 451. These blood-vessels, however, are absent from the fovea centralis and reduced in size in the macula lutea, figures 451 and 452.

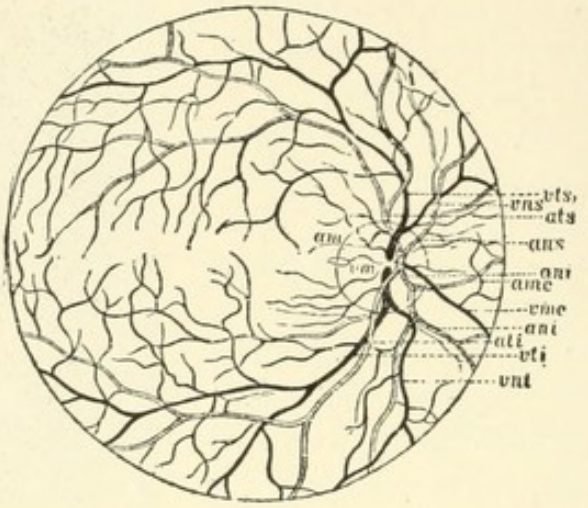


FIG. 451.—Diagram of the Blood-vessels of the Human Retina. (Leber, after Jaeger.) *ans*, *vns*, Superior nasal artery and vein; *ats*, *vts*, superior temporal artery and vein; *ani*, *vni*, inferior nasal artery and vein; *ati*, *vti*, inferior temporal artery and vein; *am*, *vm*, macular artery and vein; *ame*, *vme*, median artery and vein.

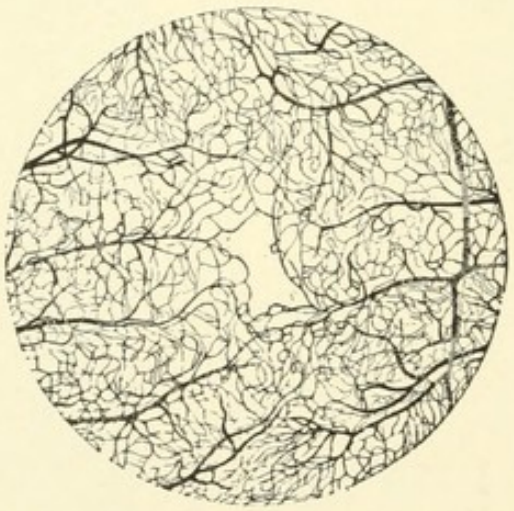


FIG. 452.—Blood-vessels of the Macula Lutea. The part that is totally free from vessels is the fovea centralis.

THE OPTICAL APPARATUS.

The optical apparatus may be supposed, for the sake of description, to consist of several parts; 1, A system of transparent refracting surfaces and media by means of which images of external objects are brought to a focus upon the back of the eye; 2, a sensitive screen, the retina, which is a specialized sensory apparatus in connection with the terminations of the optic nerve, and capable of being stimulated by luminous objects, and of sending such impressions as to produce in the brain visual sensations. To these main

parts may be added, 3, an apparatus for focussing light from objects at different distances from the eye; and 4, since both eyes are usually employed in vision, an arrangement by means of which the eyes may be turned in the same direction so that binocular vision is possible. The arrangement of the optic nerve fibers, and of the continuation of these backward in the optic chiasma, and thence to special districts of the brain have already been discussed.

The eye may be compared to a photographic *camera*, and the transparent refracting media correspond to the photographic lens. In a camera images of external objects are thrown upon a screen, the sensitive plate, at the back of the camera box. In the eye, the camera proper is represented by the eyeball with its choroidal pigment, the sensitive screen by the retina, and the lens by the refracting media. In the case of the camera, the screen is adjusted to receive clear images of objects at different distances by an apparatus for focussing. The corresponding adjustment in the eye is accomplished by the accommodating apparatus.

Refractive Media and Surfaces. At first sight it would seem as if the refracting apparatus of the eye were very complicated, since it consists of so many parts. These parts are: the anterior surface of the cornea itself, the posterior surface of the cornea, the aqueous humor, the anterior surface of the lens, the substance of the lens itself (which is unequally refractive), the posterior surface of the lens, and the vitreous humor. Thus there are four surfaces, and at least, including the air, five media. For all practical purposes, however, we may leave out of consideration all but three refracting surfaces and their adjacent media. These are: the anterior surface of the cornea, separating the air and the corneal substance; the anterior surface of the lens, separating the aqueous humor and the lens substance; and the posterior surface of the lens, separating the lens surface from the vitreous humor.

Image Formation. In the refraction through a simple transparent spherical surface there are certain cardinal points to be considered. The rays of light which fall perpendicularly on such a surface pass through without refraction. All such rays cut the center of the radius of curvature of the lens, called the *nodal point*. A line that passes through the center of curvature of a lens and thus pierces the nodal point is called the *optical axis*, and the point on the surface pierced by the optical axis is the *principal point*. In every optical system there are certain other cardinal facts to be considered. All rays which do not strike vertical to the curved surface are refracted toward the optical axis. Rays which impinge upon the spherical surface of a lens parallel to the optical axis will meet at a point upon the axis called the *posterior principal focus*, figure 453, *F*. The posterior principal focus is outside of the nodal point. Again, there is a point in the optical axis in front of the surface, rays of light from which strike the surface so that they are

refracted in a line parallel with the axis, df''; such a point, F_2, is called the *anterior principal focus.*

In any given system the principal foci can be found by erecting verticals at the nodal and principal points of the optical axis and laying off lengths on each, *a* and *b*, proportional to the refractive indices of the media. A line drawn through *a* on the principal vertical and *b* on the nodal vertical will cut the optical axis at the posterior principal focus, and *vice versa.*

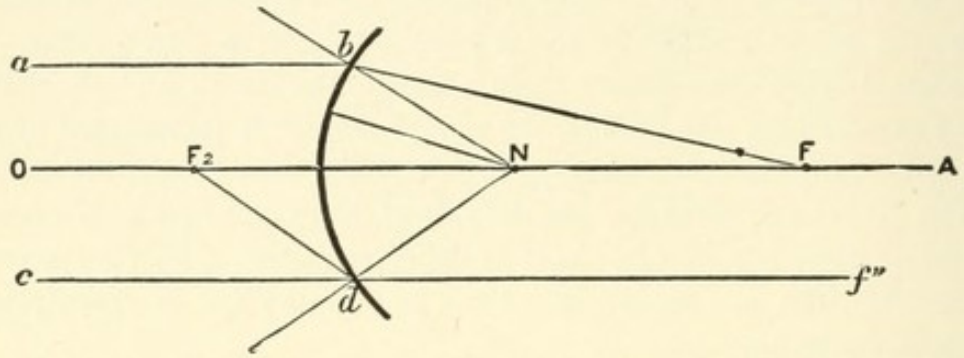


FIG. 453.—Diagram of a Simple Optical System. (Foster.) The curved surface, *bd*, is supposed to separate a less refractive medium toward the left from a more refractive medium toward the right.

If a luminous point outside the anterior principal focus is considered, it is obvious that rays from it will be so refracted when they enter the convex surface that they will become converging and will ultimately meet again in a point or focus. Two such points form conjugate foci, figure 454. If the anterior focus of a conjugate is moved away from the anterior principal focus, then the posterior conjugate will move toward the posterior principal focus, and the converse. If one conjugate is known, the other can be found as

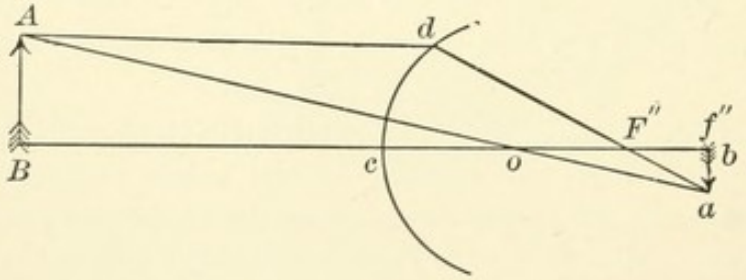


FIG. 454.—Diagram to Show the Relations of Conjugate Foci. *cd*, Refracting surface; *AB* and *ba*, conjugate foci; *o*, nodal point; *F''*, posterior principal focus.

follows: From a point in the plane of the known conjugate, but outside the principal axis, draw two rays, one perpendicular to the refracting surface which will pass through the nodal point, the other parallel to the principal axis. The latter will be refracted through the posterior principal focus and when prolonged will meet the first ray in the plane of the second conjugate, figure 454, *a*. This relationship between conjugate foci is played upon in the focussing of a camera.

It is quite obvious that the eye, even considering only the three surfaces above indicated, is a much more complicated optical apparatus than the one described in the figure. It is, however, possible to reduce the refractive surfaces and media to a simpler form when the refractive indices of the different media and the curvature of each surface are known. All of these data have been very carefully collected. They are as follows:

Index of refraction of aqueous and vitreous,	=	1.3365
" " " " the lens,	=	1.4371
Radius of curvature of cornea,	=	7.829 mm.
" " " anterior surface of lens,	=	10.0 "
" " " posterior " "	=	6.0 "
Distance from anterior surface of cornea and anterior surface of lens,	=	3.6 "
Distance from posterior surface of cornea and posterior surface of lens,	=	7.2 "

With these data it has been found comparatively easy by mathematical calculation to reduce the different refractive surfaces of the different curvatures into one mean curved surface of known curvature, and the differently refracting media into one mean medium the refractive power of which is known.

The simplified or so-called schematic eye, formed upon this principle, suggested by Listing as *the reduced eye*, has the following dimensions:

From the anterior surface of the cornea to the principal point,	=	2.3448 mm
From the nodal point to the posterior surface of lens,	=	0.4764 "
Posterior chief focus lies behind cornea,	=	22.8237 "
Anterior chief focus in front of cornea,	=	12.8326 "
Radius of curvature of ideal surface,	=	5.1248 "

In this reduced or simplified eye the principal posterior focus, about 23 mm. behind the spherical surface, would correspond to the position of the retina behind the anterior surface of the cornea. The refracting surface would be situated about midway between the posterior surface of the cornea and the anterior surface of the lens.

The *optical axis* of the eye is a line drawn through the centers of curvature of the cornea and lens, and when prolonged backward it cuts the retina between the optic disc and the fovea centralis. This differs somewhat from the visual axis which passes through the nodal point of the reduced eye to the fovea centralis, and forms an angle of five degrees with the optical axis. The visual or optical angle is the angle included between the lines drawn from the borders of any object through the nodal point. It has been shown by Helmholtz that the smallest angular distance between two points which can be appreciated is fifty seconds, the size of the retinal image being 3.65 μ; this practically corresponds to the diameter of the cones at the fovea centralis which is 3 μ, the distance between the centers of two adjacent cones being 4 μ.

The image of an object formed upon the retina may be considered as a series of points, from each of which a pencil of light diverges to the eye, and

this pencil has for its center or axis a ray which impinging upon the refractive surface perpendicularly to the surface is not refracted, but passes through the nodal point and is prolonged backward to the retina, whereas the diverging rays are also made to converge to a principal posterior focus behind the lens,

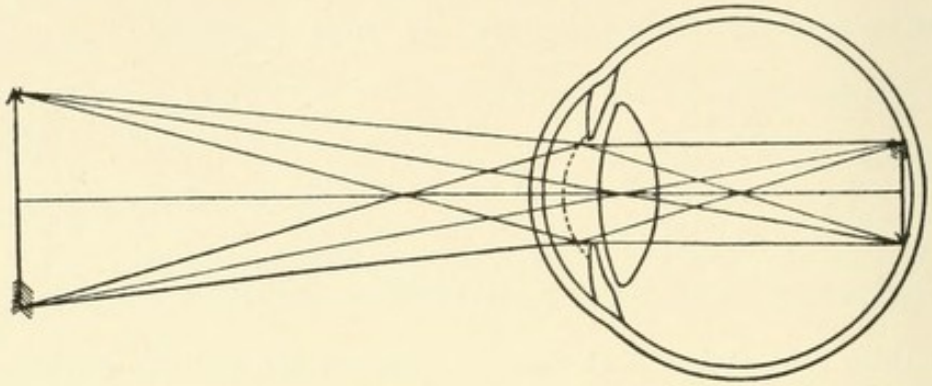


FIG. 455.—Diagram of the Method of the Formation of an Inverted Image Exactly Focussed upon the Retina. The dotted line is the ideal surface of curvature.

or the chief axis of the pencil of light proceeding from the point in question, and this focus, if the image is to be clear, should fall on the retina.

Thus from each point of an object a corresponding image is formed on the retina, so that an image of the distant object is produced. It is an inverted image. Whether the image is blurred or not depends upon the refractive power of the media, and upon the distance of the anterior surface of the cornea from the retina. If the refractive media are too powerful, or the eye too long, the image is formed in front of the retina, figure 456; if the reverse, the image

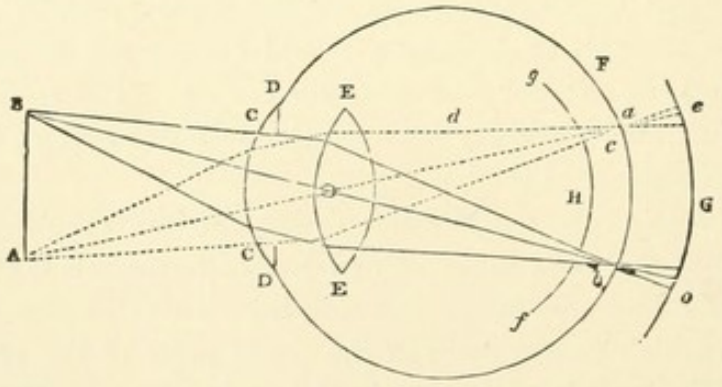


FIG. 456.—Diagram of the Course of a Ray of Light, to Show how a Blurred or Indistinct Image is Formed if the Object be not Exactly Focussed upon Retina. The surface *CC* should be supposed to represent the ideal curvature. The nodal point should be nearer the posterior surface of lens as in figure 455.

is formed behind the retina, and in both cases an indistinct and blurred image is the result.

Accommodation. The distinctness of the image formed upon the retina is mainly dependent on the perfection with which the rays emitted by each luminous point of the object are brought to a focus upon the retina.

If this focus occurs at a point either in front of or behind the retina, indistinctness of vision ensues, in the way we have just described, with the production of a halo. The *focal distance, i.e.*, the distance of the point at which the luminous rays are collected from a lens, besides being regulated by the degree of convexity and density of the lens, varies with the distance of the object from the lens, being greater as this is shorter, and *vice versa*. In other words, the luminous points on the object and the focal points on the retina are conjugate foci. Hence, since objects placed at various distances from the eye can within certain limits be seen with almost equal distinctness, there must be some provision by which the eye is enabled to adapt itself, so that, at whatever distance the luminous object may be, the focal point may always fall exactly upon the retina.

Accommodation is the act of adapting the eye to vision at different distances. It is obvious that the effect might be produced in either of two ways, viz., 1, by altering the convexity, and thus the refracting power, either of the cornea or of the lens; or 2, by changing the position of the lens relative to the retina, as in the focussing of a camera, so that whether the object be near or distant, the focal points to which the rays are converged by the lens may always fall exactly on the retina. The amount of either of these changes which is required in even the widest range of vision is extremely small, for from the refractive powers of the media of the eye the difference between the focal distances of the images of an object at a distance and of one at four inches is only about 3.5 mm. On this calculation the change in the distance of the retina from the lens required for vision at all distances, supposing the cornea and lens to remain the same, would not be more than about one line. Beer has shown that the second method is indeed the type of accommodative apparatus in fishes. But in man and the higher animals accommodation occurs by the first method, *i.e.*, by changing the convexity of the refracting surface.

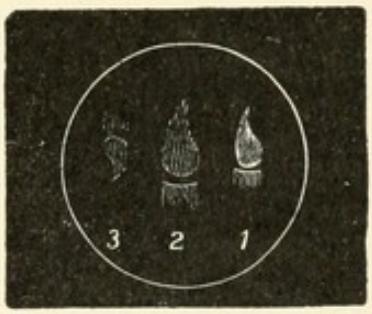


FIG. 457.—Diagram Showing Three Reflections of a Candle. 1, From the anterior surface of cornea; 2, from the anterior surface of lens; 3, from the posterior surface of lens. For further explanation, see text. The experiment is best performed by employing an instrument invented by Helmholtz, termed a *Phakoscope*.

The accommodation of the human eye for objects at different distances is primarily due to a varying shape of the lens, its front surface becoming more or less convex, according as the distance of the object looked at is near or far. The nearer the object, the more convex the front surface of the lens, up to a certain limit, and *vice versa;* the back surface takes little or no share in accommodation. The following simple experiment illustrates this point: If a lighted candle be held a little to one side of a person's eye, an observer looking at the eye from the other side sees three distinct images of the flame,

figure 457. The first and brightest is, 1, a small erect image formed by the anterior convex surface of the cornea; the second, 2, is also erect, but larger and less distinct than the preceding, and is formed at the anterior convex surface of the lens; the third, 3, is smaller, inverted, and indistinct; it is formed at the posterior surface of the lens, which is concave forward, and

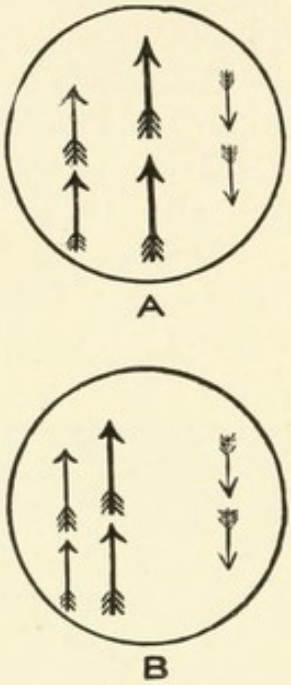


FIG. 458.

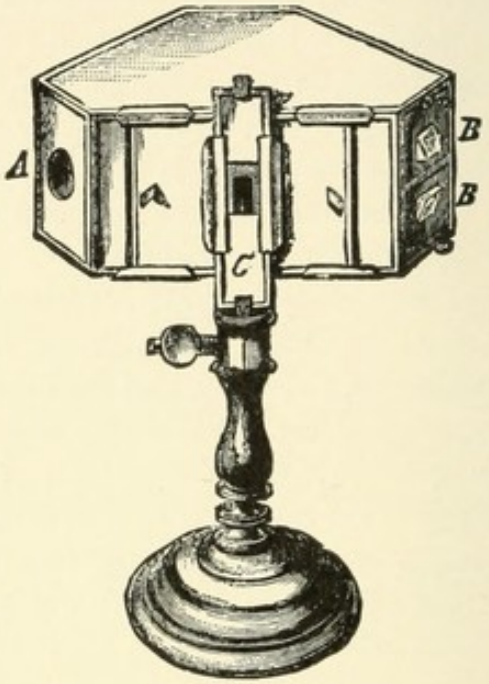


FIG. 459.

FIG. 458.—Diagram of Sanson's Images. *A*, When the eyes are focussed for far objects, and *B*, when they are focussed for near objects. The figure to the right in *A* and *B* is the inverted image from the posterior surface of the lens.

FIG. 459.—Phakoscope of Helmholtz. At *B*, *B'*, are two prisms, by which the light of a candle is concentrated on the eye of the person experimented with at *C*. *A* is the aperture for the eye of the observer. The observer notices three double images, as in figures 457 and 458, reflected from the eye under examination when the eye is fixed upon a distant object; the position of the images having been noticed, the observed eye is then focussed on a near object, such as a reed pushed up by *C*; the images from the anterior surface of the lens will be observed to move toward each other, in consequence of the lens becoming more convex.

therefore, like all concave mirrors, gives an inverted image. If now the eye under observation be made to look at a near object, the second image becomes smaller, clearer, and approaches the first. If the eye be now adjusted for a far point, the second image enlarges again, becomes less distinct, and recedes from the first. In both cases alike the first and third images remain unaltered in size, distinctness, and relative position. This proves that during accommodation for near objects the curvature of the cornea, and that of the *posterior* surface of the lens, remain unaltered, while the *anterior* surface of the lens becomes more convex and approaches the cornea.

The experiment, figure 458, is more striking when the two prisms of the phakoscope which form two images of the candle are used. The pair of images of the candle from the front surface of the lens not only approach those from the cornea during accommodation, but also approach one another, and become somewhat smaller, Sanson's images.

The Mechanism of Accommodation. The mechanism of accommodation depends primarily upon the inherent tendency of the lens to approximate the shape of a sphere. When the eye is at rest the intra-ocular tension is such as to put stress on the suspensory ligament around its equator, which compresses the elastic lens in its antero-posterior dimension. The elasticity of the lens can make itself apparent when the tension of the suspensory ligament is relaxed. This takes place completely after a division of the fibers of the zonula. When we remove the lens from the eye of a young person, we see it assume the spherical shape immediately upon the division of its connections. In life this slackening of the tension of the suspensory ligament of the lens is brought about by the contraction of the fibers of the ciliary body. This allows the anterior surface of the lens to become more convex, by its own elastic powers, thus focussing entering rays of light from a near object upon the retina, figure 460. It therefore appears that when the eye is at rest it is focussed for distant objects, inasmuch as the suspensory ligament is taut and the anterior surface of the lens more flattened. The normal eye is passive when in focus for distant objects. It is the active contraction of the muscles of accommodation that focusses for near objects. The iris acts in coordination with the accommodative contractions of the ciliary muscles. In viewing near objects the pupil contracts, and upon viewing distant ones it dilates.

Range of Distinct Vision. *Near-point.* In every eye there is a limit to the power of accommodation. If a book be brought nearer and nearer to the

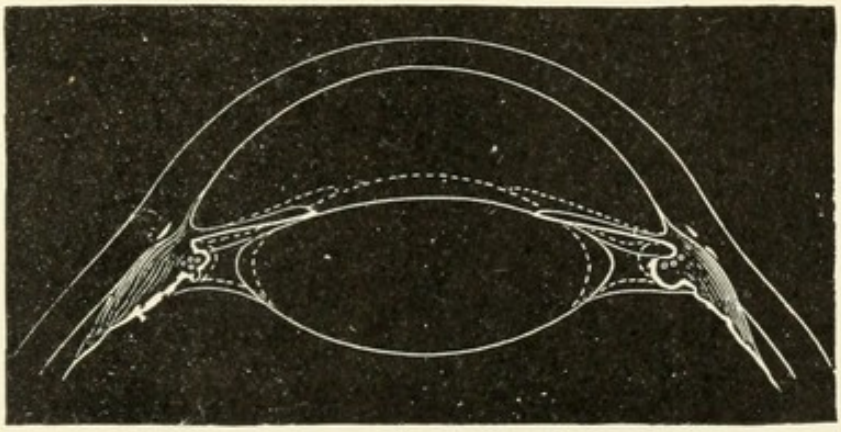


FIG. 460.—Diagram Representing by Dotted Lines the Alteration in the Shape of the Lens on Accommodation for Near Objects. (E. Landolt.)

eye, the type at last becomes indistinct, and cannot be brought into focus by any effort of accommodation, however strong. This limit, which is termed the *near-point*, can be determined by the experiment of Scheiner. Two small holes not more than 2 mm. apart are pricked in a card with a pin; at any rate their distance from each other must not exceed the diameter of the pupil. The card is held close in front of the eye, and a small needle viewed

through the pin-holes. At a moderate distance it can be clearly focussed, but when brought nearer, beyond a certain point, the image appears double and more or less blurred. This point where the needle ceases to appear single is the near-point of vision. Its distance from the eye can of course be readily

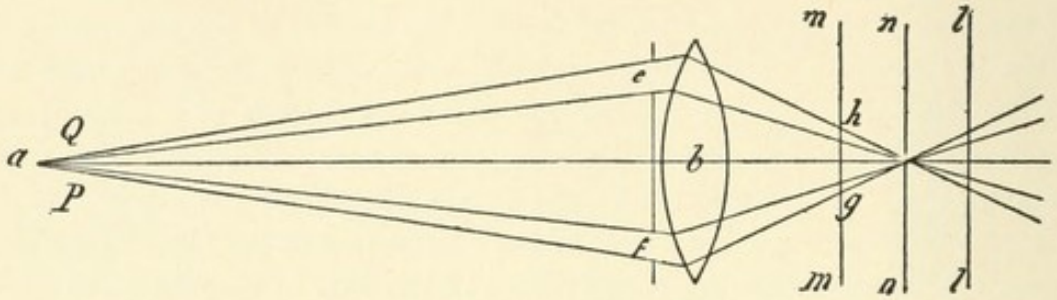


FIG. 461.—Diagram of Experiment to Ascertain the Minimum Distance of Distinct Vision.

measured. It is usually about five or six inches, 12 to 15 cm. In the accompanying figure, 461, the lens *b* represents the eye; *e*, *f*, the two pin-holes in the card, *nn* the retina; *a* represents the position of the needle. When the needle is at a moderate distance, the two pencils of light coming from *e* and *f* are focussed at a single point on the retina *nn*. If the needle be brought nearer

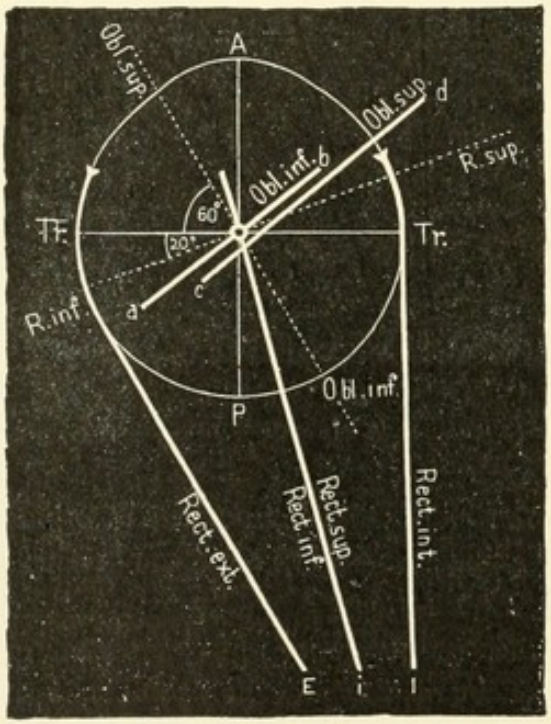


FIG. 462.—Diagram of the Axes of Rotation of the Eye. The thin lines indicate axes of rotation, the thick the position of muscular attachment.

than the near-point, the strongest effort of accommodation is not sufficient to focus the two pencils, they meet at a point behind the retina. The effect is the same as if the retina were shifted forward to *mm*. Two images *h*, *g*, are formed, one from each hole. It is interesting to note that when in this way

two images are produced, the lower one g really appears in the position Q, while the upper one appears in the position P. This may be readily verified by covering the holes in succession.

During accommodation two other changes take place in the eyes. *The eyes converge* by the action of the extra-ocular muscles, chiefly by the internal and inferior recti or internal and superior recti. The pupils contract.

Movements of the Eye. The eyeball possesses movement around three axes indicated in figure 462, viz., an antero-posterior, a vertical, and a transverse, passing through a center of rotation a little behind the centre of the optic axis. The movements are accomplished by pairs of muscles.

Direction of Movement.	By what muscles accomplished.
Inward,	Internal rectus.
Outward,	External rectus.
Upward,	Superior rectus. and Inferior oblique.
Downward,	Inferior rectus. and Superior oblique.
Inward and upward,	Internal and superior rectus. and Inferior oblique.
Inward and downward,	Internal and inferior rectus. and Superior oblique.
Outward and upward,	External and superior rectus. and Inferior oblique.
Outward and downward,	External and inferior rectus. and Superior oblique.

The contraction of all of the muscles during the act of accommodation, viz., of the ciliary muscle, of the recti muscles, and of the sphincter pupillæ, is under the control of the fibers of the third nerve. But the superior oblique may also be employed, in which case the fourth nerve is concerned.

Reflexes of the Pupil. Contraction of the iris may occur under the following circumstances: 1, On exposure of the eye to a bright light; 2, On the local application of eserine (active principle of Calabar bean); 3, On the administration internally of opium, aconite, and in the early stages of chloroform and alcohol poisoning; 4, On division of the cervical sympathetic or of stimulation of the third nerve. Dilatation of the pupil occurs, 1, in a dim light; 2, when the eye is focussed for distant objects; 3, on the local application of atropine and its allied alkaloids; 4, on the internal administration of atropine and its allies; 5, in the later stages of poisoning by chloroform, opium, and other drugs; 6, on paralysis of the third nerve; 7, on stimulation of the cervical sympathetic, or of its center in the floor of the front of the aqueduct of Sylvius. The contraction of the pupil is under the control of a center in the floor of the aqueduct beneath the anterior corpora quadrigemina. This center is reflexly stimulated by a bright light, and the dilatation when the center is not in action is due to the stimulation of the radial fibers of the iris by sympathetic nerves. In addition, it appears that both

contraction and dilatation may be produced by a local action of certain drugs which is independent of and probably often antagonistic to the action of the central apparatus of the third and sympathetic nerves.

The close coordination between the two eyes is nowhere better shown than by the condition of the pupil. If one eye be shaded by the hand its pupil will of course dilate; the pupil of the other eye will also dilate, though unshaded, due to crossed reflex action.

Defects in the Optical Apparatus. Under this head we may consider the defects known as: 1, Spherical Aberration; 2, Chromatic Aberration; 3, Astigmatism; 4, Myopia; 5, Hypermetropia.

The normal or emmetropic eye is so perfect that parallel rays are brought exactly to a focus on the retina without any effort of accommodation, figure 466. Hence all objects except near ones (in practice all objects at a distance of twenty feet or more) are seen without any effort of accommodation; in other words, the far-point of the normal eye at rest is at an infinite distance. In viewing near objects we are conscious of the effort (the contraction of the ciliary muscle) by which the anterior surface of the lens is rendered more convex, and rays which would otherwise be focussed behind the retina are converged upon the retina.

Spherical Aberration. The rays of a cone of light from an object situated in the field of vision do not all meet in the same point, owing to the greater refraction of the rays which pass through the circumference of a lens than that of those traversing its central portion. This defect is known as *spherical aberration.* In the camera, telescope, microscope, and other optical instruments it is remedied by the interposition of a screen with a circular aperture in the path of the rays of light, cutting off all the marginal rays and allowing the passage only of those near the center. Such correction is effected in the eye by the iris, which forms a diaphragm to cover the circumference of the lens, and prevents the rays from passing through any part of the lens but its center, which corresponds to the pupil. The iris is pigmented to prevent the passage of rays of light through its substance. The image of an object will be most defined and distinct when the pupil is small, if the light is abundant; so that, while a sufficient number of rays are admitted, the narrowness of the pupil may prevent the production of indistinctness of the image by *spherical aberration.* But even the image formed by the rays passing through the circumference of the lens, when the pupil is much dilated, as in the dark, or in a feeble light, may, under certain circumstances, be well defined.

Distinctness of vision is further secured by the pigment of the outer surface of the retina and of the posterior surface of the iris and the ciliary processes, which absorbs any rays of light that may be reflected within the eye, and prevents their being thrown again upon the retina so as to interfere with the images formed there. The pigment of the retina is especially important in this respect; for with the exception of its outer layer the retina is

very transparent; and if the surface behind it were not of a dark color, but capable of reflecting the light, the luminous rays which had already acted on the retina would be reflected again and would fall upon other parts of the same membrane, producing indistinctness of the images.

Chromatic Aberration. In the passage of light through the periphery of an ordinary convex lens, decomposition of each ray into its elementary colored parts commonly ensues, and a colored margin appears around the image, owing to the unequal refraction which the elementary colors undergo. This is termed *chromatic aberration.* It is corrected by the use of lenses constructed of alternate layers of glass of different refractive indices so ground that they produce chromatic dispersion in opposite directions and thus mutually correct any chromatic aberration which may have resulted. The human eye has considerable chromatic aberration, as may readily be demonstrated, experiment 13, page 673.

An ordinary ray of white light in passing through a prism has its constituent rays refracted in unequal degrees, and therefore appears as colored bands fading off into each other, known as the spectrum. The colors of the spectrum are arranged as follows: red, orange, yellow, green, blue, indigo, violet; of these the red ray is the least, and the violet the most, refracted. Hence, as Helmholtz has shown, the rays from a white point cannot be accurately focussed on the retina, for if we focus for the red rays, the violet are out of focus, and *vice versâ:* such objects, if not exactly focussed, are often seen surrounded by a pale yellowish or bluish fringe.

For similar reasons a red surface looks nearer than a blue one at an equal distance, because, the red rays being less refrangible, a stronger effort of accommodation is necessary to focus them, and the eye is adjusted as if for a nearer object, and therefore the red surface appears nearer, experiment 13.

Astigmatism. This defect, which was first discovered by Airy, is due to a greater curvature of the refractive surfaces of the eye in certain meridians than in others. Thus vertical and horizontal lines crossing each other cannot both be focussed on one plane; one set stands out clearly, and the others are blurred and indistinct. This defect, which is generally present in a slight degree in all eyes, is usually seated in the cornea, but occasionally in the lens as well.

The plane of greatest curvature in the cornea is usually in the vertical meridian, a fact which doubtless comes from the pressure of the eyelids during development. If one looks at figure 463, *A* or *B*, with one eye, the three lines in the radii of the figure will be seen with unequal distinctness. Certain sets will stand out sharp and black and others dim and with indistinct outlines, and if the astigmatism is great enough the three lines may not be distinguished. Figures *C* and *D* of this series enable one to detect minute traces of astigmatism with great accuracy.

It is somewhat difficult to picture the rays from a luminous point in their

courses through eyes which have this defect, but an examination of figure 464 will show their refraction. In this figure four rays coming from the point L in the arrows are represented as striking on the refractive surface of the eye at A, B, C, D, and being converged toward a focus. The rays A, C, separated by vertical line on the refractive surface, are focussed at f_1, while the lines A, B, separated by the horizontal distance on the refractive surface, are

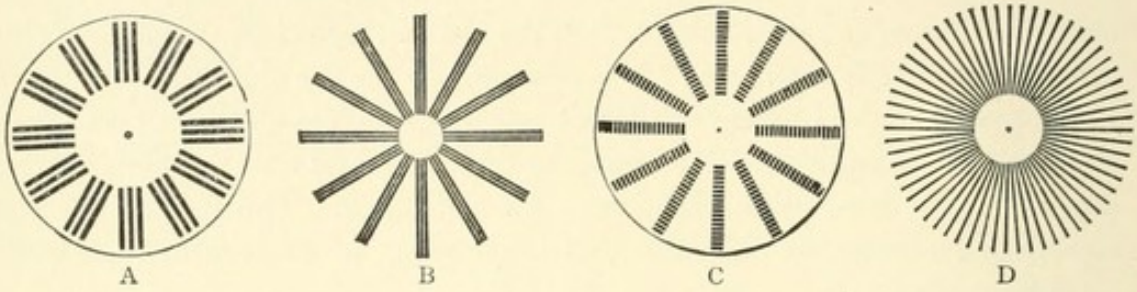


FIG. 463.—Astigmatic Charts.

brought to a focus at f_2. The point L, therefore, has two apparent focal points, one point composed of the rays that strike in a horizontal plane, f_2, the other of rays that strike in a vertical plane, f_1. If the retina of the eye be placed at f_1 it will see an image of a point with indistinct horizontal rays. If placed at the position f_2 it will see a luminous point with indistinct rays in the vertical plane. If the series of points in the arrow MN be considered, it is evident that at the position f_1 the rays which fall in the vertical plane will form distinct foci, while those that fall in the horizontal plane will form overlapping diffuse images in that plane. Since they are overlapping, they will not appear separate except at the ends of the image of the arrow, and the arrow will therefore be seen distinctly. If the position f_2 is considered where the rays of the horizontal plane are focussed, then it is evident that

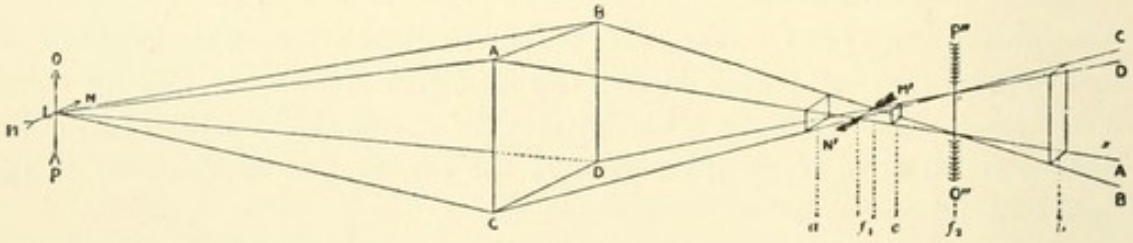


FIG. 464.—The Unequal Refraction of Rays in an Astigmatic Eye. (John Green.)

the points in the arrow MN will present a series of rays or halos in the vertical plane, thus rendering its outline very dim or indistinct. The condition with the arrow OP is exactly the reverse. Hence, in the astigmatic eye the images of the horizontal arrow MN will be distinct at the focus f_1, while the image of the vertical arrow OP will be distinct in the focus f_2, and the eye cannot see the two lines distinctly at the same time. This condition is

further illustrated in figure 465 which represents the position f_1 shown in figure 464.

Myopia. This is that refractive condition of the eye in which parallel rays are brought to a focus *in front* of the retina, 4, figure 466. It is due either to an abnormal elongation of the eyeball, antero-posteriorly, or to an increase in the convexity of the refracting surfaces, or to both of these conditions. Parallel rays are focussed in front of the retina, and, crossing, form circles on the retina. Thus, the images of distant objects are blurred and indistinct. The eye is, as it were, permanently adjusted for a near point. Rays from a point near the eye are exactly focussed on the retina. But those which issue from any object beyond a slight distance, the myopic *far-point*, which is less than twenty feet, cannot be distinctly focussed. This defect is corrected by *concave* glasses, which cause parallel rays entering the eye

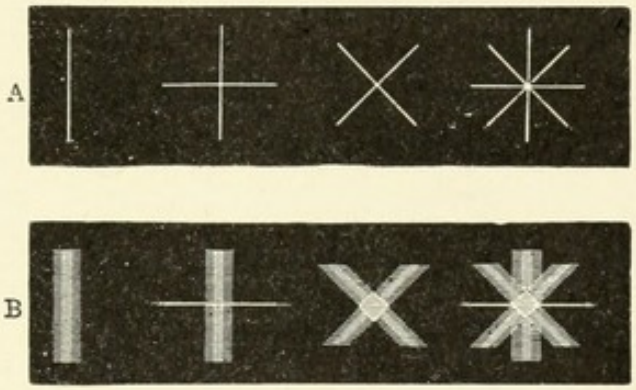


FIG. 465.—Diagram of Character of Retinal Images in Astigmatism. (John Green.)

to diverge. Such glasses of course are needed only to give a clear vision of distant objects. For near objects they are not required.

Hypermetropia. This is that refractive condition of the eye in which parallel rays are brought to a focus *behind* the retina, 3, figure 466. It is the opposite of myopia, and is due either to an abnormal shortening of the eyeball, antero-posteriorly, or to a decrease in the convexity of the refracting surfaces, or both. Parallel rays entering the eye at rest are focussed *behind* the retina. An effort of accommodation is therefore required to focus parallel rays on the retina. When the rays are sharply divergent, as in viewing a very near object, the accommodation is insufficient to focus them. Thus, both near and distant objects require an effort of accommodation, and the eye is under a constant strain which produces in the end various nervous, as well as ocular, disorders. This defect is obviated by the use of *convex* glasses, which render the pencils of light more convergent. Such glasses are especially needed for near objects, as in reading, etc. They are also required for distant vision to rest the eye by relieving the ciliary muscle from constant work.

Presbyopia. Presbyopia is a condition of diminished range of accommodation. It takes place with considerable uniformity from youth to old age.

It is not a disease, but a physiological process which every eye undergoes as its owner grows older. It is due to a gradual diminution of elasticity of the lens by a sort of sclerosis from the center toward the periphery. It begins even in childhood, but advances so slowly that it is not until the age of twenty-five or so that a distinct, though small, nucleus is present. With advancing years the process goes on until finally the lens becomes inelastic

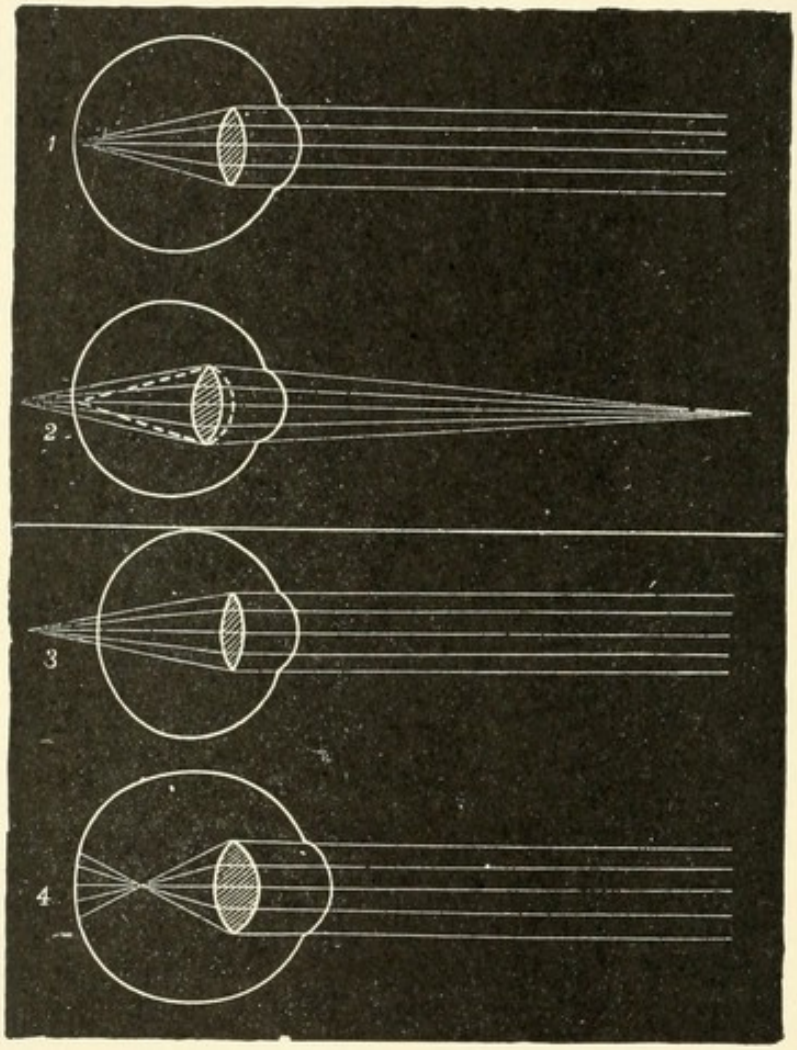


FIG. 466.—Diagram Showing: 1, Normal or *emmetropic* eye bringing parallel rays exactly to a focus on the retina; 2, normal eye at rest, showing that light from a near point is focussed behind the retina, but by increasing the curvature of the anterior surface of the lens (shown by dotted lines) the rays are focussed on the retina; 3, *hypermetropic* eye. In this case the axis of the eye is shorter, and the lens normal (or the lens may be flatter than normal and the eyeball normal); parallel rays are focussed behind the retina; 4, *myopic* eye. In this case the lens is too convex (or the axis of the eye is abnormally long); parallel rays are focussed in front of the retina.

and is unable to assume a shape convex enough to focus rays from a near object upon the retina, as in reading. The defect is remedied by the use of convex lenses equivalent to the loss in accommodation.

Visual Sensations, from Excitation of the Retina. Light is the normal agent in the excitation of the retina. The only portion of the retina capable of reacting to the stimulus is the rod and cone layer. The proofs of this statement may be summed up thus: 1. The point of entrance of the optic

nerve into the retina, where the rods and cones are absent, is insensitive to light and is called the *blind spot*. The phenomenon itself is very readily demonstrated. If we close one eye, and direct the other upon a point at such a distance to the side of any object that the image of the latter must fall upon the retina at the point of entrance of the optic nerve, its image is lost. If, for example, we close the left eye, and direct the axis of the right eye steadily toward the circular spot in figure 467, while the page is held at a distance of about six inches from the eye, both dot and cross are visible. On gradually increasing the distance between the eye and the object, by removing the book farther and farther from the face, keeping the right eye steadily on the dot, it will be found that suddenly the cross disappears from view, while on removing the book still farther it suddenly comes into view again. The cause of this phenomenon is simply that the portion of retina which is occupied by the entrance of the optic nerve is quite blind; and therefore that when it alone occupies the field of vision objects cease to be visible.

FIG. 467.—Diagram for Demonstrating the Blind Spot.

2. In the fovea centralis and macula lutea, which contain rods and cones but no optic-nerve fibers, light produces the greatest effect. In the latter, cones occur in large numbers, and in the former cones without rods are found, whereas in the rest of the retina, which is not so sensitive to light, there are fewer cones than rods. We may conclude, therefore, that cones are even more important to vision than rods. 3. If a small lighted candle be moved to and fro at the side of and close to one eye in a dark room while the eyes look steadily forward into the darkness, a remarkable branching figure, *Purkinje's figures*, is seen floating before the eye, consisting of dark lines on a reddish ground. As the candle moves, the figure moves in the opposite direction, and from its whole appearance there can be no doubt that it is a reversed picture of the retinal vessels projected before the eye. The two large branching arteries passing up and down from the optic disc are clearly visible, together with their minutest branches. A little to one side of the disc, in a part free from vessels, is seen the yellow spot in the form of a slight depression. This remarkable appearance is due to shadows of the retinal vessels cast by the candle. The branches of these vessels are chiefly distributed in the nerve fibers and ganglionic layers; and since the light of the candle falls on the retinal vessels from in front, the shadow is cast behind them, and hence those elements of the retina which perceive the shadows must also lie behind the vessels. Here, then, we have a clear proof that the light-perceiving elements of the retina are not the fibers of the optic nerve forming the innermost layer of the retina, but the external layers of the retina, the rods and cones.

When light falls on the rods and cones it produces changes which develop nerve impulses that are transmitted by the chain of neurones extending through the retina, the optic nerve and chiasma, the geniculate bodies, etc., to the cerebral cortex of the occipital lobe, which is the sensorium for visual sensations. We have already seen that the eye possesses a wonderful mechanical perfection for receiving and focussing light on definite parts of the retina. A comparison of visual sensations shows that there are corresponding qualities in the sensation, as, for example, its intensity, duration, localization, complexity, etc.

Duration of Visual Sensations. The duration of the sensation produced by a luminous impression on the retina is always greater than that of the stimulus which produces it. However brief the luminous impression, the effect on the retina always lasts for about one-twentieth of a second. Thus, suppose an object in motion, say a horse, to be revealed on a dark night by a flash of lightning, the image remaining on the retina during the time of the flash. The object is really revealed for such an extremely short period (a flash of lightning being almost instantaneous) that no appreciable movement could have taken place in the period during which the stimulus was produced on the retina of the observer. The horse would appear standing in the position of motion for about a twentieth of a second, though he would not be seen to make any motions. And the same fact is proved in a reverse way. The spokes of a rapidly revolving wheel are not seen as distinct objects, because at every point of the field of vision over which the revolving spokes pass, a given impression has not faded before another comes to replace it. Thus every part of the interior of the wheel appears filled.

The duration of the *after-sensation* produced by an object is greater in a ratio proportionate to the duration of the impression which caused it. Hence, the image of a bright object, as of the light of a window, may be perceived in the retina for a brief period, the *positive after-image.* If, however, the primary stimulation is sharp and intense there will follow presently an appearance of the window in which all the contrasted lights are reversed, the *negative after-image.*

Intensity of Visual Sensations. It is quite evident that the more luminous a body the more intense is the stimulus it produces. But the intensity of the sensation is not *directly* proportional to the intensity of the luminosity of the object. It is necessary for light to have a certain intensity before it can excite the retina, but it is impossible to fix an arbitrary limit to the power of excitability. As in other sensations, so also in visual sensations, a stimulus may be too feeble to produce a sensation. If it be increased in amount sufficiently, it reaches a point that is intense enough to produce an effect; this is a minimal or threshold stimulus. The amount of increase in the stimulus that produces a perceptible change in the sensation is at first very slight, but later quite great. It does not depend on the absolute

change of intensity of the stimulus, but is proportional to the intensity of the stimulus already acting, Weber's law.

This law, which is true only within certain limits, may be best understood by an example. When the retina has been stimulated by the light of one candle, the light of two candles will produce a difference in sensation which can be easily and distinctly felt. If, however, the first stimulus is that of an electric arc-light, the addition of the light of a candle will make no difference in the sensation. So, generally, for an additional stimulus to be felt, it may be proportionately small if the original stimulus is small, and must be greater if the original stimulus is great. The stimulus increases as the numbers expressing its strength, while the sensation increases as the logarithms.

Every one is familiar with the fact that it is quite impossible to see the *fundus* or back of another person's eye by simply looking into it. The interior of the eye forms a perfectly black background to the pupil. The same

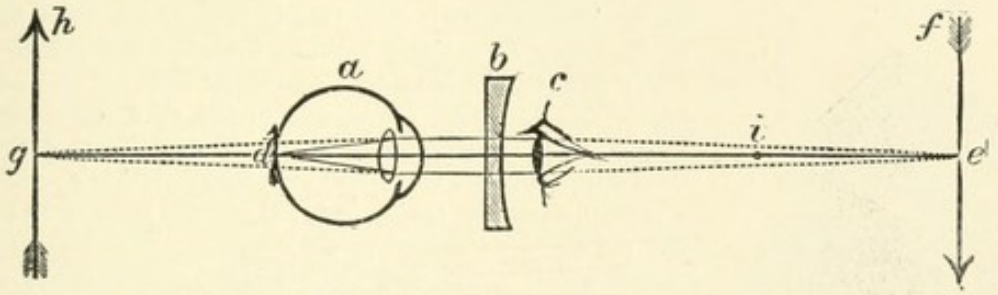


FIG. 468.—Diagram to Illustrate the Action of the Ophthalmoscope when a Plane Concave Glass is Used. *c*, Observer's eye. The light reflected from any point, *d*, on retina of *a*, would naturally be focussed at *e*; if the lens *b* is used it would be focussed at *i*, in other words, at back of *c*. The image would be enlarged, as though of *g*, and would be inverted. (After McGregor Robertson.)

remark applies to an ordinary photographic camera, and may be illustrated by the difficulty we experience in seeing into a room from the street through the window, unless the room be lighted from within. In the case of the eye this fact is partly due to the feebleness of the light reflected from the retina, most of it being absorbed by the retinal pigment. But the difficulty is due more to the fact that every such ray is reflected back to the source of light and cannot be seen by the unaided eye without intercepting the incident light as well as the reflected rays from the retina. This difficulty is surmounted by the use of the *ophthalmoscope*.

The ophthalmoscope, brought into use by Helmholtz, consists in its simplest form of a concave mirror with a hole in it. The one described is one of the less intricate of the modern instruments. It consists of, *a*, a slightly concave mirror of metal or silvered glass perforated in the center, and fixed into a handle; and *b*, a biconvex lens of 6 to 8 cm. focal length. Two methods of examining the eye with this instrument are in common use —the *direct* and the *indirect:* both methods of investigation should be employed. A normal eye should be examined. A drop of a solution of atropine (two grains to the ounce) or of homatropine hydrobromate should be dropped into the right eye only about twenty minutes before the examination is commenced; the ciliary muscle is thereby paralyzed,

the power of accommodation is abolished, and the pupil is dilated. This will materially facilitate the examination; but it is quite possible to observe all the details to be presently described without the use of this drug. The room being now darkened, the observer seats himself in front of the person whose eye he is about to examine, placing himself upon a

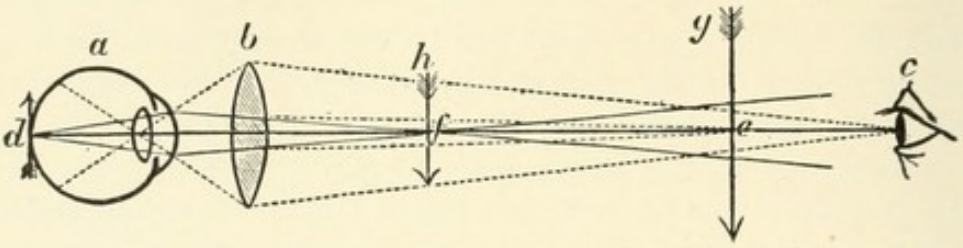


FIG. 469.—Diagram to Illustrate Action of Ophthalmoscope when a Biconvex Glass is Used. The figure *d* on retina of *a* is under ordinary conditions focussed at *f* and inverted. If the lens *b* be placed between eyes, the image *h* is seen by the eye *c* as an enlarged image. (After McGregor Robertson.)

somewhat higher level. A subdued but steady light is placed close to the left ear of the patient in the examination of the right eye. Guiding the mirror in his right hand, and looking through the central hole, the operator directs a beam of light into the eye of the patient. A red glare, called in practice the *reflex*, due to the illumination of the retina, is seen. The patient is then told to look at the little finger of the observer's right hand as he holds the mirror; to effect this the eye is rotated somewhat inward, and at the same time the reflex changes from red to a lighter color, owing to the reflection from the optic disc. The observer now approximates the mirror, and with it his eye to the eye of the patient, taking care to keep the light fixed upon the pupil, so as not to lose the reflex. At a certain distance, which varies with the refractive power in different eyes, but is usually an interval of about two or three inches between the observed and the observing eye, *the vessels of the retina* will become visible as lines running in different directions. The smaller and brighter red arteries can be distinguished from the larger and darker colored veins. An examination of the fundus of the eye reveals the *optic disc* and the entrance of the blood-vessels, the macula lutea, and the fovea centralis. No blood-vessels are seen in the fovea. This constitutes the direct method of examination, figure 468; by it the various details of the fundus are seen as they really exist, and it is this method which should be adopted for ordinary use.

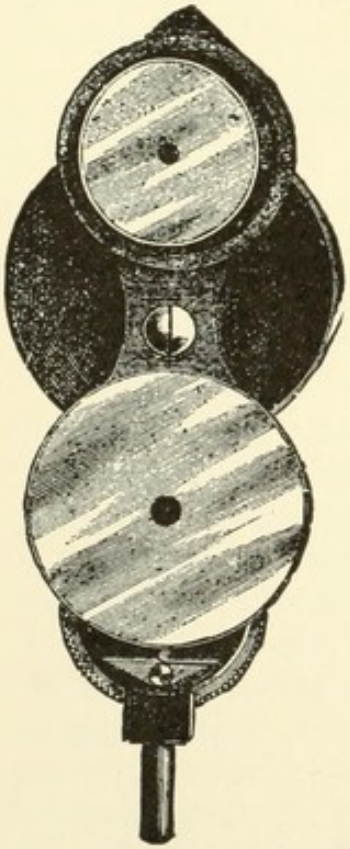


FIG. 470.—The Ophthalmoscope. The small upper mirror is for direct, the larger for indirect, illumination.

If the observer is ametropic, *i.e.*, is myopic or hypermetropic, he will be unable to employ the direct method of examination until he has remedied his defective vision by the use of proper glasses.

In the indirect method, figure 469, the patient is placed as before, and the operator holds the mirror in his right hand at a distance of 30 to 40 cm. from the patient's right eye. At the same time he rests his left little finger lightly upon the patient's right temple, and holding the lens between his thumb and forefinger, two or three inches in front of the patient's eye, directs the light through the lens into the eye. The red reflex, and subsequently the white one, having been gained, the operator slowly moves his mirror, and with it his eye, toward or away from the face of the patient, until the outline of one of the retinal vessels becomes visible, when very slight movements on the part of the operator will suffice to bring into

view the details of the fundus above described, but the image will be much smaller and inverted. The lens should be kept at a fixed distance of two or three inches, the mirror being alone moved until the disc becomes visible: should the image of the mirror obscure the disc, the lens may be slightly tilted.

The Field of Vision. The field of vision of an eye is that part of the external world which can be seen by it when the eye is fixed. Under such circumstances objects near the axis of vision stimulate points in the retina near the fovea or on it, while objects at an angle of 60° to 90° from the axis

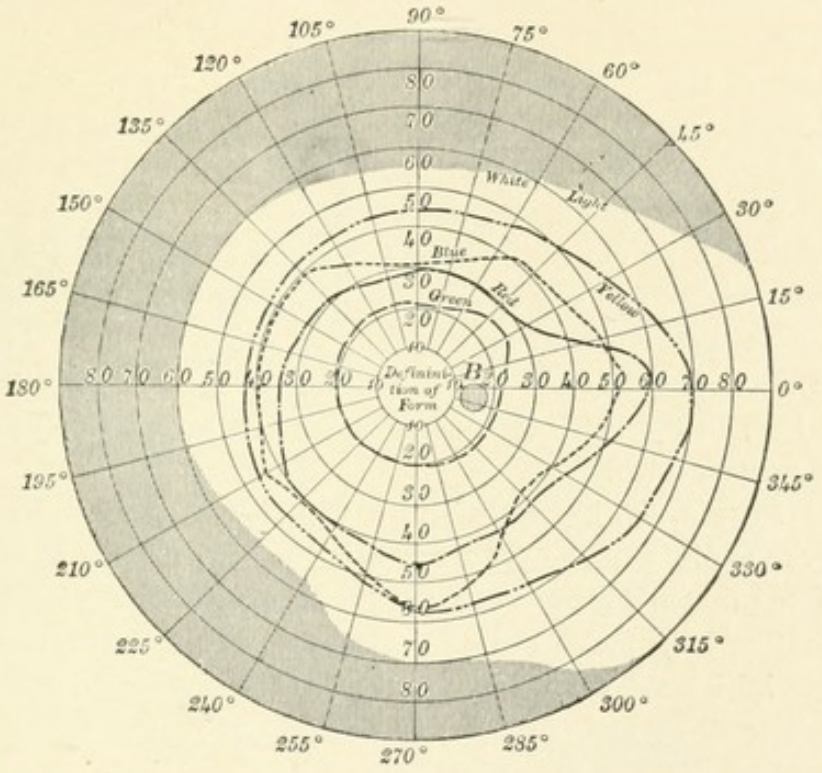


FIG. 471.—Perimeter Chart, Showing Extent of Field of Vision for White Light and to the Colors Red, Green, Yellow, and Blue. (Krapart.)

of vision stimulate regions of the opposite side of the retinal cup, *i.e.*, the retinal field is inverted.

The perimeter is an instrument for measuring the field of vision in terms of angular measure. When a field is charted by means of the perimeter it is revealed that objects can be seen further out in the field in some directions than in others. For example, objects in the temporal field can be seen at an angle of 90° to 100°, while on the nasal side they are seen only 60° to 70°. If the head is turned to the right or the left while keeping the eye fixed, it is found that objects are seen at a greater angle. This shows that the limitations are due to the facial boundaries of the eye preventing the light from entering the eye and not from lack of sensitiveness of the retina. In fact the retina is sensitive to light out to the ora serrata.

Localization in the Retina. Careful exploration of the retina with the perimeter gives a measure not only of the extent of the visual field but of

its acuteness and localization in different areas toward the periphery. Considering the minimal distance apart which two luminous points must be to be distinguished as two, it is found that when the image falls on the fovea the two points may be very near together, as little as one minute or even less. Two stars can be seen only at a somewhat greater angular distance, two to three minutes. One minute angular measure covers an area on the retina of a trifle over 4 μ. The diameter of the cones is about 2 μ, so that the stimuli in the fovea fall on at least two separate cones. The inference seems reasonable that the retina in its most sensitive part can localize stimuli that fall on adjacent cones.

The area of the fovea centralis is small, from 0.5 to 1.5 mm. Outside of its area the acuteness of vision quickly falls off. The fact is roughly estimated by fixing the vision on a letter in the printed line in the book before the reader and then determining the number of letters to either side that can be identified. The height of these letters is 1.5 mm.; by measuring the distance of the page from the eye one can quickly calculate the area of distinct vision on the retina. Test types are printed on the basis of an angle of five minutes.

In the outer limits of the retina the power of localizing stimuli is very slight; in fact, in the extreme borders of the field it is difficult to determine other than general form.

Visual Purple. The method by which a ray of light is able to stimulate the endings of the optic nerve in the retina is not yet understood. It is supposed that the change effected by the agency of the light which falls upon the retina is in fact a chemical alteration in the protoplasm, and that this change initiates a nerve impulse that is transferred to the optic nerve endings. The discovery of a certain temporary reddish-purple pigmentation of the outer limbs of the retinal rods in certain animals, *e.g.*, frogs, which had been killed in the dark, forming the so-called *rhodopsin* or *visual purple*, appeared likely to offer some explanation of the matter, especially as it was also found that the pigmentation disappeared when the retina was exposed to light, and reappeared when the light was removed, and that it underwent distinct changes of color when other than white light was used. It was also found that if the operation were performed quickly enough and in the dark, the image of an object, *optogram*, might be fixed in the pigment on the retina by soaking the retina of an animal in alum solution.

The visual purple cannot, however, be absolutely essential to the due production of visual sensations, as it is absent from the retinal cones, and from the macula lutea and fovea centralis of the human retina, and does not appear to exist at all in the retinæ of some animals, *e.g.*, bat, dove, and hen, which are, nevertheless, possessed of good vision.

However, the fact remains that light falling upon the retina *bleaches the visual purple*, and this must be considered as one of its effects. It has been found that certain pigments, also sensitive to light, are contained in the inner

segments of the cones. These colored bodies are said to be oil globules of various colors—red, green, and yellow—called *chromophanes*, and are found only in the retinæ of animals other than mammals. The rhodopsin at any rate appears to be derived in some way from the retinal pigment, since the color is not renewed after bleaching if the retina be detached from its pigment layer. The second change produced by the action of light upon the retina is the *movement of the pigment cells*. On the stimulation by light the granules of pigment in the cells which overlie the outer part of the rod and cone layer of the retina become diffused into the parts of the cells between the rods and cones, the *melanin* granules, as they are called, passing

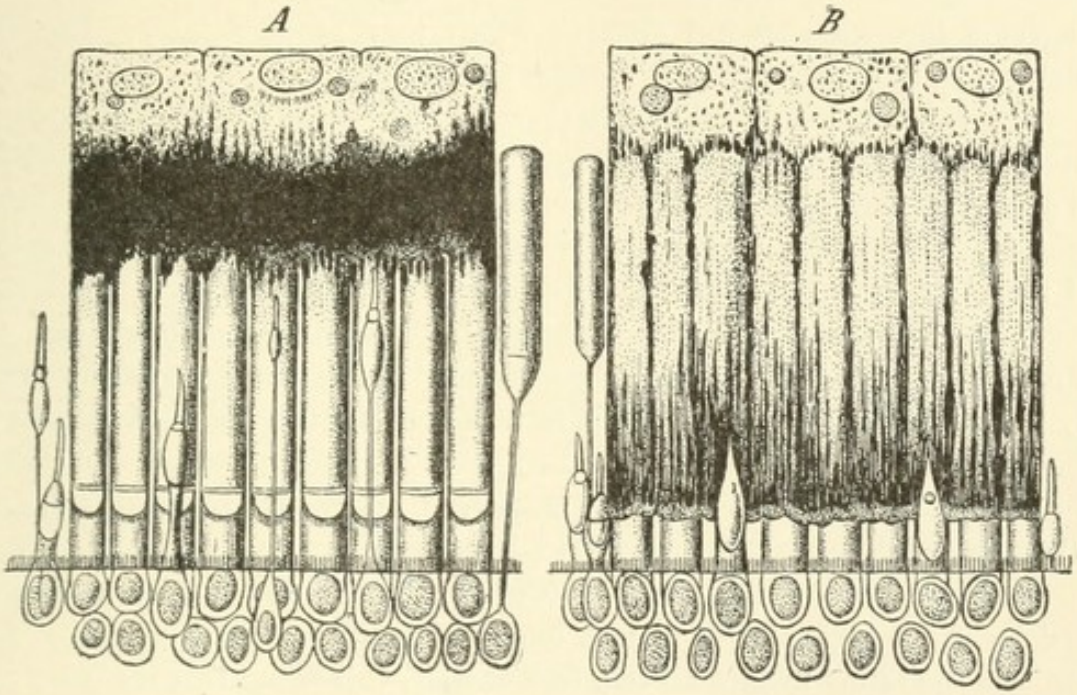


FIG. 472.—Sections of Frog's Retina Showing the Action of Light upon the Pigment Cells and upon the Rods and Cones. (von Gendesen-Stort.) *A*, From a frog which had been kept in the dark for some hours before death; *B*, from a frog which had been exposed to light just before being killed. Three pigment cells are shown in each section. In *A* the pigment is collected toward the nucleated part of the cell, in *B* it extends nearly to the basis of the rods. In *A* the rods, outer segments, were colored red (the detached one green); in *B* they had become bleached. In *A* the cones, which in the frog are much smaller than the rods, are mostly elongated; in *B* they are all contracted.

down into the processes of the pigment cells. A *movement of the cones* and possibly of the rods is also said to occur, as has been already incidentally mentioned. Under the influence of the stimulus of light the outer parts of the cones, which in an eye protected from light extend to the pigment layer, are retracted. It is even thought by some that the contraction is under the control of the nervous system. Finally, according to the careful researches of Dewar and McKendrick, and of Holmgren, it appears that the stimulus of light is able to produce *an action current* in the retina. McKendrick believes that this is the electrical expression of those chemical changes in the retina of which we have already spoken.

Color Sensations. When a ray of sunlight enters the eye it pro-

duces a sensation of white light. But if the ray first passes through a prism, then it produces sensations corresponding to the colors of the spectrum. As is well known, white light is produced by vibrations of the luminiferous ether through a wide range of vibration rates. When a beam of white light is passed through a dispersing prism those vibration rates of low frequency are refracted less than those of higher frequency, giving rise to the spectrum. Vibrations of the luminiferous ether of rates just outside of the spectral rates exist, those which have a lower rate giving rise to heat rays, and those of higher rate to the so-called actinic or chemical rays, because they exert a powerful chemical action. Those spectral colors which stimulate the retina to produce sensations of color presumably affect the retinal elements through chemical changes which they produce there. But this matter will be discussed under theories of color vision.

The examination of color sensations reveals certain correspondences between the physical color of the stimulus and the resulting color perception. If a pure spectral color be allowed to fall on the retina, a corresponding simple sensation is produced. If two colors fall on the same portion of the retina at the same time, a sensation is produced that is different from that which occurs when either color alone stimulates. The same fact holds true for three colors or more. In fact, three spectral colors can be selected which by proper combination can be used to produce sensations of all the colors of the spectrum. Such colors are called the fundamental colors, and while the choice is more or less arbitrary, red, green, and violet are the colors usually considered.

Extent of the Visual Field for Color. The retina is most sensitive to color in the region of the macula lutea. If by means of the perimeter one explores the retina to spectral red, for example, it is found that the color can be identified only at a distance of from 30° to 50° from the macula; the limits extending out somewhat farther on the nasal side of the retina, that is, the part corresponding to the temporal visual field. In the same way yellow can be identified for from 40° to 70°, blue from 40° to 50°. The visual field for green is quite restricted, usually extending only from 20° to 30°. The extent of the color visual field varies greatly in different individuals.

Complemental Colors, and After-images of Color. Certain colors, when allowed to stimulate the retina at the same time, tend to neutralize each other. That is, they produce sensations approaching white, usually some shade of gray, which will have a tinge of one or the other primary colors according to the proportion of stimulation. These pairs of colors are called *complemental colors*. Each spectral color has its complemental color, a fact that is represented in figure 473. The complemental colors of greatest physical significance are red and green (greenish blue), yellow and deep blue (indigo blue), green (greenish yellow), and violet.

Positive after-images of color exist for a brief moment, but the greatest

significance attaches to the negative after-images. The negative after-images of color following the stimulus of colored light upon the retina are not the sensation of color produced by the color of an object, but are the opposite or complemental color. The after-image of red is, therefore, green, and that of green, red; that of violet, yellow and of yellow, violet, etc. The same relation holds with the other colors. A condition for the development of a strong after-image is that the primary image shall have continued to a certain degree of fatigue. The colors which reciprocally excite each other

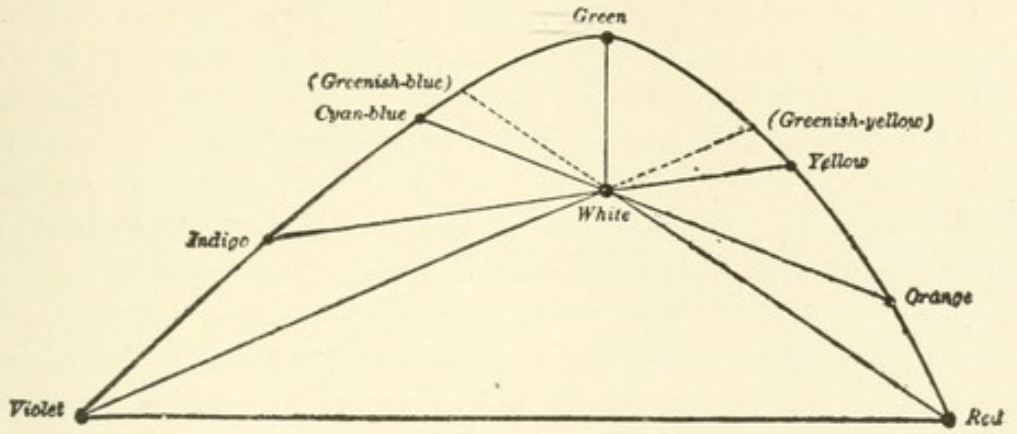


FIG. 473.—Geometrical Color Table for Determining the Complemental Colors.

in the retina are those placed at opposite points in the color table, figure 473. The after-images of color are most intense in the axis of the visual field and are not always present in the periphery of the retina, as can readily be seen by examining the chart, figure 471.

Color sensations may also be produced by contrast. Thus, a very small dull gray strip of paper, lying upon an extensive surface of any bright color, does not appear gray, but has a faint tint of the color which is the complement of that of the surrounding surface. A strip of gray paper upon a green field, for example, appears to have a tint of red, and when lying upon a red surface, a greenish tint; it has an orange-colored tint upon a bright blue surface, and a bluish tint upon an orange-colored surface; a yellowish color upon a bright violet, and a violet tint upon a bright yellow surface. The color excited thus must arise as an opposite or antagonistic condition of the retina, and the opposite conditions of which it thus becomes the subject, would seem to balance each other by their reciprocal reaction. A necessary condition for the production of the contrast colors is that the part of the retina in which the new color is to be excited shall be in a state of comparative repose; hence the small object itself must be gray. A second condition is that the color of the surrounding surface shall be very bright.

Color-Blindness. Many persons are unable to distinguish one or more of the fundamental colors, and therefore have different perceptions

of the color combination from that of the normal individual. It is said that from 4 to 5 per cent of men and about 1 per cent of women are defective in color vision. This defect is called *color-blindness*.

In very rare cases complete color-blindness exists. Such individuals distinguish lights and shades only, that is, form. A more common defect, however, is the absence of one or more of the fundamental color sensations, the most common of all being the red-blind, or the red-green blind. The red-green blind individual cannot distinguish red and green colored yarns from each other or from shades of gray which reflect light with the same intensity. When they are given the color test by the Holmgren yarns, they indiscriminately mix the reds, greens, and grays. Cases have been described in which the individual was red-blind alone, or green-blind alone. A less common color defect is the inability to distinguish yellows and blues, yellow-blue blindness.

Color-blindness may occasionally arise from disease or accident, but it is usually congenital. The individual often does not discover his defect until examined especially for his color vision. He may have learned to apply the terms green and red to surrounding objects, such as the grass, bricks, etc., but he distinguishes these objects by slight differences in intensity of lumination, form, etc., and not by the sensations of color which the normal individual experiences.

Theories of Color Vision. We have no way of determining the method by which the colors stimulate the retina other than our inferences from indirect evidence. It is probable that the energy of light vibration is transformed in the retinal structures into either physical or chemical change, perhaps the latter. Those interested in the phenomena of color vision generally accept one of two theories, or their modifications, in explanation of the facts.

The Young-Helmholtz Theory of Color Vision. This theory assumes that there are three fundamental sensory elements in the retina which correspond to and are stimulated primarily by the three primary colors—red, green, and violet. The theory in its present form further assumes that each color-perceiving element is slightly stimulated by others of the spectral rays, as shown in figure 474. When red rays fall upon the retina, they stimulate the red-perceiving elements strongly and the green and violet very feebly. The resulting sensation is that of red. So also is it with green and violet rays. When the retina is stimulated by both red and green rays, the two corresponding color-perceiving elements are strongly stimulated. The resulting color perception, however, is a combination of the two sensations and corresponds to some region of the spectrum between the red and green, according to the relative intensity of the two stimuli. When all three color-perceiving elements are stimulated at the same time, this theory assumes that white light will be perceived. In a similar manner all the various color sensations are arrived at.

Hering's Theory of Color Vision. This theory is based on the assumption that there are chemical substances in the retina, photogenic substances, which are stimulated by the colors of the spectrum. It assumes three photogenic substances which are called the red-green, the yellow-blue, and the

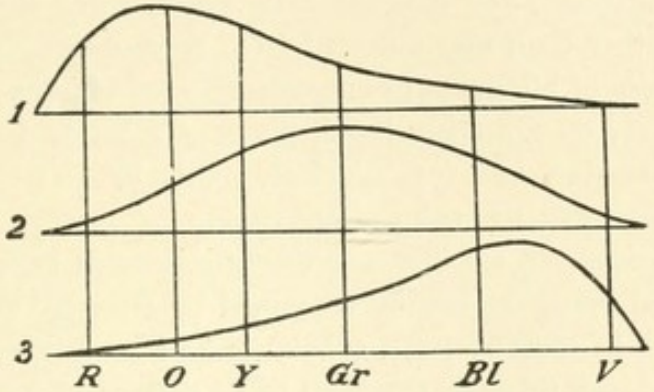


FIG. 474.—Diagram to Illustrate the Stimulating Effects of the Three Primary Colors. (Young-Helmholtz theory.) 1 is the red; 2, green, and 3, violet, primary color sensations. The lettering indicates the colors of the spectrum. The diagram indicates by the height of the curve to what extent the several primary sensations of color are excited by vibrations of different wave lengths. (Helmholtz.)

white-black substances. By the theory, when the red-green substance is stimulated by red or green light, respectively, the former produces destructive or catabolic changes, the latter constructive or anabolic changes, in the substance. When red light falls upon the retina, it produces catabolism in the red-green substance, which in turn develops a nerve impulse that arouses

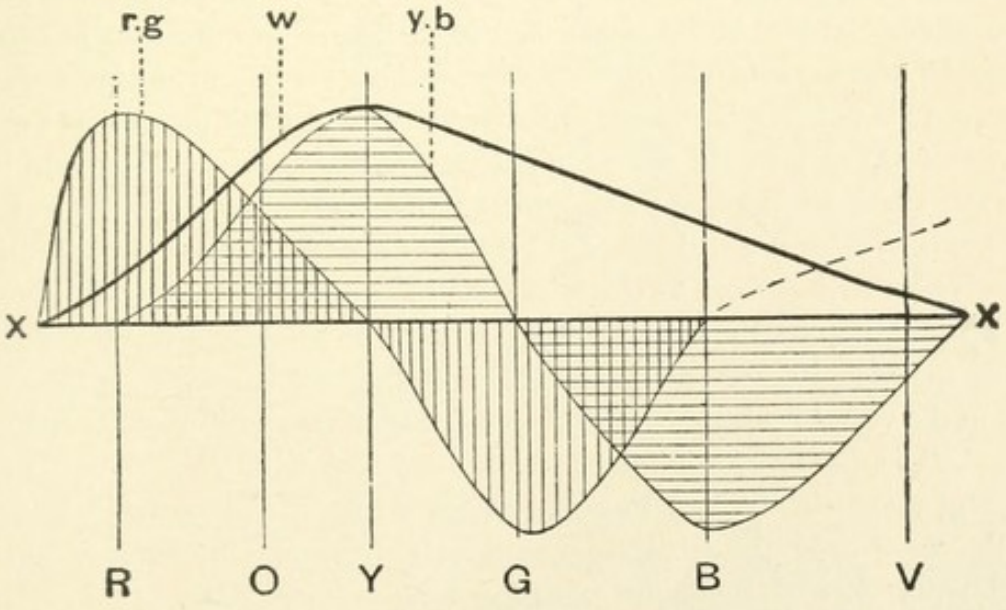


FIG. 475.—Diagram to Illustrate the Reactions of the Three Photogenic Substances, according to Hering's Theory. (Foster.)

the sensation of red. When green light, on the other hand, stimulates the retina, it produces anabolism of the red-green substance and the sensation of green. The same rule holds with the other two substances. It will be noticed that this theory is based on the complemental colors.

When we apply the theories mentioned above to the phenomena of color-contrast and color-blindness, we find that each is defective in some point. By the Young-Helmholtz theory it is difficult to understand the perception of the sensation black, for by the theory black could be perceived only as the absence of all colors, and it is generally granted that there is a distinct black sensation other than and different from mere darkness. This theory explains those cases of blindness to one color, as red-blindness, for example. The Hering theory, on the other hand, gives us a rational explanation for positive black sensation, and is particularly applicable to the observed facts of color-contrast and negative color after-images.

Color after-images, as for instance the after-images of green following stimulation by red light, are readily explained by Hering's theory, since the strong catabolism in the red-green substance will be followed immediately by anabolism to bring this substance up to its normal in the eye, thus producing the after-image. This phenomenon can be explained by the Young-Helmholtz theory only by assuming that following the stimulation by red light and the consequent fatigue of red-perceiving elements there is sufficient light entering the eye to stimulate the relatively sensitive green and violet perceiving elements, thus producing an after-image. Strong after-images are perceived in the dark room, so that the Hering theory is most applicable in the explanation of these cases.

Binocular Vision. When one looks at an object with a single eye, the eye is so adjusted that the axis of vision is directed toward the object investigated. This is called *ocular fixation*. The ocular fixation is accomplished by the coordinated contractions of the six pairs of ocular muscles. Its purpose is to bring the image of the object examined in the external visual field as nearly as possible upon the macula lutea. In binocular vision both eyes are fixed on the same point in the visual field. A projection of the visual axis of each eye will pierce the point of fixation in the external object. It is evident that objects to either side of the point of fixation will give off rays which will enter the eyes, stimulating fields in the retina on the opposite side of the visual axis. An examination of figure 476 will show that each point in the visual field, A, B, C, D, stimulates corresponding points, a, b, c, d, a', b', c', d', in the retinas of the two eyes. a, b, c, d, and a', b', c', d', are corresponding points in the two retinas. When a and a' are stimulated at one and the same time, the resulting sensation is attributed to one object in the visual field, A, and these are corresponding points. This can be shown by pressing one eye out of its normal fixation so that the axes of the two eyes are not directed toward the same point. If one eye is pressed lightly by the thumb while examining a given object, as soon as the pressure is applied two objects will appear. This phenomenon is known as *diplopia*. Diplopia is due to the fact that the images of visual objects do not fall on corresponding points in the two retinæ.

The parts of the retinæ in the two eyes which thus correspond to each other in the property of referring the images which affect them simultaneously to the same spot in the field of vision, are, in man, just those parts which would correspond to each other if one retina were placed exactly in front of and over the other, as in figure 477. Thus, as we have noticed in speaking of the distribution of the optic nerve fibers, the temporal portion of one eye corresponds to or is identical with the nasal portion of the other eye. The upper part of one retina is also identical with the upper part of

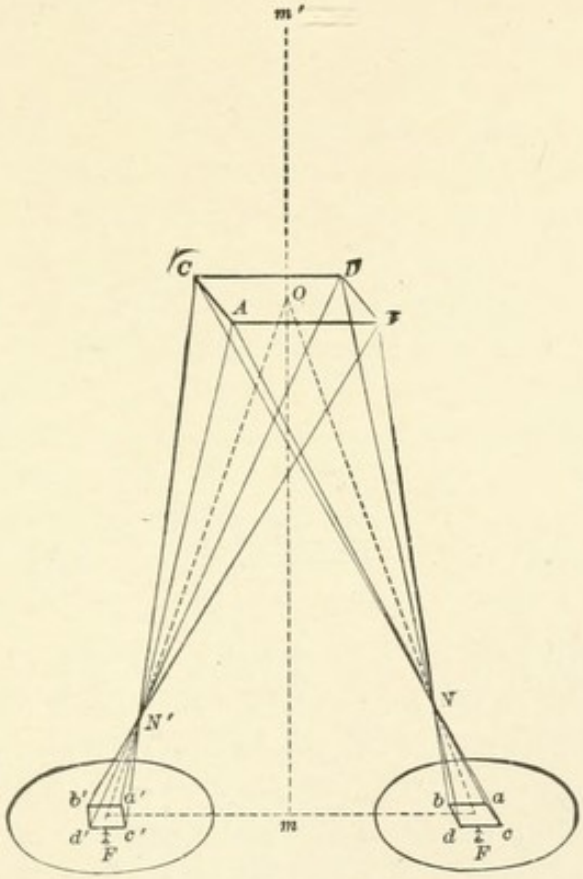


FIG. 476.—Diagram Showing the Symmetrical Correspondence of the Retinal Fields. *N*, Nodal point; *F*, fovea centralis. The observer is supposed to be looking down upon the optical apparatus from above. Note that the line *CD*, which is on the lower side of the object, is the upper side of the image; and that the line *BD*, which is the right side of the object, is the left side of the image, which brings it at the inner segment of the right retina and the outer segment of the left retina.

the other; and the lower parts of the two eyes are identical with each other. The distribution of the optic nerve fibers corresponds with the distribution of the identical points. The identical points on the upper and lower parts of the retinæ may also be shown by the following simple experiment.

Pressure upon any part of the ball of the eye, so as to affect the retina, produces a luminous circle, seen at the opposite side of the field of vision to that on which the pressure is made. If, now, in a dark room, we press with the finger at the upper part of one eye, and at the lower part of the other, two luminous circles are seen, one above the other; so, also, two figures are

seen when pressure is made simultaneously on the outer or the inner sides of both eyes. But if pressure be made with the fingers upon both eyes simultaneously at their lower part, one luminous ring is seen at the middle of the upper part of the field of vision. If the pressure be applied to the upper part of both eyes, a single luminous circle is seen in the middle of the field of vision below. So, also, if we press upon the outer side of one eye and upon the inner side of the other eye, a single luminous spot is produced, and is appar-

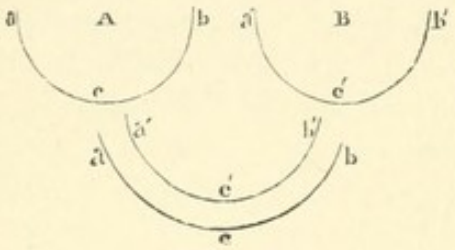


Fig. 477.

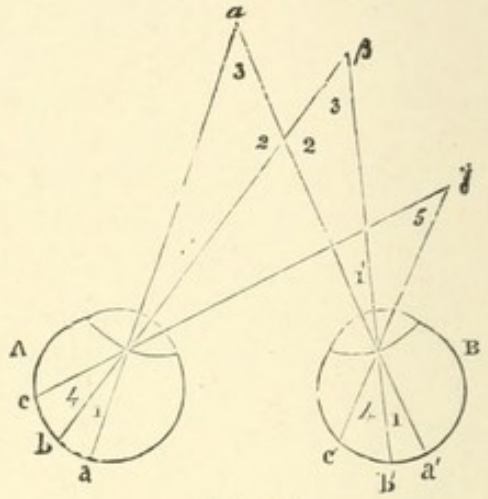


Fig. 478.

Fig. 477.—Diagram to Show the Corresponding Parts of the Retinæ.

Fig. 478.—Diagram to Show the Simultaneous Action of the Eyes in Viewing Objects in Different Directions.

ent at the extreme right of the field of vision. The hemispheres of the two retinæ may, therefore, be regarded as lying one over the other, as in *C*, figure 477; so that the left portion of one eye lies over the identical left portion of the other eye, the right portion of one eye over the identical right portion of the other eye; and with the upper and lower portions of the two eyes, *a* lies over *a'*, *b* over *b'*, and *c* over *c'*. The points of the one retina intermediate between *a* and *c* are again identical with the corresponding points of the other retina between *a'* and *c'*; those between *b* and *c* of the one retina, with those between *b'* and *c'* of the other. If the axes of the eyes, *A* and *B*, figure 478, be so directed that they meet at α, an object at α will be seen singly, for the point *a* of the one retina and *a'* of the other are identical. So, also, if the object β be so situated that its image falls in both eyes at the same distance from the central point of the retina—namely, at *b* in the one eye and at *b'* in the other—β will be seen single, for it affects identical parts of the two retinæ. The same will apply to the object γ.

The reason why the impressions on the identical points of the two retinæ give rise to but one sensation, and the perception of but a single image, must either lie in the structural organization of the deeper or cerebral portions of the visual apparatus, or it must be the result of a mental operation;

for in no other case is it the property of corresponding nerves of the two sides of the body to refer their sensations to one spot.

Many attempts have been made to explain this remarkable relation between the eyes, by referring it to anatomical relation between the optic nerves. The circumstance of the inner portion of the fibers of the two optic nerves decussating at the commissure, and passing to the eye of the opposite side, while the outer portion of the fibers continue their course to the eye of the same side, so that the left side of both retinæ is formed from one root of the nerves, and the right side from the other root, naturally led to an attempt to explain the phenomenon by this distribution of the fibers of the nerves. And this explanation is favored by cases in which the entire half of one side of the retina sometimes becomes insensible.

Visual Judgments. *Form and Solidity.* The estimation of the form of bodies by sight is the result partly of the visual sensation and partly of the association of ideas. The form of the image perceived by the retina depends wholly on the outline of the part of the retina affected; the sensation alone is adequate only to the distinction of superficial forms from each other which lie in one plane, as of a square from a circle. But the idea of a solid body, as a sphere, or a body of three or more surfaces, *e.g.*, a cube, can be attained only by the action of the mind in constructing it from the different superficial images seen in different positions of the eye with regard to the object, and (as shown by Wheatstone and illustrated in the *stereoscope*), from two different perspective projections of the body being presented simultaneously to the mind by the two eyes. Hence, when, in adult age, sight is suddenly restored to persons blind from infancy, all objects in the field of vision appear at first as if painted flat on one surface; and no idea of solidity is formed until after long exercise of the sense of vision combined with that of touch. The clearness with which an object is perceived, irrespective of accommodation, would appear to depend largely on the definiteness of stimulation of the rods and cones which its retinal image covers. Hence, the nearer an object is to the eye, within the limits of vision, the more clearly are all its details seen. Moreover, if we want carefully to examine any object, we always direct the eyes straight toward it, so that its image shall fall on the yellow spot, which has already been shown to be the area of most acute vision.

In binocular vision the images of an object, while they fall in approximately corresponding points on the two retinæ, are never absolutely the same.

When an object is placed so near the eyes that to view it the optic axes must converge, a different perspective projection of it is seen by each eye, these perspectives being more dissimilar as the convergence of the optic axes becomes greater. Thus, if any figure of three dimensions, an outline cube, for example, be held at a moderate distance before the eyes, and viewed with each eye successively while the head is kept perfectly steady, *A*, figure 479, will be the picture presented to the right eye, and *B* that seen by the left eye.

Wheatstone has shown that on this circumstance depends in a great measure our conviction of the solidity of an object, or of its projection in relief. If different perspective drawings of a solid body, one representing the image seen by the right eye, the other that seen by the left, for example, the drawing of a cube, *A*, *B*, figure 479, be presented to corresponding parts of the two retinæ, as may readily be done by means of the stereoscope, the mind will perceive not merely a single representation of the object, but a body projecting in relief, the exact counterpart of that from which the drawings were made.

Size and Distance. The estimation of the size of an object and its distance away from the observer is based in part upon the visual image and in part upon judgments due to past experience. The two elements are inseparable and mutually dependent. Thus, a lofty mountain many miles away may subtend the same visual angle as a small hill near at hand. While the size

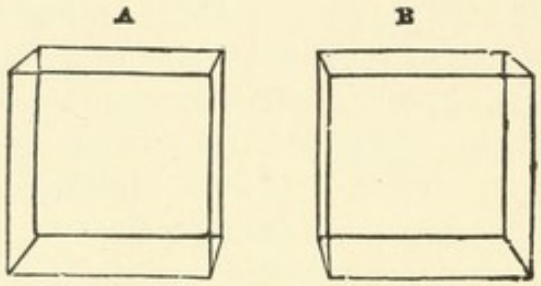


FIG. 479.—Diagrams to Illustrate how a Judgment of a Figure of Three Dimensions is Obtained.

and shape of the two images may be identical, yet the image of the hill near at hand is more distinct, its details are perceived, and its outlines are sharper than in the image of the mountain. If the atmosphere be charged with moisture or with dust, the image of the mountain will be still more indistinct and dim. From previous experiences we have learned that the dimness and indistinctness of the one and the definiteness of the other are associated with distance.

If two objects are very near at hand then there will be a difference in the convergence of the two eyes in binocular vision. It is now well known that the ocular muscles are possessed of a very delicate muscle sense. This muscle sense leaves the impression which enables us to judge that the one object is nearer and the other farther. In the common and familiar objects about us we have from long experience and intimate contact learned their actual size and the character of the retinal image formed at definite, but known distances. When such an object forms an image of the common size and usual distinctness on the retina, the judgment as to its distance is quickly made.

In the case of unknown objects which are associated with known objects, the judgment of the size and distance of the latter is used in forming

a judgment of the size and distance of the former by comparison. Many visual deceptions are based on these comparisons, a fact that is often taken advantage of by photographers. It is also well known that people living in a moist, hazy climate are utterly unable accurately to estimate distances when suddenly transferred to a clear mountain climate.

LABORATORY DIRECTIONS FOR EXPERIMENTS ON THE SENSE ORGANS.

1. **Touch.** Use the small compasses with rounded tips provided for the purpose, and determine the power of localization of the sense of touch as follows: Have the person observed close his eyes, then touch different parts of the skin, of the hand, arm, face, neck, etc., and let the observed one announce the exact point touched.

The localization can also be determined by touching two points on the skin with the points of the compasses separated by varying distances. Examine especially the skin on the forearm, on the back of the hand, on the palm of the hand, the tips of the fingers, and at different points on the face, including the lips and tip of the tongue. Touch these regions of the skin

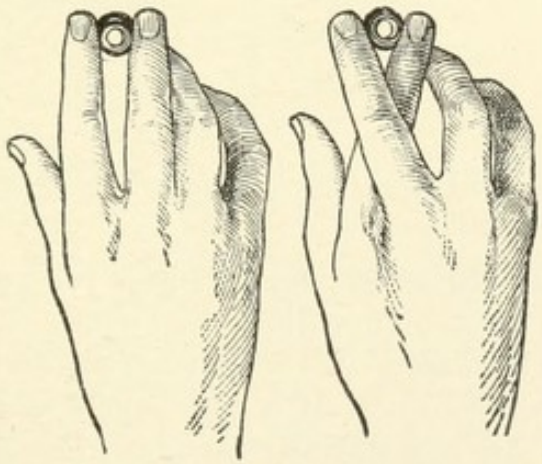


FIG. 480.—Aristotle's Experiment.

with either one or with two points of the compasses, and allow the person observed to announce results, drawing your conclusions according to the principle of trial and error. Make a table showing the power of local discrimination in the different regions.

2. **Aristotle's Touch Experiment.** Roll the tips of the middle and index fingers over a marble and note that the sensation from the two fingers is interpreted as that of a single object. Now cross the fingers and repeat the experiment. This time there is the sensation of touching two spheres.

3. **Temperature Sensations.** It is a common experience that the hand brought in the neighborhood of a warm or a cold object develops the

sensation of warmth or cold. Examine a given small area of the back of the hand with the thermoesthesiometer. Certain points will give stronger sensation of heat than others. Map these out carefully. Examine the same area for the cold. A large number of cold spots will be found and they will not coincide with the warm spots, figure 421.

The stimulation for the hot and cold spots does not depend upon the absolute temperature, but on the relative temperature. Insert the hand in

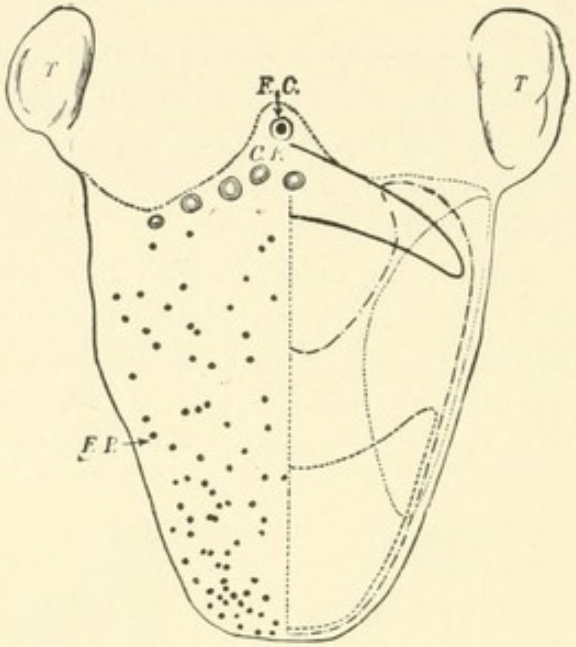


FIG. 481.—Localization of Taste. Bitter ——; acid ....; salt, —·—·—; sweet - - - - -; *T*, tonsils; *FC*, foramen cecum; *CF*, circumvallate papillæ; *FP*, fungiform papillæ. (Hall.)

water that feels lukewarm. Place the same hand in a cup of quite warm water for a moment, then reinsert it in the lukewarm water. This will now feel cold.

4. **Sensations of Taste.** The distribution of taste organs in the tongue is shown in figure 481. Examine your own tongue for organs of sweet, acid, saline, and bitter, using solutions of 1 to 2 per cent salt, 10 per cent sugar, 2 to 5 per cent acid, 5 per cent acetic acid, and 0.1 per cent quinine.

Wipe the tongue dry and apply the solution named from the tip of a glass rod. The best form of rod is about 15 cm. long by 0.5 cm. in diameter, and has one end drawn out to a slender pencil-shaped tip and of a size which will suspend a very small drop. Too large a drop diffuses over too great an area of the tongue. Occasionally small crystals of sugar, salt, etc., give more satisfactory results.

Perform the experiments on yourself before a mirror and map the results as shown in figure 481.

If the experiments are done with care certain papillæ will be found which give one or two of the taste sensations, but not all.

5. **Sensations of Smell.** Quantitative experiments on the sense

of smell are difficult to determine. Inhale vapor of ammonia so dilute that it can just be detected. Note that the sensation is strongest at the moment of drawing the vapor into the nostril. Fill the nostrils with the diluted vapor and close the external opening; the sensation quickly disappears. Keeping the nostrils closed, walk into the open air, then inhale fresh air. At the moment of the inhalation of fresh air the ammonia is again perceptible. Repeat with bergamot, rose water, etc.

6. **The Limits of the Sense of Hearing.** Use a set of tuning forks for the purpose, and determine the lowest vibration per second which can be perceived as sound. Determine the highest limits in the same way.

7. **Acuteness of the Sense of Hearing.** Listen to the vibrations of a tuning fork, or, better, to the ticking of a watch which is moved back and forth from the ear. Measure the distance at which it can just be distinguished. This experiment should be performed with the person blindfolded, and extraneous noise should, of course, be suppressed.

8. **Refraction.** Light passes out from a luminous point in straight lines so long as the line of propagation is in a medium of uniform density. If the rays pass form a transparent medium of one density into a second medium of different density, they will usually be turned out of their course, or refracted. If the rays enter the second medium at right angles to its surface, they will continue in straight lines, but if they enter at any other angle they will be refracted. If the second medium is denser than the first, the rays will be refracted toward the perpendicular; if it is less dense, away from the perpendicular.

Use a Hall's refraction-measuring apparatus (constructed of a carpenter's try square). Adjust it in a water-pan, and fill to the exact level with clear water. Clamp a rule to the vertical limb of the apparatus at an angle with the axial point of the instrument. Read the horizontal scale of the instrument along the edge of the clamped rule. Remove the instrument from the pan, using care not to disturb the adjustment of the ruler, and construct the angle of refraction on coordinate paper. Determine the relation of the angle of incidence and of refraction, and compute the refractive index of the water, the air having a refractive index of one.

Repeat the determination using a block of glass.

9. **To Determine the Refractive Power of a Convex Lens.** Use a meter stick which is provided with a movable diaphragm or screen, and a holder for a lens. Measure the focal distance of lens number 1 as furnished from the optical set. Put the lens in its holder and focus the image of the sun or of an electric bulb on the screen, moving the screen back and forth until the sharp focus is determined. If the lens is accurately ground, the focus will be at a distance of one meter, which is the refractive power of a one-diopter lens, by definition. In the same way determine the refractive power of lenses numbers 2, 3, and 4.

Construct the path of the light in the formation of the image in these cases.

If the measurement in the above case is made through two parallel openings or diaphragms about 5 mm. in diameter each, and separated by 4 or 5 mm., the point of focus can be more accurately determined (see Scheiner's experiment, No. 14.) Construct the mathematical figure showing the course of both cones of rays in this test.

10. **Determination of Near and Far Limits of Vision.** Support a meter stick in a horizontal position at a comfortable level for the eye. Mount a needle in a cork and set it on the meter stick about 25 cm. in front of the eye. Make two pin-holes in a card at a distance of about 2 mm. from each other. Hold this card with the pin-holes close in front of one eye, and bring the eye up to the end of the meter stick; cover the other eye. Observe that when the needle is brought nearer and nearer to the eye, at a certain distance it becomes double. Determine this distance very accurately. It is the *near-point of accommodation* for the right eye. Make the same determination for the left eye.

Hold the punctured card in front of the right eye, and move the needle (it is better to use something larger) farther and farther away until it becomes

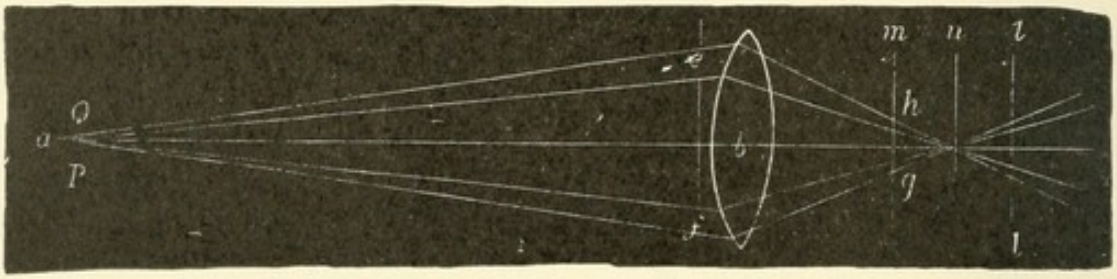


FIG. 482.—Diagram of Experiment to Ascertain the Minimum Distance of Distinct Vision.

again double, if it does so. This is the *far-point of accommodation*. In normal eyes there is no far limit. In practice an eye that has no far limit under twenty feet is considered normal. This test should be made on each eye.

11. **Inverted Image on the Retina.** Dissect off a segment of the sclerotic of a fresh ox eye, or use a fresh eye from an albino rabbit. Make a tube of black paper of the size of the eye, and insert the eye in one end, with the cornea directed into the tube. In the dark room examine the image of the candle flame as formed on the retina of the eye in the tube. In a favorable experiment, a clear inverted image of the candle can be seen on the retina through the semi-transparent membranes of the eye. The same experiment can be demonstrated with the camera, or with a small lens, using a ground-glass plate to make the image more apparent.

12. **Spherical Aberration.** In physical optics it is found that it is difficult to grind lenses so that they will refract equally in the center or

optical axis and in the periphery. Unequal refraction of these two regions is called spherical aberration. It is corrected in optics by diaphragms which shut out the light, either from the borders of the lens or from its center. The former method is used in the eye. To demonstrate Spherical Aberration, look at an object two meters from the eye, such as part of the window. Pass a card across the eye until the light enters only at the margin of the pupil, *i.e.*, the borders of the lens. It will be found that the object is no longer in focus and the outlines are dim and diffused. Normal eyes are near-sighted for the rays that are refracted by the borders of the lens.

13. **Chromatic Aberration.** Look toward the borders between the sash and the bright light of an open window, at a distance of twenty feet or more. Use the right eye only. Bring a card across the pupil approaching from the side of the light until the eye is almost covered with the card. The window sash will seem to have a blue-violet fringe. If the card is brought across from the opposite side, the sash will have a reddish-yellow fringe.

Make a cross of two strips of Bradley's pure color paper, one red and the other blue, on a black surface. When held at the proper distance the red appears nearer than the blue. This phenomenon is brought out more strongly by covering the colored papers with very thin white tissue paper. The judgment of distance is based on the effort of accommodation which is greater for the red than for the blue and violet rays.

14. **Scheiner's Experiment.** Use two needles on corks, the method described in experiment 1, placing one at a distance of 20 cm., and the other about 60 cm. from the eye. Use only the right eye, look through two pinholes in a card at the far needle. The near needle will appear double, but the images will be somewhat blurred. While looking at the far needle, bring a cardboard across the right hole, note that the left image of the near needle disappears, and *vice versa*. If one accommodates for the near needle, the far needle appears double, and upon covering the right hole with the card the right image of the far needle disappears. This is known as Scheiner's Experiment. Construct a diagram to explain these phenomena.

15. **Purkinje-Sanson's Images.** Examine the eye of another person in a dark room as follows: With the observing eye focus for a far object, let the observer hold a candle slightly to one side of the axis of vision and about one foot from the eye. If the observer looks into the other eye from the side opposite the candle, he will be able to see three reflected images, figures 457 and 458. One, from the anterior surface of the cornea, is bright and distinct, and of medium size and erect. In the middle of the pupil there will be a second image, larger and quite dim. This is a reflection from the front of the lens. The third image, reflected from the posterior surface of the lens, will seem to be farther back in the eye, quite small and inverted. These images can all three be seen at once with careful adjustment of the relative

positions of the candle and the observer, with reference to the axis of vision of the eye observed.

If the observer protects his own eye from the direct light of the candle by a blackened cardboard between his eye and the candle, and asks the observed person to accommodate now for near objects, now for far, keeping the axis of vision constant, he will be able to note that the middle image, *i.e.*, the one from the anterior surface of the lens, changes in size and in relative position with reference to the other two, which are essentially constant. With near accommodation this image becomes smaller and seems to move toward the image from the cornea; with far accommodation it becomes larger and appears to move to the image reflected from the posterior surface of the lens. This shows that the act of accommodation consists in a change in the convexity of the front of the lens.

16. **The Phakoscope of Helmholtz.** This classical instrument was invented by Helmholtz to demonstrate the act of accommodation, as out-

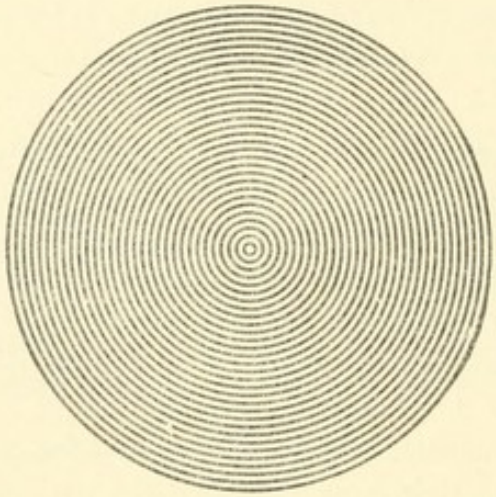


FIG. 483.—Disc of Concentric Lines for the Astigmatic Test.

lined in the second paragraph of the preceding experiment. Repeat the preceding experiment, using this instrument in a dark room.

17. **Astigmatism.** Astigmatism is a term used to describe the condition of unequal curvature of the refracting surfaces of the eye in the different meridia. The cornea is the surface which usually shows the greatest astigmatism. This defect is demonstrated by numerous forms of astigmatic charts, the most serviceable of which are the barred-letter test type, the clock dial, or the dials shown in figure 463 or 483. Hang an astigmatic dial at a distance of six meters and test the right and left eyes separately, as follows: When the vision is focussed on the center of the dial, if the eye is normal, the three bars in each radius of the clock dial will be seen with equal distinctness and have sharp black lines. In an astigmatic eye one or more of these radii will appear sharp and distinct, while the other will appear dim and

indistinct, the relative difference depending upon the degree of astigmatism. Note the meridian of astigmatism in the right and left eyes separately. Use the test set, and find the cylinder necessary to correct the astigmatism in each eye and determine its meridian.

Astigmatism is commonly shown by the presence of radii when one looks at the stars at night, or by the ragged outline of a pin-hole in a card, when held at arm's length against a white sky. In extreme cases outlines like

FIG. 484.—Diagram for Demonstrating the Blind Spot.

the bars in the window sash or checks in clothing may be distorted, or some of the lines may not even be seen.

18. **The Blind Spot.** Look with the right eye at the spot in the accompanying figure at a distance of about 20 to 25 cm., covering the left eye. Hold the spot in the line of direct vision and move the book to and from the eye; in some cases it is necessary to rotate the book slightly. It will be found that the cross to the right will, at a certain position, completely disappear. This happens when its image falls on the retina directly over the entrance of the optic nerve, which has no visual cells, and is, therefore, the blind spot.

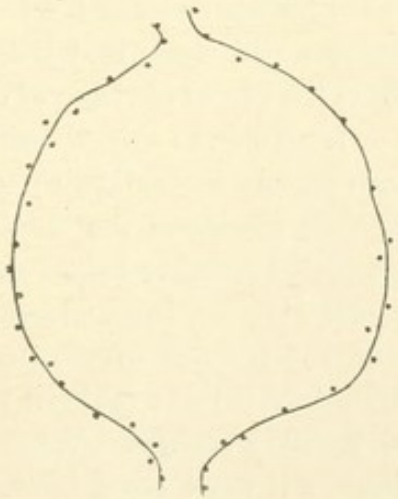


FIG. 485.—The Blind Spot with the Eye 30 cm. from the Paper.

This area is large enough to cause a man completely to disappear at a distance of about one hundred meters.

Place a sheet of white paper at a distance of 30 cm. in front of the eye, holding the head in a fixed position by some support; look with the right eye at the top of the cross made on the left of the sheet of paper. Covering the sharpened portion of a lead pencil with white paper, leaving the black tip exposed, move this pencil across the paper from the visual center to the right. At a certain distance the black lead will suddenly disappear.

Mark this point. Continue to move the pencil until the lead reappears. Mark this point. These two points represent the limits of the blind spot in the horizontal plane, as magnified by the conditions of the experiment. Mark the limits in the other meridians in the same manner. Compute from the figures obtained the exact size of the blind spot in your right eye, figure 485. Repeat on the left eye. Usually these areas are not symmetrical. The computation may be based on the following proportion: a, the diameter of the mapped blind spot is to the distance of the map from the nodal point of the eye, x, as c, the distance from the nodal point to the retina, which is 1.5 cm., is to x, the diameter of the actual blind spot in the retina. x varies from 1.5 to 3 or more mm. $a : b : : c : x$.

19. **Relations of the Size of the Retinal Image to Distance.** Compute the size of the retinal images of familiar objects by the equation given in the last experiment. Compute the size of the image formed on the retina by a man six feet tall at a distance of 100 feet. Compute the size of the image formed by a tower 125 feet tall at a distance of 575 feet.

20. **Purkinje's Shadows.** Stand in front of a blackened wall in the dark room. While looking toward the wall with the right eye accommodated for distant objects, move a lighted candle back and forth about 10 to 20 cm. to the right of the eye and a little below its level. Presently many branching shadows will be seen as though they stood in space in front of the individual. These are the shadows of the blood-vessels cast upon the retina. A careful examination will show that these shadows seem to converge to a point to the right of the center of vision of the right eye. By moving the candle up and down or from side to side, the shadows seem also to move slightly. Many persons can readily see Purkinje's figures by looking through the narrow spaces between the fingers of the hand moved close in front of the eye, when the vision is directed toward a bright sky. One can demonstrate by this means that the macula is free from blood-vessels, since the pattern of the blood-vessels around the borders of the macula is very readily determined. This is especially true if there is slight retinal congestion.

21. **Duration of the Retinal Image.** When a beam of light falls upon the retina for an instant it produces a stimulus which endures for a time after the stimulus is removed. This interval can be measured by the proper mechanical device. Place on the color wheel a disc, which has a small segment cut out at one point on the periphery. Put a printed page behind the segment with the observer standing in front. Rotate the segment faster and faster until the printed page is seen continuously. At this point the visual image made at one revolution of the disc lasts until the next impression on the same spot. The speed of the revolution of the color wheel can be measured by attaching an electric contact key and signal magnet to the disc wheel and measuring the rate of interruptions against the known vibrations of a tuning fork. The same phenomenon may be determined by placing on the disc

two complemental colors and judging the speed of revolution required for complete fusion.

22. **Limits of the Field of Vision.** The limits of the visual field are determined by direct measurement with the perimeter. Set the person whose retina is to be measured in a comfortable erect position, with one eye at the center of the arc of the perimeter and the other covered by an eye-shade. The observed eye must be fixed on the center of the field of vision, and care must be used to prevent obstruction of the field. The examination is made with greatest accuracy by bringing an object into the field of vision from behind the person observed. When the individual examined first detects the presence of the object, he announces it and the angle is read off from the arc of the perimeter and recorded on the chart for the purpose. These readings should be made in about twelve radii. They should be made for each eye.

23. **Limits for the Field of Vision for Color.** To measure the limits of the field of vision for colors one should proceed as in the preceding experiment, except that small squares of colored papers are brought into the field from the rear. The retina should be mapped for red, green, yellow, and blue. Use Bradley's pure color papers. Take four penholders and mount on the end of one a centimeter square of red paper, on the others green, yellow, and blue. To make a determination bring the color up from behind and, as soon as it is certainly detected and announced, remove it from the field of vision. Examine the eye for all four colors at one sitting, mixing them indeterminately in the individual tests. Occasionally an eye will be found which exhibits a well-marked restriction of the color field, though the individual himself may not be completely color-blind.

24. **Color-Blindness.** Make an examination for color-blindness, using Holmgren's colored yarns. Spread the yarns out on a table in the best of light. Place the three confusion skeins in front of the individual to be examined and ask him to match them quickly from the skeins on the table, paying no attention to lights and shades of the same color. A color-blind individual will confuse colored skeins, most usually the reds, greens, and grays.

25. **Color Mixing.** Use Bradley's color wheel and test the effect of simultaneous stimulation of the retina with two or more colors, by placing on the wheel two or more colored discs, rotating the wheel at a speed sufficient to cause complete fusion. The sensation produced by two colors applied simultaneously will be entirely different from that produced by either alone. Red and green (or greenish blue), when mixed in the proper proportion, produce a sensation of gray. The same effect may be had from yellow and blue, orange and violet, or any of the complementary colors chosen according to the geometrical color table, figure 473. By mixing three colors, red, green, and violet, in the proper proportion one can produce a sensation almost the same as that produced by white light.

26. **Color After-Images.** Color after-images can be demonstrated

by looking continuously at the center of one of the primary colors of Bradley's color charts against a white or gray wall until there is apparent fatigue, then suddenly removing the chart. An after-image of approximately the complementary color will appear in the course of a few seconds. Occasionally these images are very vivid. The experiments are brilliant if performed in the dark room, using colored gelatin screens through which an intense light shines. When the light is turned off, a brilliant after-image of the complementary color appears.

27. **Retinoscopy.** Use the ordinary small ophthalmoscope and examine the retina of the eye of a cat or rabbit. Dilate the eye by the use of atropine. Place the animal whose eye is to be examined on a support in front of a bright but uniform light (an Argand burner). Reflect the light from the mirror of the ophthalmoscope through the pupil into the retinal cup of the animal. Usually the ophthalmoscope has to be focussed for a cat's retina. When a good light is secured, the retinal cup will appear as a brilliantly colored disc, with the branching blood-vessels, and usually with some brilliant bluish-green pigment in the lower portions of the retinal disc.

After some practice on the cat or the rabbit, the student should examine the retina of one of his mates, preferably an eye that has an unusually wide pupil. In some cases a light dosage of homatropine may be used on one eye. This will dilate the pupil and the examination will be much easier.

Students are not recommended to use atropine unless under conditions which permit the eye to rest for two or three days following.

28. **Visual Acuity.** The visual acuity of the eye should be tested first for the right eye, then for the left. Hang a test chart at a distance of twenty feet, so that its disc is well illuminated, and allow the individual tested to read off the letters on the chart, beginning with the larger ones at the top. The letters on this chart are constructed on the basis of a visual angle of five degrees. When the letters marked "twenty feet" or "six meters" represent the limit of accurate identification, the visual acuity is said to be 1, or normal. If the line marked "thirty feet" is the limit, then the acuity is one and a half; if "fifteen feet," then the visual acuity is three-fourths, etc.

If the eyes tested are astigmatic, or have other optical defects, these must first be corrected before testing for visual acuity.

29. **The Test Set.** The student is recommended to close the experiments on the eye by fitting glasses for himself and at least two others. He should correct for the defects that have been revealed in the preceding experiments, especially for astigmatism; myopia, or hypermetropia; and presbyopia. Of course each eye must be tested and fitted separately.

CHAPTER XVI

THE REPRODUCTIVE ORGANS

THE REPRODUCTIVE ORGANS OF THE MALE.

THE male reproductive organs comprise the *Testes*, the *Vas Deferens*, the *Vesicula Seminalis*, the *Prostate Gland*, and the *Penis*.

The Testes. The testes consist of two parts, 1, the testicle, which is covered by the tunica vaginalis and secretes the germinal cells, and 2, the conducting tubules, which compose the *epididymis* and *vas deferens*.

The testicle is divided by connective-tissue septa into lobules, the *tubuli seminiferi*. Each tubule is limited by a membrana propria on which rests the *germinal epithelium*.

On the approach of sexual maturity the process of spermatogenesis begins.

FIG. 486.

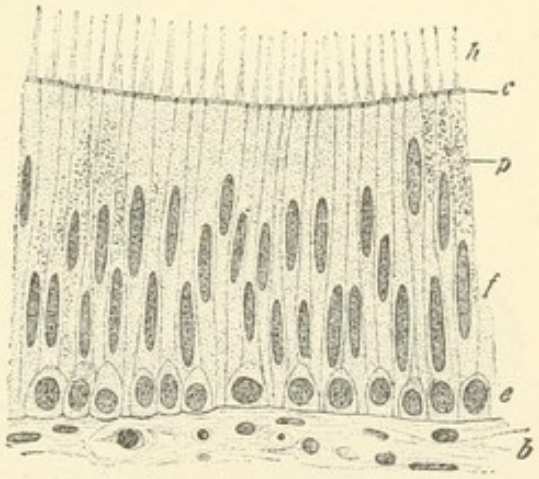


FIG. 487.

FIG. 486.—Plan of a Vertical Section of the Testicle, Showing the Arrangement of the Ducts. The true length and diameter of the ducts have been disregarded. *a*, *a*, Tubuli seminiferi coiled up in the separate lobes; *b*, tubuli recti or vasa recta; *c*, rete testis; *d*, vasa deferentia ending in the coni vasculosi; *l*, *e*, *g*, convoluted canal of the epididymis; *h*, vas deferens; *f*, section of the back part of the tunica albuginea; *i*, *i*, fibrous processes running between the lobes; *s*, mediastinum.

FIG. 487.—Vertical Section through the Wall of the Tubules of Epididymis. × 700 (Kölliker.) *b*, Connective tissue and smooth muscle cells; *e*, basal layer of epithelial cells; *f*, high columnar cells; *p*, pigment granules in columnar cells; *c*, cuticula; *h*, cilia.

The germinal cells multiply rapidly, and, by a complex series of mitotic divisions or stages, form ultimately the male reproductive cells, or sperm cells.

The important stages in order are: archispermiocyte, spermatogonia, primary and secondary spermatocytes, spermatids, and spermatozoa. The spermatogonia stage is the stage of rapid multiplication; the spermatocyte, that of maturation, comparable to the maturation stage of the ovum.

The sperm cells are the essential male reproductive cells. Each spermatozoan consists of a minute oval head, a middle piece, and a tail. The head is 4 μ by 2.5 μ. The middle piece and tail are about 50 to 60 μ long. Sperm cells possess the power of flagellate movement.

The Vas Deferens. This is the single duct proceeding from each testicle to join its fellow at the base of the bladder. Each has an ampulla or

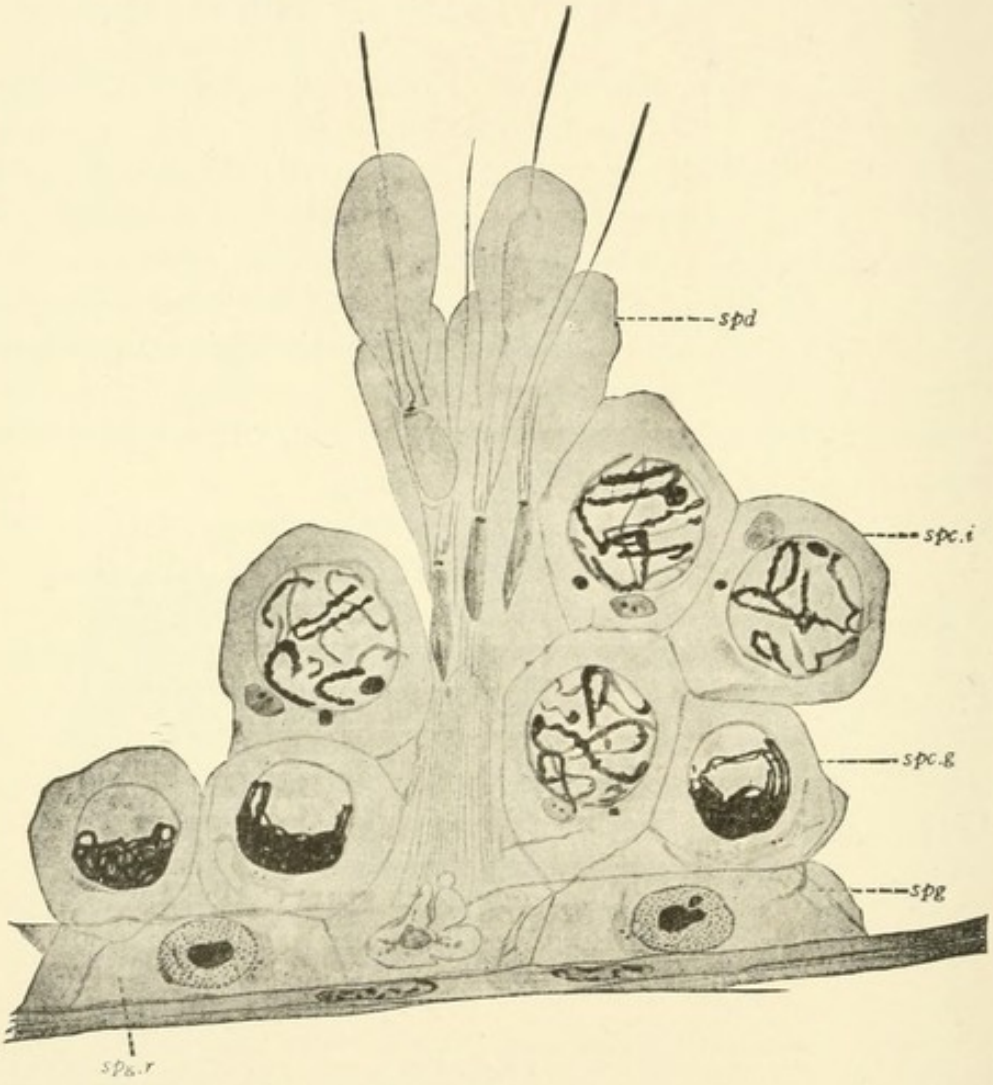


FIG. 488.—Later Stages in Spermatogenesis of the Bull. *spg.r*, Reserve spermatogonium; *spg*, spermatogonium; *spc.g*, spermatocyte in late synapsis stage; *spc.i*, spermacyte in stage just preceding the maturation divisions; *spd*, spermatids in advanced stage of histogenesis, with heads deeply embedded in Sertoli cell. Highly magnified. (After Schoenfeld.)

enlargement just before it unites with its fellow. The vas deferens has muscular walls and is lined with ciliated epithelial cells.

The Vesiculæ Seminales. The seminal vesicles have the appearance of outgrowths from the base of the vasa deferentia. Each vas deferens, just before it enters the prostate gland, through part of which it passes to terminate in the urethra, gives off a side branch which bends back from it at an acute angle. This branch, dilating, variously branching, and pursuing in

both itself and its branches a tortuous course, forms the vesicula seminalis. Each vesicula is a single-branching convoluted and sacculated tube.

The structure resembles closely that of the vasa deferentia.

The Penis. The penis is attached to the symphysis pubis by its root. It is composed of three long, more or less cylindrical masses enclosed

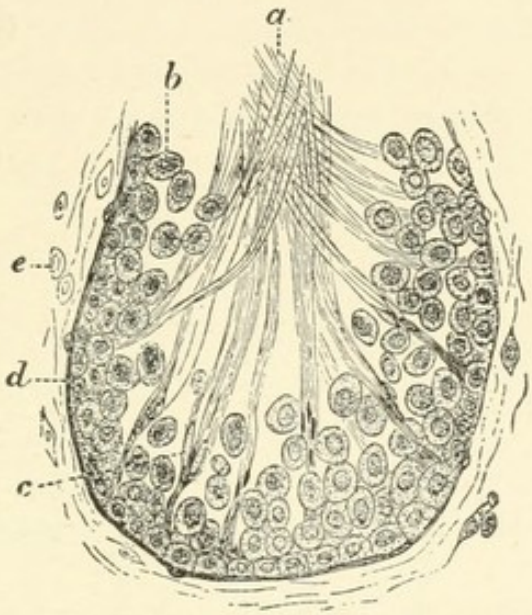


FIG. 489.—Section of a Tubule of the Testicle of a Rat, to Show the Formation of the Spermatozoa. *a*, Spermatozoa; *b*, seminal cells; *c*, spermatoblasts, to which the spermatozoa are still adherent; *d*, membrana propria; *e*, fibro-plastic elements of the connective tissue. (Cadiat.)

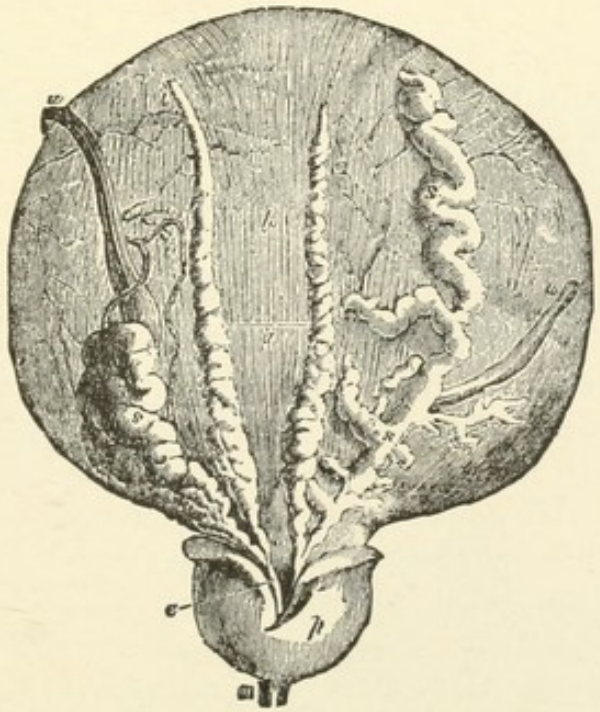


FIG. 490.—Dissection of the Base of the Bladder and Prostate Gland, Showing the Vesiculæ Seminales and Vasa Deferentia. *a*, Lower surface of the bladder at the place of reflection of the peritoneum; *b*, the part above covered by the peritoneum; *i*, left vas deferens, ending in *e*, the ejaculatory duct; the vas deferens has been divided near *i*, and all except the vesical portion has been taken away; *s*, left vesicula seminalis joining the same duct; *s,s*, the right vas deferens and right vesicula seminalis, which has been unraveled; *p*, under side of the prostate gland; *m*, part of the urethra; *u*, *u*, the ureters (cut short), the right one turned aside. (Haller.)

in remarkably firm fibrous sheaths. Two, the *corpora cavernosa*, are alike and are firmly joined together. They receive below and between them the third part, or *corpus spongiosum*. The *urethra* passes through the *corpus spongiosum*. The enlarged extremity, or glans penis, is continuous with the corpus spongiosum. *Cowper's* glands are at its base, and their ducts open into the base of the urethra.

The Prostate Gland. The prostate is situated at the neck of the urinary bladder, and encloses the base of the urethra. The prostate is made up of small compound tubular glands embedded in an abundance of mus-

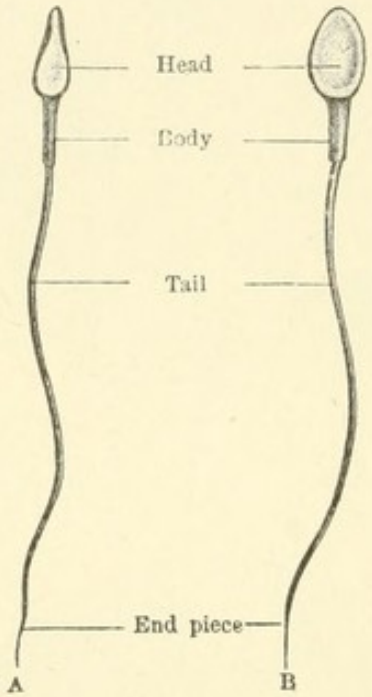


FIG. 491.—Human Spermatozoa (after Retzius). *A*, Side view; *B*, front view.

cular fibers and connective tissue. The glandular substance consists of numerous small sacculés, opening into elongated ducts, which unite into a smaller number of excretory ducts. *The acini* of the upper part of the prostate are small and hemispherical, in the middle and lower parts the tubes are longer and more convoluted. *The ducts*, twelve to twenty in number, open into the urethra. They are lined by a layer of columnar cells, beneath which is a layer of small polyhedral cells.

The muscular tissue of the prostate not only forms the chief part of the stroma of the gland, but also forms a continuous layer inside the fibrous sheath, as well as a layer surrounding the urethra continuous with the sphincter of the bladder.

The Seminal Fluid. The sperm cells of the testes are joined on their way to the exterior by the fluids secreted by the mucous lining of the various tubules and glands. Of the fluids the chief ones are the secretions of the

seminal vesicles, of the prostate gland, and of Cowper's glands. The sperm cells and the secretions together constitute the seminal fluid.

After the period of puberty the seminal fluid is secreted constantly but slowly, except under sexual excitement. It is ordinarily received into the seminal vesicles, whence it is expelled at the time of coitus. In celibates the seminal fluid may at times escape in small quantity into the urethra to be washed away by the urine, or periodic reflex emissions may occur. The seminal vesicles contribute a secretion, as well as a vesicle to receive the sperm.

The secretion of the seminal vesicles and that of the prostate gland are in some way concerned in maintaining the activity and prolonging the life of the spermatozoa. These cells remain alive in the fluid for as much as forty-eight hours after removal from the body, and remain alive quite indefinitely in the vesicles in the body. The secretions have been proven necessary to the life and function of the spermatozoa by the results of operations in which the seminal vesicles and the prostate were removed, whereby the animal became sterile.

THE REPRODUCTIVE ORGANS OF THE FEMALE.

The female genital organs consist of the *ovaries*, the *Fallopian tubes*, the *uterus*, and the *vagina*.

The Ovaries. The ovaries are paired bodies, situated in the cav-

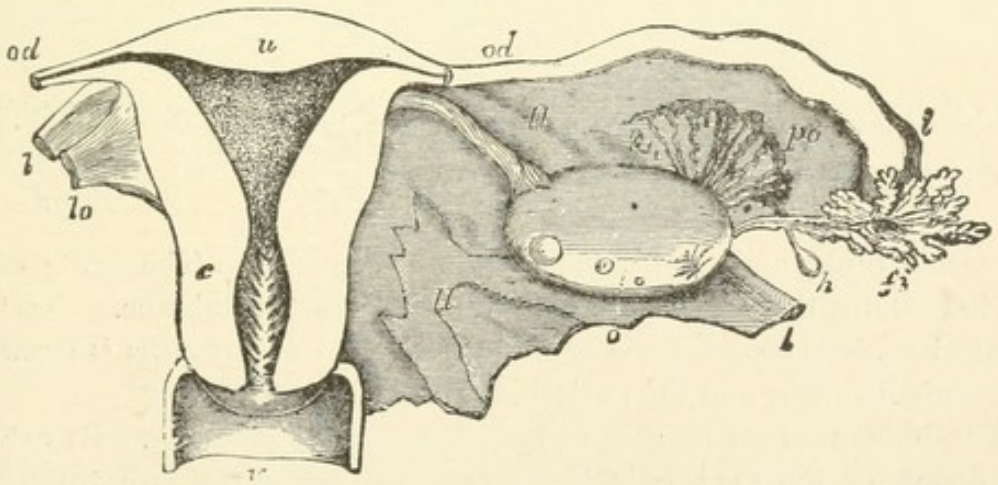


FIG. 492.—Diagrammatic View of the Uterus and Its Appendages, as Seen from Behind. The uterus and upper part of the vagina have been laid open by removing the posterior wall; the Fallopian tube, round ligament, and ovarian ligament have been cut short, and the broad ligament removed on the left side. *u*, The upper part of the uterus; *c*, the cervix opposite the os internum; the triangular shape of the uterine cavity is shown, and the dilatation of the cervical cavity with the rugæ termed arbor vitæ; *v*, upper part of the vagina; *od*, Fallopian tube or oviduct; the narrow communication of its cavity with that of the cornu of the uterus on each side is seen; *l*, round ligament; *lo*, ligament of the ovary; *o*, ovary; *i*, wide outer part of the right Fallopian tube; *fi*, its fimbriated extremity; *po*, parovarium; *h*, one of the hydatids frequently found connected with the broad ligament. ½. (Allen Thomson.)

ity of the pelvis, and adherent to the posterior surface of the broad ligament. The border of the ovary is called the hilum, and it is at this point that the

blood-vessels and nerves enter it. Each ovary is about 4 cm. long, 2 cm. wide, and 1.25 cm. thick. It is supported by the suspensory ligament.

The internal structure of the ovary consists of a peculiar soft fibrous connective tissue, *stroma*, abundantly supplied with blood-vessels. The surface of the ovary is covered with cubical epithelium. Embedded in the stroma in various stages of development are numerous minute follicles or vesicles, the *Graafian follicles*, containing the ova, figure 494. They are small and numerous near the surface of the ovary, either arranged as a continuous layer, as in the cat or rabbit, or in groups, as in the human ovary. Nearer the center are large and fully developed follicles.

Each follicle has an external membranous envelope, or *membrana propria*, which is lined with a layer of nucleated cells, forming a kind of epithelium

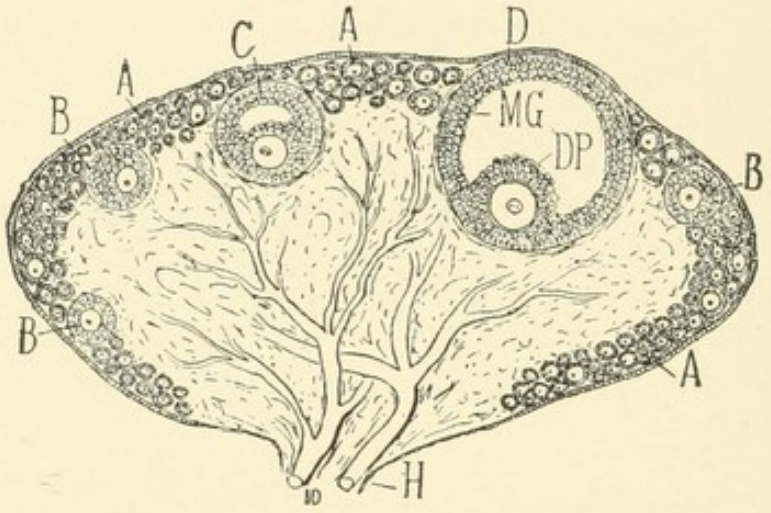


FIG. 493.—Diagrammatic Section of the Ovary, Showing its Cortical or Ovigenous Layer, Formed of Ovisacs in Various Stages of Evolution. (Duval.) *A*, *A*, *A*, Primordial ovisacs; *B*, *B*, *B*, ovisacs further developed; *C*, ovisac approaching maturity; *D*, ripe ovisac with its proligerous disc (*DP*) containing the ovum; *MG*, membrana granulosa; *H*, hilum of ovary.

or internal tunic, and named the *membrana granulosa*. The cavity of the follicle contains the ovum enclosed in a very delicate membrane. The large spherical nucleus contains one or more nucleoli. The nucleus is known as the *germinal vesicle*, and the nucleolus as the *germinal spot*.

The human ovum measures about 0.2 mm. in diameter. Its external investment, or the *zona pellucida*, or *vitelline membrane*, is a transparent membrane, about 10 μ in thickness, which under the microscope appears as a bright ring, figure 495. The ovum itself has the characteristic structure of the typical cell, with the exception that its cytoplasm is filled with numerous yolk granules. The larger granules or globules, which have the aspect of fat-globules, are in greatest number at the periphery of the yolk.

The nucleus, or *germinal vesicle*, is about 0.05 mm. in diameter. The vesicle is of greatest relative size in the smallest ova.

The Graafian follicles are formed in the following manner: The em-

bryonic ovary is covered with short columnar cells, or the so-called germinal epithelium. The cells of this layer undergo proliferation so as to form several strata, and grow into the ovarian stroma as longer or shorter columns or tubes. By degrees these tubes become cut off from the surface epithelium, and form cell nests, small if near the surface, larger if in the depth of the stroma. The nests increase in size from multiplication of their cells. Certain cells of the germinal epithelium enlarge, and form ova; and the formation of ova takes place in the nests within the stroma. The small cells of a nest surround the ova, and form their membrana granulosa, and the stroma growing up separates the surrounded ova into so many Graafian follicles.

The smallest follicles are formed at the surface, and make up the cortical

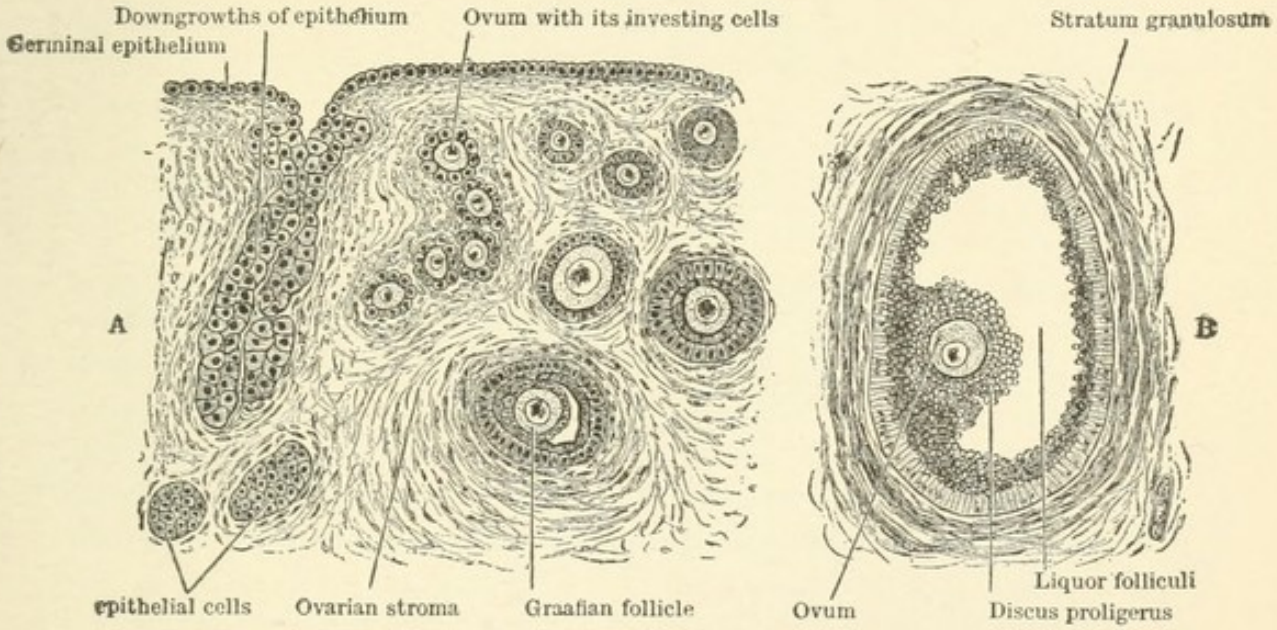


FIG. 494.—*A*, Diagrammatic Representation of the Manner in which the Graafian Follicles Arise During the Development of the Ovary. *B*, Diagram Illustrating the Structure of a Ripe Graafian Follicle. (Cunningham.)

layer. It is said by some that the superficial follicles as they ripen become more deeply placed in the ovarian stroma; and, again, that as they increase in size, they make their way toward the surface.

When the Graafian follicles mature, they form little prominences on the exterior of the ovary covered only by a thin layer of condensed fibrous tissue and epithelium. From the earliest infancy, and through the whole fruitful period of life, there appears to be a constant formation, development, and maturation of Graafian vesicles, with their contained ova. Until the period of puberty, however, the process is comparatively inactive. But, coincident with the other changes which occur in the body at the time of puberty, the ovaries enlarge and become very vascular, the formation of Graafian vesicles is more abundant, the size and degree of development attained by them are greater, and the ova are capable of being fertilized.

The Fallopian Tubes, or Oviducts. The Fallopian tubes are about 10 cm. in length and extend between the ovaries and the upper angles of the uterus. At the point of attachment to the uterus, each tube is very narrow; but in its course to the ovary it increases to about 3 mm. in thickness. At its distal extremity, which is free and floating, it bears a number of *fimbriæ*, one of which is longer than the rest and is attached to the ovary. The canal

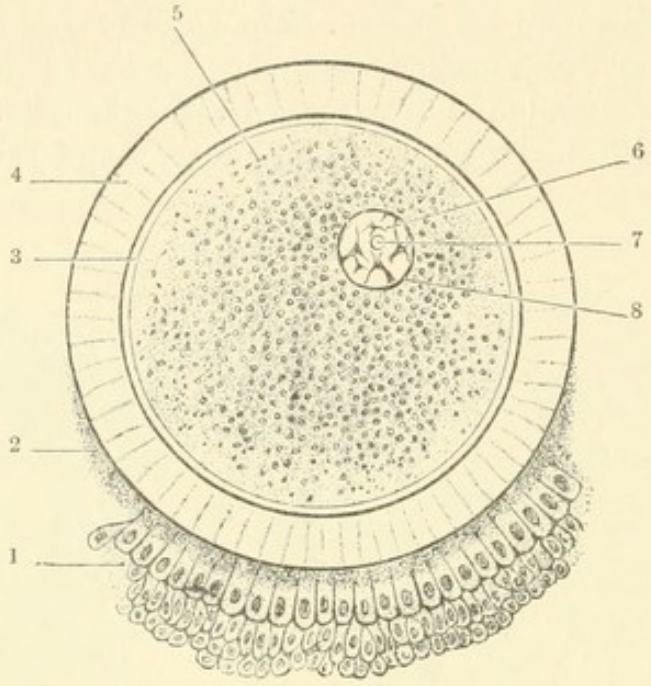


FIG. 495.—Diagrammatic Representation of a Human Ovum and Its Coverings. (Cunningham.)

The corona radiata, which completely surrounds the ovum, is represented only in the lower part of the figure.

1, Corona radiata;
2, granular layer;
3, vitelline membrane;
4, zona pellucida (oolemma);
5, vitellus or yolk;
6, germinal vesicle (nucleus);
7, germinal spot (nucleolus);
8, nuclear membrane.

of the tube is narrow, especially at its point of entrance into the uterus. Its other extremity is wider and opens into the cavity of the abdomen by the fimbriæ. The Fallopian tube is invested with peritoneum, and its canal is lined with ciliated epithelium.

The Uterus. The uterus, *u*, *c*, figure 492, is a somewhat pyriform organ, and is about 7.5 cm. in length, 5 cm. in breadth at its upper part or *fundus*, but at the *neck* or *cervix* only about 1.25 cm. The part between the fundus and neck is termed the *body* of the uterus; it is about 2.5 cm. in thickness.

The uterus is constructed of three principal layers, or coats: serous, fibrous and muscular, and mucous. The *serous* coat, which has the same general structure as the peritoneum, covers the organ except the front surface of the neck. The *middle* coat is a thick mass of unstriped muscle. The muscle fibers become enormously developed during pregnancy. The arteries

and veins are found in large numbers in the outer part so as to form almost a special vascular coat. The *mucous* membrane of the uterus is composed of columnar ciliated epithelium, which extends also to the interior of the tubular glands, of which the mucous membrane is largely made up. In the cervix of the uterus the mucous membrane is arranged in permanent longitudinal folds, *palmæ plicatæ*. The glands of this part branch repeatedly, and extend deeply into the substance of the cervix. The body has numerous simpler tubular glands. The glands are also lined with ciliated epithelium. They secrete a thick glairy mucus, resembling white of egg.

The Vagina. The vagina is a membranous canal 8 to 10 cm. long, extending obliquely downward and forward from the neck of the uterus, which it embraces, to the external organs of generation. It is lined with mucous membrane, covered with stratified squamous epithelium, which in the ordinary contracted state of the canal is thrown into transverse folds. External to the mucous membrane, the walls of the vagina are constructed of unstriped muscle and fibrous tissue, within which in the submucosa, especially around the lower part of the tube, is a layer of erectile tissue. The lower extremity of the vagina is embraced by an orbicular muscle, the *sphincter vaginæ*. The external organs of generation are the *clitoris*, the *labia interna* or *nymphæ;* and, the *labia externa* or *pudenda*, formed of the external integument, and lined internally by mucous membrane. Numerous mucous follicles are scattered beneath the mucous membrane of the external organs of generation; and two larger lobulated glands, the glands of Bartholin, analogous to Cowper's glands in the male, are located at the sides of the lower part of the vagina. The ducts of these glands are about 12 mm. long and open immediately external to the hymen at the mid-point of the lateral wall of the vaginal orifice.

Ovulation and Menstruation. In the process of development in the ovary, the individual Graafian follicle increases in size and gradually approaches the surface of the ovary. When fully ripe or mature, it forms a little projection on the exterior. Coincident with the increase in size, which is caused by the augmentation of its liquid contents, the external envelope of the distended vesicle becomes very thin and eventually bursts. The ovum and fluid contents of the vesicle escape on the exterior of the ovary, whence they pass into the Fallopian tube.

In man and mammals ovulation apparently occurs only at certain periods. These periods seem to precede or occur during the changes in the woman that constitute the phenomenon of *menstruation*, or, in the lower mammals, of *heat*.

That ovulation and discharge occur periodically, and only during the phenomenon of heat, in the lower mammalia, is made probable by the facts that, in all instances in which Graafian vesicles have been found presenting the appearance of recent rupture, the animals were at the time or had recently been in heat. There are few authentic and detailed accounts of Graafian

vesicles being found ruptured in the intervals of heat; and females do not admit the males, and never become impregnated, except at those periods. Although conception is not confined to the periods of menstruation, yet it is more likely to occur about a menstrual epoch than at other times.

The exact relation between the discharge of ova and menstruation is not very clear. It was formerly believed that menstruation was the result of a congestion of the uterus arising in association with the enlargement and rupture of a Graafian follicle; but though a Graafian follicle is, as a rule, ruptured at each menstrual epoch, yet instances are recorded in which menstruation has occurred where no Graafian follicle can have been ruptured, and

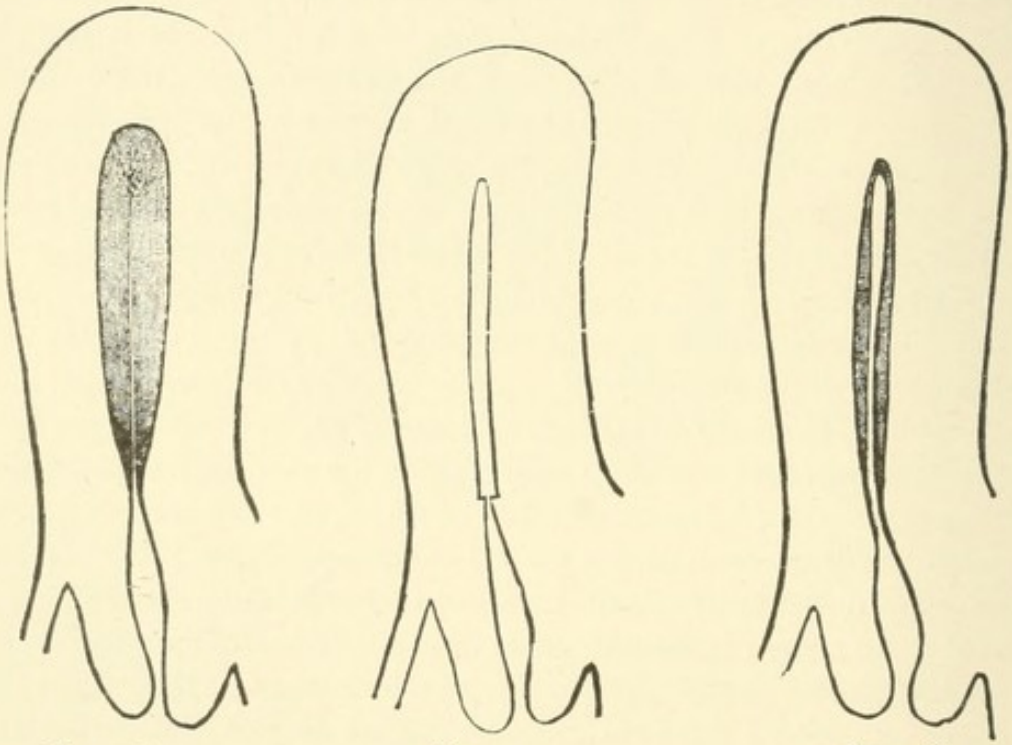


FIG. 496. FIG. 497. FIG. 498.

FIG. 496.—Diagram of Uterus just Before Menstruation. The shaded portion represents the thickened mucous membrane.

FIG. 497.—Diagram of Uterus when Menstruation has just Ceased, Showing the Cavity of the Uterus Deprived of Mucous Membrane.

FIG. 498.—Diagram of Uterus a Week After the Menstrual Flux has Ceased. The shaded portion represents renewed mucous membrane. (J. Williams.)

cases where ova have been discharged in amenorrheic women. It must therefore be admitted that menstruation is not dependent on the maturation and discharge of ova.

Observations made after death, and facts obtained by clinical investigation, support the view that rupture of a Graafian follicle does not happen on the same day of the monthly period in all women. In the minority of cases it may occur toward the close or soon after the cessation of a flow. On the other hand, in almost all subjects examined after death, of which there is record, rupture of the follicle appears to have taken place before the commencement of the menstrual flow.

However, the presence of the ovaries seems necessary for the performance of the menstrual function; for women do not menstruate when both ovaries have been removed by operation. (See page 432 for a discussion of the functional effects of removal of the ovary.)

Source and Character of Menstrual Changes. The menstrual periods usually occur at intervals of a lunar month, the duration of each being from three to six days. In some women the intervals are so short as three weeks or even less; while in others they are longer than a month. The periodical return is usually attended by pains in the loins, a sense of fatigue in the lower limbs, and other symptoms, which vary extremely in different individuals.

The menstrual discharge is a thin sanguineous fluid, and consists of blood, epithelium, and mucus from the uterus and vagina. The menstrual flow is preceded by a general engorgement of all the pelvic organs with blood. The cervix and vagina become darker in color and softer in texture, and the quantity of mucus secreted by the glands of the cervix and body is increased. The uterine mucous membrane is swollen and the glands are enlarged. The discharge of blood, the source of which is the mucous membrane of the body of the uterus, is probably associated with uterine contractions. There is great difference of opinion as to whether or not any of the uterine mucous membrane is normally shed during the process of menstruation. John Williams believes that the whole of the mucous membrane of the body of the uterus is thrown off at each monthly period, forming a true *decidua menstrualis*, figure 496, while Möricke and others believe that the mucous membrane remains intact. Leopold believes that red blood-corpuscles escape from the congested capillaries and undermine the superficial epithelium, and that in this way the superficial layer of the mucous membrane is eroded and subsequently regenerated. There is a period of regeneration followed by a period of rest before the next repetition. Minot distributes the variations in time as follows:

Tumefaction	5 days
Menstrual discharge	4 "
Restoration of mucosa	7 "
Period of rest	12 "

The menstrual period is often accompanied by profound disturbances in other parts of the body, especially of the vascular and of the nervous systems and of the nutritive processes.

Corpus Luteum. Immediately before, as well as subsequent to, the rupture of a Graafian follicle and the escape of its ovum, changes ensue in the interior of the follicle, which result in the production of a yellowish mass, termed a Corpus luteum.

When fully formed, the corpus luteum of mammals is a roundish solid body, of a yellowish or orange color, and composed of a number of lobules,

which surround, sometimes a small cavity, but more frequently a small stelliform mass of substance, from which delicate processes pass as septa between the several lobules. The processes gradually change till they nearly fill the cavity of the follicle, and even protrude from the orifice in the external covering of the ovary. Subsequently this orifice closes, but the fleshy growth within still increases during the earlier period of pregnancy, the color of the substance gradually changing to yellow, and its consistence becoming firmer. After the orifice of the follicle has closed, the growth of the yellow substance continues during the first half of pregnancy, till the cavity is reduced to a comparatively small size or is obliterated; in the latter case, merely a white stelliform cicatrix remains in the center of the corpus luteum.

The first changes of the internal coat of the Graafian follicle in the process of formation of a corpus luteum seem to occur in every case in which an ovum escapes. If the ovum is impregnated, the growth of the yellow substance continues during nearly the whole period of gestation and forms the large corpus luteum commonly described as a characteristic mark of impregnation.

The significance of the corpus luteum is found in the belief that it is the portion of the ovary especially concerned in the production of an internal secretion that affects the uterus, especially stimulating it at and before the menstrual period.

Menstrual Life. The occurrence of a menstrual discharge is one of the most prominent indications of the commencement of puberty in the female sex; though its absence even for several years is not necessarily attended with arrest of the other characters of this period of life or incapability of impregnation. The average time of its first appearance in females of this country and others of about the same latitude is from fourteen to fifteen: but it is much influenced by the kind of life to which girls are subjected, being accelerated by habits of luxury and indolence, and retarded by contrary conditions. Its appearance may be slightly earlier in persons dwelling in warm climates than in those inhabiting colder latitudes. The menstrual functions continue through the whole fruitful period of a woman's life, and usually cease between the forty-fifth and fiftieth years, which time is known as the climacteric. Menstruation does not usually occur in pregnant women.

CHAPTER XVII

DEVELOPMENT

Changes Which Occur in the Ovum Prior to Impregnation. The ovum when ripe and detached from the ovary is a single cell enclosed within the zona pellucida, and containing the germinal vesicle and germinal spot. The ovum undergoes a series of changes preparatory to fertilization, known as *maturation*, the general effect of which is to reduce the chromatin in anticipa-

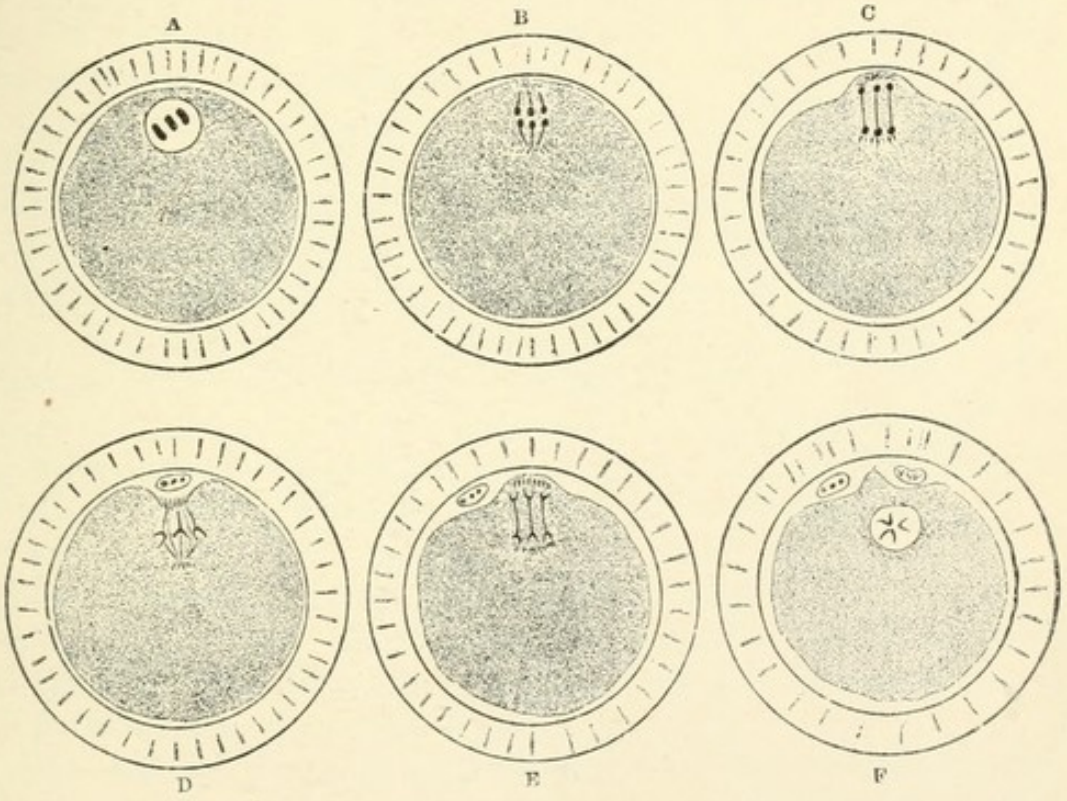


FIG. 499.—The Maturation of the Ovum; Extrusion of the "Polar Bodies." (Diagrammatic.) *A*, An ovum at the commencement of the process; *B*, after the formation of the spindle. The chromosomes are gathered at the equator of the spindle. *C*, One apex of the spindle has projected into a bud on the surface, and half of the divided dyads have passed to each pole; *D*, the separation of the first polar body; *E*, the commencement of the second polar body; *F*, the completion of the second polar body. (Cunningham.)

tion of the added chromatin from the sperm nucleus. The primary change observed in the ovum consists in the migration of the germinal vesicle or nucleus to the surface, and the disappearance of its nuclear membrane, with a consequent indistinctness of its outline. Its protoplasm becomes to a considerable extent confounded with the yolk substance, and its germinal spot disappears. The next step in the process is the appearance in the yolk of two

centrosomes in a clear space near the poles of the elongated vesicle, and the formation of a *nuclear spindle*, with the aster at either end lying near the surface of the yolk. The nucleus now divides into two parts, and that nearer the surface is extruded from the ovum enveloped in a very small amount of protoplasm. This forms the first *polar body*. The nucleus again divides by mitosis, one-half of the chromatin is extruded from the ovum, forming a second polar cell; the chromatin that remains behind constitutes the *female pronucleus*. The centrosome has disappeared and the ovum undergoes no further changes unless fertilized by the sperm.

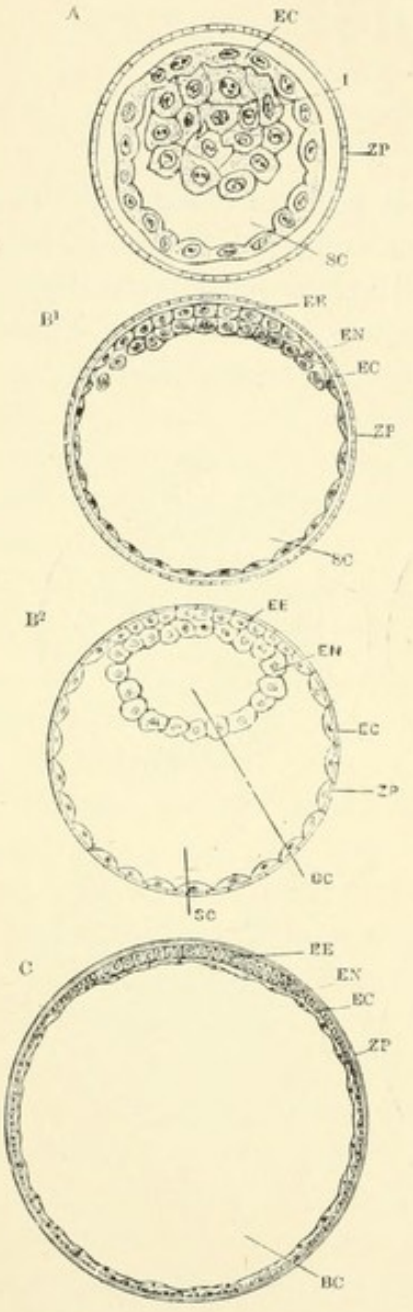


FIG. 500.—Conversion of the Morula to the Blastula. Formation of Blastodermic Vesicle and Membrane. *A*, Appearance of segmentation cavity and attachment of inner cell-mass to ectoderm at upper pole of ovum; B^1, extension and flattening of inner cell-mass as it occurs in rabbits and some other mammals; B^2, extension of entoderm as it occurs in insectivora, monkeys, apes, and man; *C*, completion of bilaminar blastodermic vesicle; *BC*, blastodermic cavity; *EC*, ectoderm; *EE*, embryonic ectoderm; *EN*, entoderm; *I*, inner cell-mass; *SC*, segmentation cavity; *ZP*, zona pellucida. (Cunningham.)

Changes Following Impregnation. The process of impregnation of the ovum has been observed most accurately in the lower types. The process is as follows: The head of a single spermatozoon joins with an elevation of the yolk substance, the tail remaining motionless and then disappearing. The head enveloped in the protoplasm then sinks into the yolk and becomes a nucleus, from which the yolk substance is arranged in radiating lines. This is the *male pronucleus*. The middle piece of the sperm is believed to furnish a new centrosome to the ovum. The centrosome now divides and moves to either side the two pronuclei, a segmentation spindle is formed, and the egg undergoes its first segmentation.

The process of segmentation begins almost immediately in each half of the yolk, and cuts it also in two. The process is repeated until at last by continued cleavages the whole yolk is changed into a mulberry-like mass, still enclosed by the zona pellucida, figure 500. Fertilization probably takes place in the Fallopian tubes, and segmentation of the fertilized ovum occurs on its passage to the uterus.

The passage of the ovum from the ovary to the uterus occupies probably eight or ten days in the human.

The peripheral cells, which are formed first, arrange themselves at the surface of the yolk into a membrane, the *ectoderm*. The deeper cells of the interior pass gradually toward the surface, thus increasing the thickness of the membrane already formed by a second, or *entoderm*, layer of cells, while the central part of the yolk, the *blastoderm cavity*, remains filled only with a clear fluid. By this means the yolk is shortly converted into a kind of secondary vesicle, the walls of which are composed externally of the original vitelline membrane, and within by the newly formed cellular layer, the *blastoderm* or *germinal* membrane, as it is called.

Important changes occur in the structure of the mucous membrane of the uterus. The epithelium and subepithelial connective tissue, together with the tubular glands, increase rapidly, and there is a greatly increased vascularity of the whole mucous membrane, while a substance composed

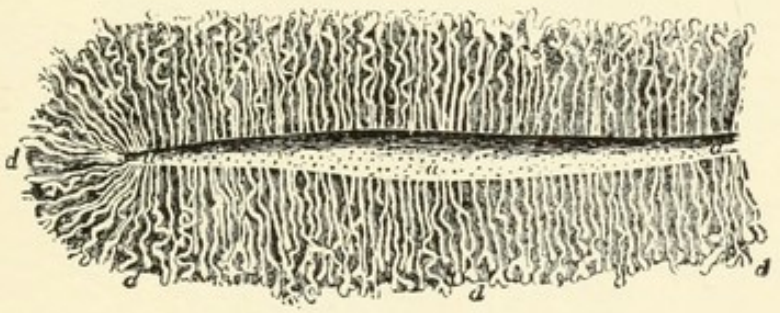


FIG. 501.—Section of the Lining Membrane of a Human Uterus at the Period of Commencing Pregnancy, Showing the Arrangement and Other Peculiarities of the Glands, *d*, *d*, *d*, with Their Orifices, *a*, *a*, *a*, on the Internal Surface of the Organ. Twice the natural size.

chiefly of nucleated cells fills up the interfollicular spaces in which the blood-vessels are contained. The effect of these changes is an increased thickness, softness, and vascularity of the mucous membrane, the superficial part of which itself forms the *membrana decidua*.

The object of this increased development is the production of nutritive materials for the ovum; for the cavity of the uterus shortly becomes filled with secreted fluid, consisting almost entirely of nucleated cells in which the chorion villi are embedded.

When the ovum first enters the uterus it becomes embedded in the structure of the decidua, which is yet quite soft, and in which soon afterward three portions are distinguishable. These have been named the *decidua vera*, the *decidua basalis*, and the *decidua capsularis*.

In connection with these villous processes of the chorion, there are developed *depressions* or *crypts* in the decidua vera, which correspond in shape to the villi they are to lodge; and thus the chorionic villi become more or less embedded in the maternal structures. These uterine crypts, it is im-

portant to note, are not, as was once supposed, merely the open mouths of the uterine follicles.

The Placenta. During these changes the deeper part of the mucous membrane of the uterus, at and near the region where the placenta is placed, becomes hollowed out by sinuses, or cavernous spaces, which communicate on the one hand with arteries and on the other with veins of the uterus. Into hese sinuses the villi of the chorion protrude, pushing the thin

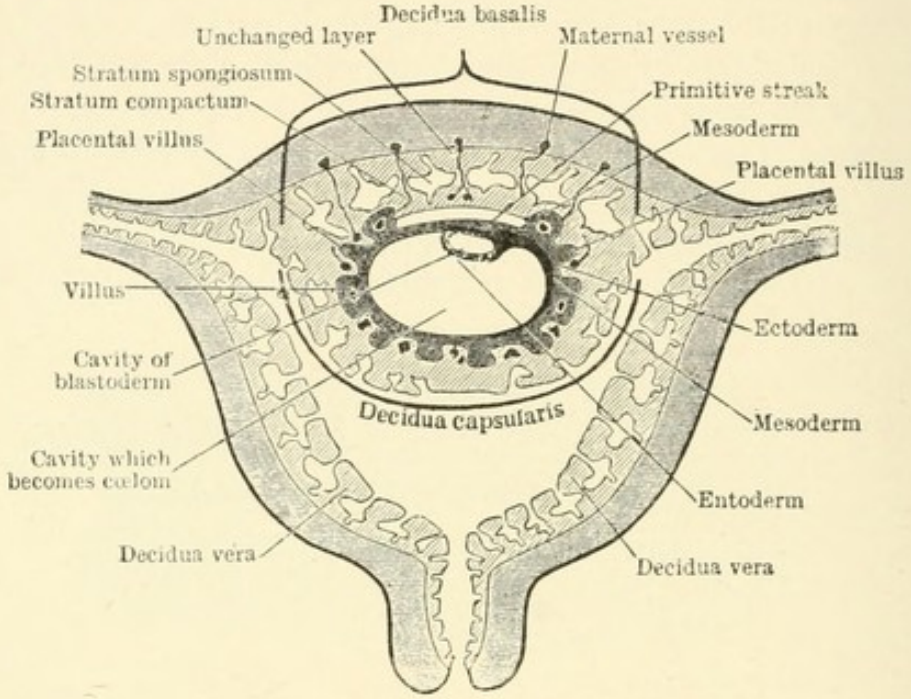


FIG. 502.—Diagram of the Early Stage of Human Embryo in Relation to the Uterus. (Cunningham.)

walls of the sinuses before them, and so come into intimate relation with the blood contained in them. *There is no direct communication between the blood-vessels of the mother and those of the fetus;* but the layer or layers of membrane intervening between the blood of the one and of the other offer no obstacle to a free interchange of matters between them by diffusion and osmosis. Thus the villi of the chorion, containing fetal blood, are bathed or soaked in maternal blood contained in the uterine sinuses.

The placenta, therefore, of the human subject is composed of a *fetal* part and a *maternal* part—the term placenta properly including all that entanglement of fetal villi and maternal sinuses, by means of which the blood of the fetus is enriched and purified after the fashion necessary for the proper growth and development of those parts which it is designed to nourish.

The whole of this structure is not, as might be imagined, thrown off immediately after birth. The greater part, indeed, comes away at that time, as the *after-birth;* and the separation of this portion takes place by a rending

or crushing through of that part at which its cohesion is least strong, namely, where it is most burrowed and undermined by the cavernous spaces before referred to. In this way it is cast off with the fetal membrane. The remaining portion is either gradually absorbed, or thrown off in the uterine discharges which occur at this period. A new mucous membrane is of course gradually developed.

Circulation of Blood in the Fetus. The circulation of blood in the fetus differs considerably from that of the adult.

Returning from the placenta by the umbilical vein the blood is first conveyed to the under surface of the liver, where the stream is divided—a part of the blood passing straight on to the inferior vena cava through a venous canal

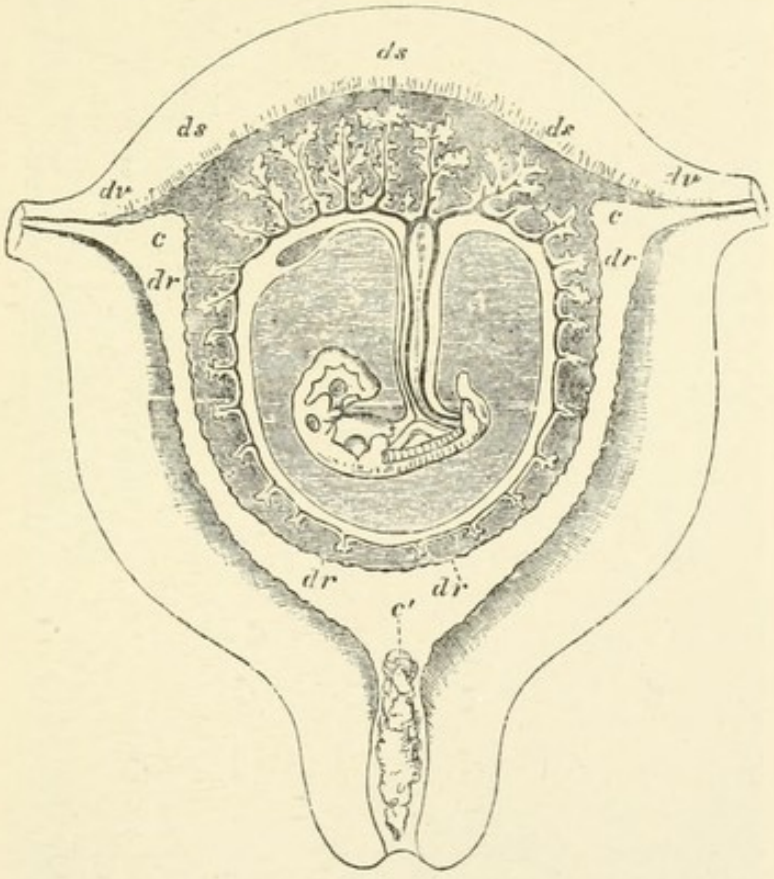


FIG. 503.—Diagrammatic View of a Vertical Transverse Section of the Uterus at the Seventh or Eighth Week of Pregnancy. *c*, *c*, *c'*, Cavity of uterus, which becomes the cavity of the decidua, opening at *c*, *c*, the cornua, into the Fallopian tubes, and at *c'* into the cavity of the cervix, which is closed by a plug of mucus; *dv*, decidua vera; *dr*, decidua reflexa, with the sparser villi embedded in its substance; *ds*, decidua serotina, involving the more developed chorionic villi of the commencing placenta. The fetus is seen lying in the amniotic sac. The umbilical cord and its vessels pass up from the umbilicus to the distribution of the blood-vessels in the villi of th chorion- and the pedicle of the yolk-sac the cavity between the amnion and chorion. (Allen Thomson.)

called the *ductus venosus*, while the remainder passes into the portal vein and reaches the inferior vena cava only after circulating through the liver. It is carried by the vena cava to the right auricle of the heart, into which cavity the blood is also pouring that has circulated in the head and neck and arms, and has been brought to the auricle by the superior vena cava. It might be

naturally expected that the two streams of blood would be mingled in the right auricle, but such is the case only to a slight extent. The blood from the superior vena cava—the less pure fluid of the two—passes almost exclusively into the right ventricle, through the auriculo-ventricular opening, just as it does in the adult. The blood of the inferior vena cava is directed by a fold

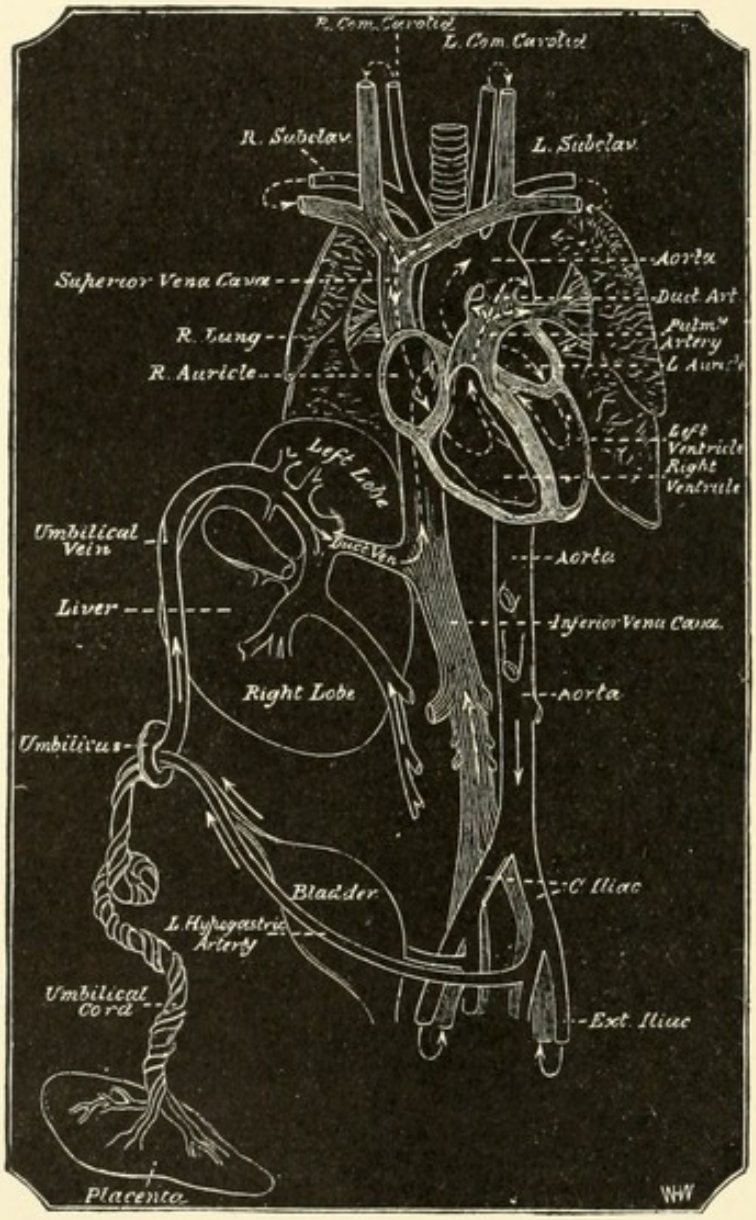


FIG. 504.—Diagram of the Fetal Circulation.

of the lining membrane of the heart, called the *Eustachian valve*, through the foramen ovale into the left auricle and into the left ventricle, and out of this into the aorta, and thence to all the body, but chiefly to the head and neck. The blood of the right ventricle is sent out in *small amount* through the pulmonary artery to the lungs, and thence to the left auricle, as in the adult, but the greater part by far passes through a canal, the *ductus arteriosus*, leading from the pulmonary artery into the aorta just below the origin of the three

great vessels which supply the upper parts of the body, and is distributed to the trunk and lower parts of the body. A large portion passes out by way of the two *umbilical arteries* to the placenta. From the placenta it is returned by the umbilical *vein* to the under surface of the liver, from which the description started.

After birth the foramen ovale, the ductus arteriosus, and ductus venosus all close, and the umbilical vessels are tied off, so that the two streams of blood which arrive at the right auricle by the superior and inferior vena cava, respectively, thenceforth mingle in this cavity of the heart, and pass into the

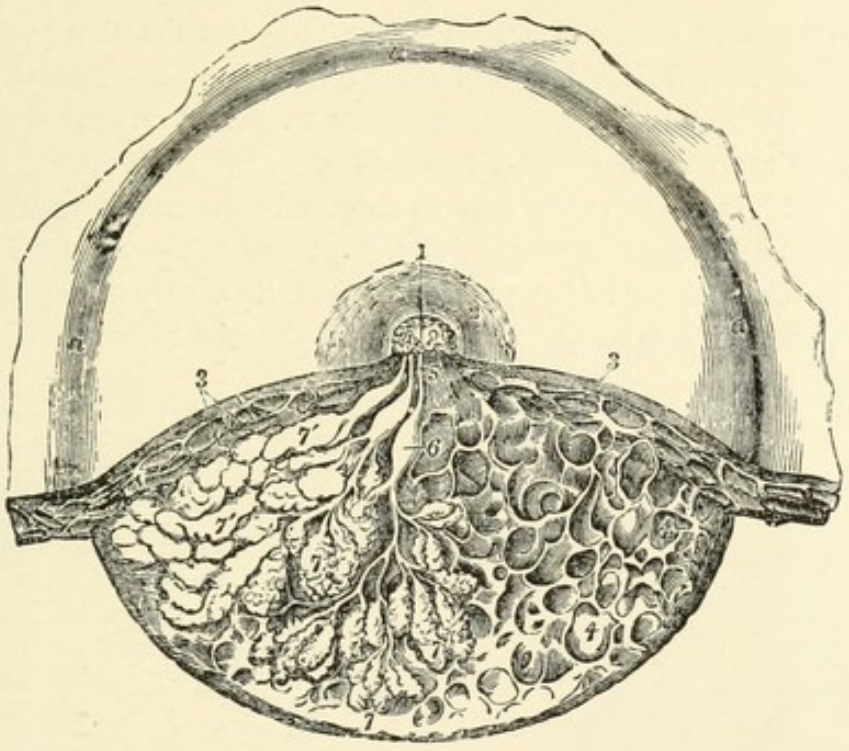


FIG. 505.—Dissection of the Lower Half of the Female Mamma During the Period of Lactation. ⅔.—In the left-hand side of the dissected part the glandular lobes are exposed and partially unravelled, and on the right-hand side the glandular substance has been removed to show the reticular loculi of the connective tissue in which the glandular lobules are placed. 1, Upper part of the mammilla or nipple; 2, areola; 3, subcutaneous masses of fat; 4, reticular loculi of the connective tissue which support the glandular substance and contain the fatty masses; 5, one of three lactiferous ducts shown passing toward the mammilla, where they open; 6, one of the sinus lactei or reservoirs; 7, some of the glandular lobules which have been unravelled; 7′, others massed together. (Luschka.)

right ventricle, by way of the pulmonary artery to the lungs, and through these, after aeration, to the left auricle and ventricle, to be distributed over the body.

Parturition. With the implantation of the embryo and the development of the placenta, the uterus grows rapidly until the end of pregnancy. The muscles of its walls increase enormously in volume, apparently by an increase in the size of the fibers, and the whole structure may become thirty or forty times its size in the resting period. Many changes take place also in other parts of the body, changes which are dependent on the presence of the fetus. Full-term pregnancy occurs when the uterus is

isolated from the nervous system, hence it has been inferred that there is some sort of special secretion, possibly of the embryo itself, that makes its way into the blood and influences the organs of the mother.

At the end of the period of pregnancy the strong uterine walls begin periodic contractions which ultimately result in the delivery of the fetus. These contractions are at first weak and at long intervals, but later become very strong and follow each other in rapid succession. The uterine contractions are supported by reflex contractions of the abdominal and thoracic muscles. After the fetus is delivered the uterine contractions become milder, but still continue until the placenta is finally expelled.

The initiation of the contractions of the uterus at delivery probably depends on the chemical stimulation of some substance or substances produced in the uterus itself or in the fetus; substances that react on the nervous mechanism and on the uterine muscles themselves. This view cannot be said to be proven, but it is supported by certain observed facts and experiments.

Lactation. There is a marked development of the mammary glands especially in the later part of the period of gestation. Upon delivery of the fetus the gland enlarges very sharply and an abundant secretion is formed.

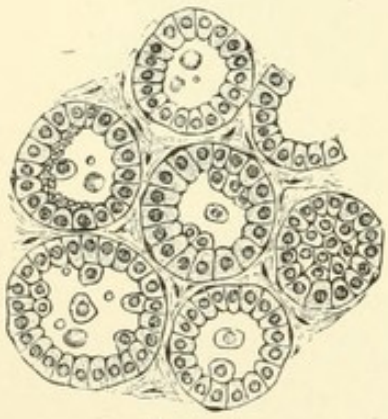


FIG. 506.

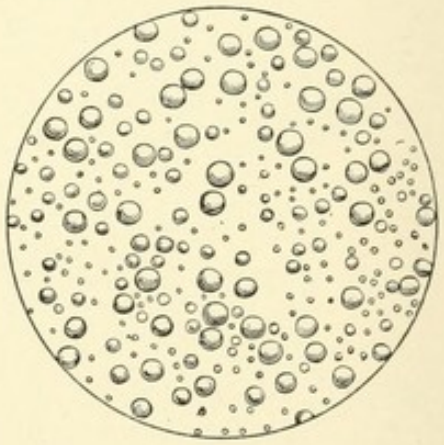


FIG. 507.

FIG. 506.—Section of Mammary Gland of Bitch, Showing Acini, Lined with Epithelial Cells of a Polyhedral or Short Columnar Form. ×200. (V. D. Harris.)

FIG. 507.—Globules and Molecules of Cow's Milk. ×400.

The secretion of the first few days is called the *colostrum*. It contains a larger per cent of solids, has the large granular colostral corpuscles, is more alkaline than ordinary milk, and has a specific gravity of 1040 to 1046.

The mammary glands have been isolated from the nervous system to determine whether or not the association in time between their changes and the changes in the uterus were of a nervous nature. The isolated mammæ develop and begin lactation at parturition as in the normal. It would seem that here, too, there is some special form of stimulation through the medium of the blood. Yet one must not draw the conclusion that the nervous system

exerts no influence on the mammary gland. Stimulation of the nerves to the gland produces vascular changes that increase or decrease the quantity of secretion. Many observations have been noted in women, which show that the secretion of milk is sharply influenced by, or even completely suppressed by, nervous states.

The Composition of Milk. Milk has a specific gravity of 1028 to 1034. Its fat is held in emulsion. Under the microscope, it is found that the milk globules vary in size, the majority being from 2 to 3 μ in diameter. The old view that they have an investing membrane of albuminous material is now generally discarded.

Composition of Colostrum (Pfeiffer).

Proteids	5.71
Fat	2.04
Sugar	3.74
Salts	0.28
Water	88.23
	100.00

Salts in Woman's Milk (Rotch).

Calcium phosphate	23.87
Calcium silicate	1.27
Calcium sulphate	2.25
Calcium carbonate	2.85
Magnesium carbonate	3.77
Potassium carbonate	23.47
Potassium sulphate	8.33
Potassium chloride	12.05
Sodium chloride	21.77
Iron oxide and alumina	0.37
	100.00

In addition to the oil or butter fat, milk contains certain *proteids*, *milk-sugar*, and several *salts*. Its percentage composition is given in the tables appended.

Chemical Composition of Milk. (After Foster, Harrington, *et al.*)

	Human.	Cow.	Mare.	Bitch.
Water	87.30	87	90	76
Solids	12.70	13	10	24
Fats	4.00	4.0	2.0	10.0
Proteids	1.50	4.0	2.5	10.0
Sugar	7.00	4.3	5.0	3.5
Salts	0.20	0.7	0.5	0.5

INDEX

Abdominal viscera, vascular nerves for, 223
Abducens nerve, 554
Absorption, 361
  conditions for, 362
  methods of, 361, 364
  places for, 362, 370
  rapidity of, 362, 370
  through the intestines, 363
    the lungs, 370
    the mouth, 362
    the skin, 369
    the stomach, 362
Accelerator centers for heart, 183
Accessory olives, 539
  thyroids, 428
Accommodation of vision, 642, 645
Achromatic layer, 17
  spindle, 19
Achromatin, 18
Achroödextrin, 311
Acid albumin, 82
Acromegaly, 431
Activating ferments, 303
Adamkiewicz reaction, 196
Addison's disease, 429, 431
Adenoid tissue, 35
Adipose tissue, 37, 38
Adrenalin, 431
Adrenals, 428
After-birth, 694
  -images, 654, 660, 677
  -sensations, 602
Agglutinative substances, 129
Air cells, 250
  changes in, during respiration, 263
  composition of, 263
  diffusion of, 267
  pressure of, 267, 285
  quantity breathed, 259, 284
  volume breathed, 284
Albumin, acid, 82
  alkali, 83
Albumin, egg, 81
  native, 80, 81
  serum, 81
Albuminates, 82
  reactions of, 97
Albuminoids, 86
  effect of diet of, 411
Albumins, 81
  reactions of, 97
Albumoses, reactions of, 97
Alcohol as a food, 300
Alkali albumin, 83
Ameba, 3
Ameboid movement, 3
Amido-acids, 89
Amitosis, 10, 19
Ammonia, effect of breathing, 279
  in the urine, 383
Ammonium carbamate, 412
Amylolytic ferments, 303
Amylopsin, 303, 334, 337
Anabolism, 6, 405
Anabolites, 405
Anacrotic limb, 206
  wave, 207, 208
Anaphase, 20
Anelectrotonus, 471
Animal heat, 433
Animals differentiated from plants, 10
Anode, 471, 473
Ano-spinal center, 526
Anterior association center, 589
Antipeptone, 336
Antiperistalsis, 350
Apnea, 277, 289
Arborization, interepithelial, 72
Archispermiocyte, 679
Archoplasm, 18
Areolar tissue, 34
Aristotle's experiment, 669
Arterial flow, 196, 198
  rhythmic, 198
  velocity of, 199

Arterial pulse, 237
blood-pressure and nervous regulation in, 239, 240
Arteries, 149
blood-pressure in, 187
nerves of, 151
Arterioles, 149
Articulate sounds, 490
Asphyxia, 278, 290
Assimilation, 6
Association centers of brain, 587
Aster, 19
Astigmatism, 649, 674
Atmosphere, composition of, 263
Attraction sphere, 18
Auditory center, 587
judgments, 626
nerve, 556
Auricles, action of, 155
Auriculo-ventricular valves, action of, 156
Autolytic substances, 129
Axis cylinder, 65
Axone, 64

Bacteria in digestive tract, 347
Basement membrane, 22
Basket cells, 562
Basophile, 113
Bezold's ganglia, 175
Bidder's ganglia, 175
Bile, 340, 360
acids, 341, 360
capillaries, 340
coloring matter of, 341
chemical composition of, 341
discharge of, 343
functions of, 342
mode of discharge of, 343
mode of secretion of, 343
pigments of, 360
salts, 341, 360
Bilirubin, 90, 341
Biliverdin, 90, 341
Binaural sensations, 627
Binocular vision, 664
Bioplasm, 2
Biuret reaction, 96
Bladder, urinary, 377
Blastema, 2
Blastoderm, 14
Blind spot, 653, 675
Blood, 101
arterial flow, 196
buffy coat, 103
capillary flow, 199
carbon dioxide of, 271
chemical composition of, 115
circulation of, 141, 186
experiments on, 226
in fetus, 695
coagulation of, 102, 137
calcium in, 106
conditions affecting, 106
fibrin in, 103
theories of, 105
corpuscles of, 107
chemical composition of, 139
colorless, 112
ameboid movement of, 113, 201
chemical composition of, 117
number of, 112
phagocytosis, 134
varieties of, 113
enumeration of, 134
percentage of, 135
red, 107
action of reagents on, 133
characters of, 108
chemical composition of, 118
development of, 110
number of, 108
origin of, 110
varieties of, 110
defibrination of, 104
differences between arterial and venous, 127
elimination of carbon dioxide by, 271
examination of, 132
ferments in, 117
flow, arterial, 196
capillary, 199
regulation of, 209
velocity of, 203
in arteries, 199
in capillaries, 201
in veins, 203
venous, 202

Blood, gases of, 267
hemoglobin, 118
isotonicity of, 136
laboratory experiments on, 132
laking of, 128
microscopical examination of, 132
morphology of, 107
oxygen of, 269
plasma, 101
chemistry of, 139
composition of, 115
percentage of, 135
reaction of, 136
plates, 115
portal, 127
pressure, 186
arterial, 187, 234, 239, 240
capillary, 195, 238
in man, 192
model, 236
respiratory undulations of, 191
variations in, 195
venous, 195
production of heat by the, 434
quantity of, 101
influence on secretion, 295
respiratory changes in, 267
serum, 102
chemistry of, 139
composition of, 117
globulicidal properties of, 128
specific gravity of, 136
uses of, 101
variations in composition of, 126
velocity of flow, 203
venous flow, 202
whipped, 138
Blushing, 215
Body, chemical composition of, 78
energy requirements of, 425
experiments on the chemistry of, 95
Bone, 41
blood-vessels of, 42
canaliculi of, 43
cells, 44
development of, 45
growth of, 50
Haversian canals of, 44
lacunæ of, 43, 44
Bone, lamellæ of, 43, 44
marrow, 41
microscopic structure of, 43
ossification in cartilage, 46
in membrane, 46
periosteum of, 42
Bowman's sarcous elements, 60
theory of urinary secretion, 386
Brain, 531
after-, 533
arrangement of different parts, 531
association centers of, 587
distinctive characters of human, 532, 574
fore-, 532
gray matter in, 568
hind-, 533
inner-, 532
mid-, 533
motor areas of, 577, 582
of human, 581
tracts in, 583
Rolandic area of, 583
sensory areas of, 584
stem, 531, 532
vascular nerve-supply of, 220
weight of, 574
Bronchi, 245
Buffy coat, 103
Bulb, the, 534, and see *Medulla*
centers in, 540
connections with cerebrum and cerebellum, 539
functions of, 540
Bundle of Vicq d'Azyr, 547
Burdach, column of, 514

Cajal, cells of, 570
Calcification, 47, 50
Calcium salts in the body, 94
in coagulation of the blood, 106
tests for, 99
Calorimeter, 290, 426
Calorimetry, 290
Canaliculi, 43
Cane sugar, 92
Capillaries, 151
blood-pressure in, 195
structure of, 152

Capillary circulation, 238
flow, 199
velocity of, 201
Carbohydrates, 91
absorption of, by intestines, 367
as foods, 297, 300
chemical reactions of, 98
metabolism of, 416
Carbon, amount excreted, 407
dioxide, determination of, 286, 287
elimination of, 263, 264, 271, 396
monoxide, effect of breathing, 279
hemoglobin, 140
Carbonates, 94
Carboxyhemoglobin, 121
Cardiac action, force of, 169
contractions, automatic, 231
experiments on, 227, 228
maximal, 174
cycle, 155, 168
impulse, 160
muscle, 61, 465, 500
action of, 465
compared with other muscles, 466, 500
automatic contractions of, 231
development of, 63
properties of, 170
refractory phase, 465
nerves, 232
Cardio-accelerator centers, 183, 543
Cardiogram, 161, 226, 228
Cardiograph, 161
Cardio-inhibitory centers, 181, 543
Cartilage, 38
development of, 41
elastic, 41
hyaline, 38
temporary, 40
white fibro-, 41
Casein, 85
Caseinogen, 85
Catabolism, 6, 405
Catabolites, 405
Catacrotic limb, 206
wave, 207
Catelectrotonus, 471
Cathode, 471, 473
Caudate nucleus, 548
Cell, 1, 8, 17, 18
body, 17
difference between plant and animal, 10
differentiation, 14, 17
division of, 10, 18
functions of, 11, 14
growth, 7, 10
multiplication, 18
nucleus of, 9, 17
reticulum of, 8
structure of, 8, 17
Cells, decay and death of, 22
derived elements of, 22
modes of connection, 21
origin of, 21
shapes of, 21
types of, 21
Cellulose, 13, 91
Center for muscle tone, 525
Centers, motor, 577, 581
sensory, 584
spinal, 526
Centrosome, 18
Cerebellar cortex, paths through, 564
Cerebellum, 561
connection with bulb, 539
functions of, 564
general structure of, 562
Cerebral cortex, fibers from, 572
structure of, 568
Cerebrum, 567
arrangement of parts, 568
connection with bulb, 509
effects of removal of, 575
functions of, 575
motor areas of cortex, 577, 582
sensory areas of, 584
weight of, 574
Cerumen, 394
Ceruminous glands, 394
Chemical composition of the body, 78
elements in the body, 78
Chemistry of the body, experiments on, 95
Chest, changes in diameter of, during respiration, 284
Cheyne-Stokes breathing, 278
Chlorides in the body, 94
in the urine, 385

Chlorides, tests for, 99
Chlorine, effect of breathing, 279
Chlorophyll, 12
Chondrigen, 87
Chondrin, 87
Chorda tympani, 306, 352, 355
Chordæ tendineæ, 148
Chromatic aberration, 649, 673
Chromatin, 18
Chromophanes, 659
Chromoplasm, 17
Chromo-proteids, 84
Chromosome, 19
Chyme, 329
Cilia, 30
Ciliary apparatus, 632
  contraction, 468, 502
  epithelium, 502
  motion, 468
Circulation, coronary, 183
  during sleep, 590
  effect of respiration on, 280
  in brain, 220
  in erectile structures, 224
  laboratory experiments on, 226
  local peculiarities of, 220
  of blood, 141
  regulation of flow, 209
  time of, 236
  through blood-vessels, 186
  velocity of, 203
  vegetable, 4
Coagulated proteids, 83
Coagulating ferments, 303
Coagulation of blood, 102, 137
  calcium salts, in 106
  conditions affecting, 106, 138
  theories of, 105
Cochlea, 619
Cohnheim's areas, 61
Cold, influence of extreme, 436
Collagen, 86
Collaterals, 68
Colloids, 129
Color, after-images, 654, 660, 677
  -blindness, 661, 677
  complemental, 660
  extent of visual field for, 660
  Hering's theory of, 663
  limits of field of vision for, 677
  -mixing, 677
Color, sensations of, 659, 661
  Young's and Helmholtz's theory of, 662
Colorless corpuscles, 112
Colostrum, 698
Column of Burdach, 514
  of Goll, 514
Columnæ carneæ, 145, 148
Comma tract, 516
Common sensations, 595
Complemental air, 259, 285
Compound proteids, 81, 84
Conductivity of muscle, 447
Conjunctiva, 630
Connective tissues, 31
  adenoid, 35
  adipose, 37
  areolar, 34, 36
  cells of, 31
  development of, 36
  fibrous, 36
  gelatinous, 34
  general structure of, 31
  intercellular substance of, 32
  lymphoid, 35
  retiform, 35
  varieties of, 32
  white fibrous, 33, 36
  yellow elastic, 33, 36
Consonants, 490
Contractility of muscle, 442
Contraction phase of muscle, 449
Contracture, 460
Convoluted tubule, 372
Cooking, effects of, 301
Cornea, 631
Corona radiata, 545, 546
Coronary circulation, 183
Corpora cavernosa, 224
  geniculata, 546
  quadrigemina, 546
  striata, 548
Corpus Arantii, 148
  dentatum, 562
  luteum, 689
  spongiosum, 224
Corpuscles, blood, 107
  Malpighian, 372
  of Bowman, 372
  of Golgi, 76
  of Krause, 74

Corpuscles of Meissner, 74
of Pacini, 73
Coughing, center for, 542
Cranial nerves, 548
Crassamentum, 102
Creatinin, 383, 402, 413, 414
Crura cerebri, 545
Crusta, 545
petrosa, 52
phlogistica, 103
Crystalloids, 129
Cutis vera, 393
Cystin in urine, 385
Cytolysis, 128
Cytoplasm, 17

Death, 7
Decay, 7
Decidua basalis, 693
capsularis, 693
menstrualis, 689
vera, 693
Decussation of the pyramids, 535
Defecation, 351
center for, 526
Degeneration in spinal cord, 515
reaction of, 474
Wallerian, 506
Deglutition, 313
center for, 316, 542
nervous mechanism of, 315
time occupied in, 315
Demarcation currents, 451, 452
Dendrites, 64
Dental papilla, 55
Dentine, 52
Depressor nerve, 215
Dermis, 393
Development, 691
Dextrin, 92
tests for, 98
Dextrose, 92
tests for, 98
Diabetes mellitus, 418
Dialysis, 129
Diapedesis, 201
Diaphragm in respiration, 254, 256
Diaster, 20
Diastole of heart, 154, 156
Dicrotic notch, 207
pulse, 208
Dicrotic wave, 207, 208
Diet, normal, requisites of, 405, 442
tables, 423
Diffusion, 129
Digestion, 297, 301
enzymes in, 301, 303
experiments in, 351
in intestines, 331, 345, 346
in mouth, 303, 353, 354
in stomach, 316
Digestive ferments, 303
Diphasic current, 453
Diplopia, 550, 664
Disassimilation, 6
Distance, estimation of, 668
Diuretics, action of, 389
Dogiel's cells, 175
Dreams, 591
Du Bois-Reymond's induction coil, 445
key, 444
Ductless glands, influence on metabolism, 427
Ductus arteriosus, 696
venosus, 695
Dyspnea, 278, 290

Ear, cochlea of, 619
external, 614
function of, 622
internal, 617
function of, 625
membranous labyrinth, 618
middle, 615
function of, 622
organ of Corti, 619
ossicles of, 616
tympanum, 615
Eck's fistula, 412
Edestine, 82
Egg albumin, 81
Eggs, composition of, 299
Eighth nerve, 556
Elasticity of muscle, 442
Elastin, 87
Electrodes, 445
Electrotonus, 471
Elements, chemical, in body, 78
Eleventh nerve, 560
Emission of semen center, 526
Emulsification, 99, 337, 342
Enamel, 53

Enamel cap, 56
germ, 55
organ, 55
papilla, 55
End-brushes, 68
-bulbs, 74
-plates, 62
Endocardiac pressure, 162
Endocardium, 143
Endomysium 59
Endoneurium, 68
Endothelium, 24
Energy, income and output of, 426
requirements for body, 425
Enterokinase, 303, 345, 360
Enzymes, 301
action of, on pancreatic juice, 359
activating, 303
amylolytic, 303
classification of, 302
coagulating, 303
digestive, 303
lipolytic, 303
proteolytic, 303
Eosinophile, 100, 113
Epiblast, 14
Epidermis, 391
Epiglottis, 245
Epinephrin, 431
Epineurium, 68
Epithelial tissues, 22
Epithelium, 22
ciliated, 29, 31
classification of, 23
columnar, 23, 24, 28
cubical, 23
functions of, 24, 31
glandular, 29
simple, 23
situations of, 23, 31
specialized, 29
squamous, 23, 27
stratified, 23, 27
transitional, 28
Equilibrium, sense of, 628
Erectile tissue, 224
Erection center, 526
Erepsin, 303, 345
Ergograph, 461
Erythroblasts, 112
Erythrocytes, 107
Erythrodextrin, 311
Eustachian tube, 615, 624
valve, 143, 696
Excreta, analysis of, 406, 407
channels of elimination of, 407
quantity of, 406
Excretion, 291, 371, 398
during starvation, 422
from skin, 395
laboratory experiments in, 398
Expiration, forced, 256
muscles of, force of, 262
quiet, 256
relative time of, 258
Expired air, carbon dioxide of, 263, 286, 287
changes in, 263
External genitals, vascular nerves for, 224
Eye, 630
anatomy of, 630
astigmatism, 649, 674
chromatic aberration of, 649, 673
image formation, 639
movements of, 647
muscles concerned in, 647
optical apparatus, 638
axis, 641
refractive surfaces and media, 639
schematic, 641
spherical aberration of, 648, 672
Eyeball, 630
blood-vessels of, 637
ciliary apparatus, 632
cornea, 631
iris, 632
lens, 632
retina, 633
Eyelids, 630

Facial nerve, 554
function of, 555
paralysis of, 555
relation to taste, 555
secretory, 555
Fallopian tubes, 686
Falsetto voice, 489
Far-point, 672
Fasciculus cuneatus, 534
gracilis, 534
of Rolando, 535

Fasciculus solitarius, 556
Fasting, 420, 421
metabolism during, 414
Fatigue, effect on muscular contraction, 497, 498
Fats, 90, 98
absorption of, by intestines, 367
as food, 297, 300
chemical reactions of, 98
digestion of, 337, 338
emulsification of, 99, 337, 342
energy value of, 414
metabolism of, 414
saponification of, 99, 337
source of, in body, 415
Fatty acids, 91
tests for, 99
Feces, 347
composition of, 348
excretion by, 407
Fermentation in intestine, 347
Ferments, 97
chemical reactions of, 97
in the blood, 117
unorganized, 301, and see *Enzymes*
Fetus, circulation of blood in, 695
Fibers of Remak, 66
Fibrin, 83
ferment, 105
Fibrinogen, 82, 105
Fictitious feeding, 321
Fifth nerve, 551
Fillet, 544
Filtration, 361
Finger, vasomotor changes in, 241
Fish, composition of, 299
Fission, 7
Food, and digestion, 297
effects of deprivation of, 420
mastication of, 803
-principles, 297
salts of, 300
Foods, 297
carbohydrates, 297, 300
classification of, 297
effect of cooking, 301
fats, 297, 300
heat production from, 426, 437
income and output of energy, 406
inorganic, 297, 300
Foods, liquid, 300
mineral, 297, 300
nitrogenous, 297
percentage composition of, 298
proteids, 297
salts, 300
water, 297
Forced movements, 567
Fore-brain, 532
Form, estimation of, 667
Fossa ovalis, 143
Fourth nerve, 550
Fovea centralis, 633
Frontal association center, 589

Galactose, 93
Gall-bladder, 340
Galvanic currents, 443
Ganglia, 508
spinal, functions of, 523
Gases in alimentary canal, 348
Gastric digestion, 316, 355
changes in food in, 327
circumstances influencing, 327
cleavage products of, 356
products of, 326
time of, 327
juice, 321, 355
acid of, 323
action on milk, 327
on proteids, 326
artificial, 356
chemical composition of, 323, 355
digestive action of, 356
enzyme action of, 356
fictitious meals, action on, 321
hydrochloric acid in, 324
pepsin in, 325
psychic secretion of, 355
quantity of, 323
secretion of, 320, 355
secretion, changes in glands during, 320
nervous mechanism of, 322
Gelatin, 86
Gelatinous tissue, 34
Gemmation, 7
Genito-spinal center, 526

Germinal epithelium, 685
matter, 9
spot, 684
vesicle, 684
Giant cells, 42
Glands, cardiac, 317
ceruminous, 394
gastric, 316
mammary, 698
pyloric, 318
reproductive, relation to metabolism, 432
salivary, 304
sebaceous, 395
secreting, 293
sudoriferous, 393
types of, 293
Globulin, serum, 82
Globulins, 81
reactions of, 97
Globus pallidus, 548
Glomerulus, 374
Glosso-pharyngeal nerve, 556
in respiration, 274
Glottis, respiratory movements of, 257
Glucoproteids, 85
Glucose, 92
Glycin, 341
Glycogen, 92, 417
destination of, 418
formation of, 416
relation to metabolism, 416
sources of, 417
tests for, 98
Glycogenesis, 416
Glycoproteids, 85
Glycosuria, 418
Goblet cells, 26
Golgi, corpuscles of, 76
Goll, column of, 514
Gowers' tract, 516
Graafian follicles, 684
Granulose, 91

HAVERSIAN canals, 44
Head, vascular nerve supply of, 220
Hearing, acuteness of, 671
limits of, 671
physiology of, 620
Heart, 142
action of, 154
Heart, anatomy of, 142
automaticity of, 178
-beat, 160
rate of, 226, 227
sequence, 227
theories of, 174
-block, 176
capacity of, 146
chambers of, 143
character of contraction, 170, 174
coronary circulation of, 183
cycle of, 155, 168
depressor nerve of, 215
development of, 146
endocardiac pressure, 162
excised, experiments on, 228, 229
force of action, 169
frequency of action, 154, 185
ganglia of, 175
impulse of, 160
influence of accelerator nerve on, 182, 543
of coronary circulation on, 183
of drugs on, 185
of inhibitory nerves on, 179, 543
of mechanical tension on, 184
of nervous system on, 179
of nutrient fluids on, 229
of sympathetic system on, 211
of temperature on, 184
of vagus on, 179
irritability of, 172
isolated, 230
metabolism of, 178
methods of investigating beat, 226
muscle, 61, 500
properties of, 170
nerves of, 179
production of heat by, 434
regulation of force and frequency of contraction, 179
relation of rhythm to nutrition, 178
rhythmic contraction of, 170, 178
size of, 146
sounds of, 158
causes of, 159
structure of, 146
tonicity of, 172

Heart, valves of, 148
action of, 156
volume of, 229
weight of, 146
work per diem, 426
Heat, animal, 433
dissipation of, 434
from lungs, 436
from skin, 434
influence of extreme, 436
of nervous system on production of, 438
produced in muscular contraction, 453
-producing tissues, 433
production of body-, 425, 433, 437
regulation of body-, 434, 438
centers for, 439
-rigor, 462
variations in loss of, 434
in production of, 437
Heidenhain's experiments on urine secretion, 386
Hemachromogen, 124
Hemacytometer, 135
Hematin, 124, 125
Hematoblasts, 110
Hematoidin, 125
Hematoporphyrin, 124
Hemianopsia, 585
Hemin, 125
Hemiopia, 585
Hemoglobin, 118, 140, 269
action on gases, 121
combining power with oxygen, 269
derivatives of, 124, 140
estimation of, 122, 136
reduced, 121
Hemoglobinometer, 122, 136
Hemolysis, 128
Hemometer, 136
Henle's membrane, 150
loop, 373
Hepatolytic sera, 128
Hind-brain, 533
Hippuric acid, 383
formation of, 383, 413
Histons, 84
Hyaline cartilage, 38
cells, 113
leucocytes, 113
Hyaloplasm, 8, 17
Hydrochloric acid, 324, 325
combined, 324
digestive action of, 325
test for free, 324
Hydrogen, amount excreted, 407
effect of breathing, 279
Hyperisotonic solutions, 130
Hypermetropia, 651
Hyperpnea, 278, 289
Hypertonic solutions, 130
Hypoblast, 14
Hypoglossal nerve, 560
Hypoisotonic solutions, 130
Hypotonic solutions, 130

Income of energy, 425
Indol, 360
Induced currents, 445
Induction coil, 445
Infundibulum, 144
Inhibition, function of nerve centers in, 527
Inogen, 464
Inorganic foods, 300
principles, 93
Inosite, 93
Insalivation, 304
Inspiration, 253
forced, 256
muscles of, 253
force of, 262
quiet, 253
relative time of, 258
Inspired air, 263, 286
Intercellular substance, 21, 32
Interepithelial arborizations, 72
Internal capsule, 545
secretions, 291, 427, 431
Intestinal digestion, 331
rôle of bile in, 342
gases, 348
juices, 344, 360
secretion, 344
functions of, 345
Intestines, absorption in, 363
action of microorganisms in, 346
defecation, 351
digestion in, 331
feces in, 347
fermentation in, 347

Intestines, gases in, 348
large, summary of digestive changes in, 346
movements of, 349
influence of nervous system on, 350
putrefaction in, 347
small, summary of digestive changes in, 345
vascular nerves for, 224
Intonation, 491
Invertase, 303
Involuntary muscle, 501
Iodothyrin, 428
Iris, 632
contraction of, 647
Iron, 94
tests for, 99
Irritability, 5
of heart-muscle, 172
of muscle, 442
Islands of Langerhans, 332
Isotonic solutions, 130
Isotonicity of blood, 136
Ivory, 52

Judgment of form and size of bodies, 604
of form and solidity, 667
of size and distance, 668
Jumping, 479

Karyokinesis, 10, 19
Karyolymph, 17
Karyoplasm, 17
Karyosomes, 18
Keratin, 87
Kidneys, 371
action of diuretics on, 389
blood supply of, 374
effect of blood pressure on, 398
factors affecting secretion from 386
function of, 371
glomeruli of, 374
Malpighian bodies of, 372
nerves of, 376, 387
structure of, 371
tubuli uriniferi of, 372
vasa efferentia of, 375
recta of, 375
Kidneys, vascular nerves of, 224
volume of, 387
Krause, corpuscles of, 74
membrane of, 60
Kronecker-Meltzer theory of deglutition, 313
Kymograph, 188

Labyrinth, 618
Lachrymal apparatus, 630
Lactalbumin, 81
Lactase, 303
Lactation, 698
Lacteals, 364
Lactic acid, test for, 324
Lactose, 92
Lacunæ, 43
Laky blood, 128
Langerhans, islands of, 332
Large intestine, summary of digestive changes in, 346
Laryngoscope, 485
Larynx, 245, 480
Latent period of muscle, 448, 495
Leaping, 479
Legumes, composition of, 299
Lens of eye, 632
Lenticular nucleus, 548
Leucocytes, 112
Leucolytic sera, 128
Levers, action of, in the body, 475
Levulose, 93
Life, phenomena of, 1
Limbs, vascular nerves for, 225
Linin, 18
Lipase, 303, 337
Lipochromes, 90
Lipolytic ferments, 303
Liquid foods, 300
Liquor sanguinis, 101
Lissauer, tract of, 516
Liver, 338
glycogenic function of, 416
secretions of, 338
structure of, 339
urea formation in, 411
vascular nerves for, 224
Localization, cerebral, 577, 584
Locomotion, 475
Locus ceruleus, 544
Ludwig's theory of urine secretion, 386

Lungs, 248
absorption from, 370
blood supply of, 252
excretion by, 407
interchange of gases in, 272
loss of heat from, 436
lymphatics of, 252
nerves of, 252
structure of, 249
Luxus consumption, 409
Lymph, 131
chemical composition of, 131
flow, 132
formation of, 131
Lymphatic sheaths, perivascular, 154
spaces, in blood-vessels, 154
Lymphocyte, 100, 113
Lymphoid tissue, 35
Lytic substances, 128

Magnesium salts in the body, 94
Malpighian bodies, 372
Maltase, 303, 311, 334
Maltose, 92, 312
Mammary glands, 698
Manometer, 188
Marrow, bone, 41
Mastication, 303
muscles of, 303
nervous mechanism of, 304
Maximal stimulus, 454
Meat, composition of, 298
Meconium, 343
Medulla oblongata, 534, 537, and see *Bulb*
as a conducting path, 540
functions of, 540
reflex centers of, 540
section of, 531
Medullary sheath, 65
Meissner's corpuscles, 74
Melanin, 90
Membrana decidua, 693
tympani, 616
Membranous labyrinth, 618
Menstrual discharge, 689
life, 690
Menstruation, 687
Mesoblast, 14
Mesothelium, 24
Metabolism, 6, 405
Metabolism, constructive, 6
destructive, 6
during fasting, 414
endogenous, 410
exogenous, 410
influence of ductless glands on, 427
reproductive glands on, 432
intermediate, 410
nutrition and diet, 405
tissue, 410
Metaphase, 19
Metaplasm, 17
Methemoglobin, 122
Microcytes, 110
Micro-organisms, action of, in intestines, 346
Microsomes, 8
Micturition, 390
center for, 526
Mid-brain, 545
Milk, composition of, 299, 699
Millon's reaction, 96
Mineral foods, 300, 419
absorption of, in intestines, 368
Minimal stimulus, 454
Mitosis, 10, 19
Monaster, 19
Motor activities, coordinated, 475
areas of cortex, 577, 582
of human brain, 581
end-plates, 62
impressions, 530
-oculi nerve, 549
tracts in human brain, 583
Mouth, absorption in, 362
digestion in, 303
in speech, 491
Movement, ameboid, 3
gliding, 4
streaming, 4
Movements, circus, 567
forced, 567
Mucigen, 309
Mucin, 85, 309
Mucous membranes, 292
Mucus in urine, 384
Murexide test, 402
Muscle, blood supply of, 62
cardiac, 61, 465, 500
chemical changes of, 451

Muscle, chemical composition of, 440, 441
clot, 440
coagulation of, 440
conditions affecting irritability of, 454
conductivity of, 447
contractility of, 442
contraction of, 443, 467
contracture, 460
currents, demonstration of, 452
development of, 62
effect of blood supply on, 458
of drugs on, 459
of nerve supply, 458
of single induction shocks on, 446
of temperature on, 456
of use on, 458
elasticity of, 442
electrical phenomena of, 451
end-plates, 62
experiments in, 492
ferments, 441
heart, 61, 465, 500
in rigor mortis, 461
involuntary, 57, 466, 501
compared with skeletal and cardiac, 466
irritability of, 442, 493
-nerve preparation, 492
nerve supply of, 62
non-striated, 57
plain, 57
plasma, 440
properties of, 442
record of contraction of, 443
serum, 440, 441
skeletal, 59
stimuli, 442, 496
striated, 58
tetanus, 459
-tone, center of, 525
voluntary, 58
Muscular action as heat producer, 433
activity, 464
center for tone of, 525
contraction, 443, 465
action currents, 452
apparatus for producing and recording, 443
Muscular contraction, changes in shape during, 449
characteristics of single, 448
chemical changes during, 451
conditions affecting character of, 454
co-ordinated, 460
differences between voluntary and involuntary, 466
effect of blood supply on, 458
of drugs on, 459
of fatigue on, 497, 498
of load on, 499
of nerve supply on, 458
of rate of stimulation on, 459
of repeated activity on, 455
of strength of stimulus on, 454, 496
of temperature on, 456, 498, 499
of use on, 458
electrical changes during, 451
energy liberated during, 454
heat produced during, 453
latent period of, 448, 495
metabolism during, 463
preparation for, 446
record of, 443, 447
recording, 446
refractory phase of, 465
response to stimuli in voluntary and involuntary, 466
simple, 448, 494
single twitch, 448
summation of contractions, 459
tetanic, 459, 499
voluntary, 459
co-ordination, 460, 629
energy, 464
tissue, 56
Musculi pectinati, 144
Mydriasis, 550
Myelin sheath, 65
Myelocyte, 100, 113
Myeloplaxes, 42
Myoalbumin, 441
Myoalbumose, 441
Myoglobulin, 44.

Myogram, 448
Myograph, pendulum, 448
Myohematin, 441
Myopia, 651
Myosin, 82, 441, 464
ferment, 441
Myosinogen, 441, 465
Myxedema, 428

Nasal region, smell, 610
Near-point, 645, 672
Nephrolytic sera, 128
Nerve cells, 70, 503
arrangement of, in spinal cord, 511
body, 70
characteristic of individual, 504
functions of, 503, 504
neurone theory, 504
nutritive influence of, 506
transmission of impulses through, 507
types of, 508
centers, 508
functions of, 508
collaterals, 68
end-brushes, 68
fibers, 64, 72
effect of battery current on, 471, 473
fatigue of, 470
functions of, 469
medullated, 64
non-medullated, 66
impulses, 469
cellulifugal, 507
cellulipetal, 507
character of, 469
specific energy of, 507
transmission through cells, 507
velocity of, 470
stimuli, 442, 469, 492
terminations, 72
tissue, 64, 66
trunks, 67
Nerves, cardiac, 232
cranial, 548
functions of, 548
depressor, 215
Nerves, effect of currents on human, 471, 473
experiments on, 492
irritability of, 492
spinal, 516
vasomotor, 211, 213, 217, 219
Nervous system, 503
functions of, 504
influence on secretion, 295
sympathetic, 591
tissues, 64, 66
axones of, 64, 507
dendrites of, 64, 507
ganglia of, 508
neuroglia of, 64, 77
Pacinian corpuscles, 73
Neuraxone, 64
Neurilemma, 64
Neuroglia, 64, 77
Neurokeratin, 87
Neurone, 64, 503
theory, 504
varieties, 508
Neutrophile, 100, 113
Ninth nerve, 556
Nitrogen in proteids, 88
Nitrogenous bodies, 79
equilibrium, 408
foods, 297
output, 409
Nitrous oxide, effect of breathing, 279
Nodes of Ranvier, 65
Nœud vital, 272
Nostrils, respiratory movements of, 257
Nuclear matrix, 17
Nuclei of optic thalamus, 546
Nucleic acid, 85
Nucleins, 85
Nucleoli, 18
Nucleoplasm, 17
Nucleoproteids, 84, 85
Nucleus, 9, 17
ambiguus, 556
ruber, 546
structure of, 17

Obesity, 416
Ocular fixation, 664
Odontoblasts, 52, 55
Oils, 90
as food, 300

Olein, 90
Olfactory apparatus, 609
bulb, 611
center, 585
glomeruli, 586
membrane, 613
nerve, 586
tract, 587
Olivary bodies, 536, 538
Olive, accessory, 539
superior, 544
Onkograph, 388
Onkometer, 388
Ophthalmoscope, 655
Optic center, 585
nerve, 633
thalami, 546
Optical apparatus, 638
defects in, 648
Organ of Corti, 619
Organized ferments, 346
Osmosis, 129
Osmotic pressure, 130
Ossein, 86
Osseous labyrinth, 618
Ossicles of ear, 616
Ossification, 45
center of, 46
in cartilage, 46
in membrane, 46
Osteoblasts, 46
Osteoclasts, 48
Osteogenetic fibers, 46
Output of energy, 426
Ovaries, 683
relation to metabolism, 432
Oviducts, 686
Ovulation, 687
Ovum, 684, 686
changes in, following impregnation, 692
prior to impregnation, 691
Oxalic acid in urine, 385
Oxygen, amount excreted, 407
in expired air, 265
in tissues, 270
determination of, in air, 286
Oxyphile, 113

Pacinian corpuscles, 73
Pain, sense of, 602
Pancreas, 332
enzymes of, 334
extirpation of, 431
extract of, 334
internal secretion of, 431
islands of Langerhans in, 332
secretion of, 333
structure of, 332
Pancreatic digestion, 358
cleavage products of, 359
fistula, 333
juice, 333, 358
artificial, 358
chemical characters of, 358
composition of, 334
conditions influencing action of, 338
enzymes of, 334, 358
action of, 335, 338, 359
secretion of, 358
action of nerves on, 334
action of secretin on, 334, 358
Papillæ of skin, 392
of tongue, 606
Paralytic secretion of saliva, 306
Paranucleoproteids, 84
Parathyroid glands, 428
Parietal association center, 589
Parotid gland, 304
nerves of, 308
Parturition, 697
center, 527
Pelvic viscera, vascular nerves for, 224
Penis, 681
Pepsin, 303
action of, 325
in gastric juice, 325
Pepsinogen, 325
Peptone plasma, 107
Peptones, 84, 325
characteristics of, 326
reactions of, 97
Perforating fibers of Sharpey, 45
Pericardium, 142
Perichondrium, 38, 46
Perimysium, 59
Perineurium, 68
Periosteum, 42
Peripheral resistance, 186, 210
Peristalsis, intestinal, 349

Peristalsis, reversed, 350
Perivascular lymphatic sheaths, 154
Perspiration, 395
Pflüger's law of contractions, 472
Phagocytes, 134
Phagocytosis, 134
Phakoscope of Helmholtz, 674
Phenomena of life, 1
Phenomenon of treppe, 497
Phosphates, 94
  tests for, 99
Phosphoric acid in urine, 384
Phosphorus in foods, 420
Phrenic nerve, influence on respiration, 289
Physiological material, source of, 15
  utilization of, 15
Physiology, 1
Pigment cells, 32
Pigments, 90
  bile, 360
Pituitary body, 431
Placenta, 694
Plants differentiated from animals, 10
Plasma, 101, 115
  chemistry of, 139
  composition of, 115
  percentage of, in blood, 135
  reaction of, 136
Plasmosomes, 18
Plethysmogram, 241
Pleuræ, 248
Pneumogastric nerve, 558, and see *Vagus*
Pneumograph, 258
Pons Varolii, 543
Postdicrotic wave, 207
Posterior longitudinal bundle, 544
  marginal zone, 516
  pyramids, 534
  roots of spinal nerves, 518, 523
Potassium salts in the body, 94
Poultry, composition of, 299
Precipitins, 129
Predicrotic wave, 207
Presbyopia, 651
Pressor nerves, 216
Pressure, endocardiac, 162
Prickle cells, 27
Pronucleus, female, 692
  male, 692
Prophase, 19
Prostate gland, 682
Protamin, 84, 89
Proteids, 79
  absorption of, from intestines, 365
  action of trypsin on, 336
  as fat formers, 410
  as glycogen formers, 410
  circulating, 409
  coagulated, 83, 97
  color reactions of, 96
  compound, 81, 84
  classes of, 80
  decomposition products, 87
  digestion of, 325
  floating, 409
  metabolism of, 408, 409
  morphotic, 409
  nitrogen in, 88
  precipitations, 96
  properties of, 79
  reactions of, 95
  simple, 80, 81
  sulphur in, 89
  tissue, 409
Proteolytic ferments, 303
Proteoses, 84, 325
Prothrombin, 106
Protoplasm, 1, 2
  chemistry of, 3
  definition of, 2
  effect of stimuli on, 5
  growth of, 7
  irritability of, 5
  movement of, 3
  physiological characteristics of, 3
  properties of, 2
  reproduction of, 7
  structure of, 8
Pseudo-nucleoproteids, 84
Ptosis, 550
Ptyalin, 303, 310
  action of, 303, 311, 354
Pulse, 204
  arterial, 237
  dicrotic, 208
  variations in rate of, 185
  -wave, rate of propagation of, 237
Pulvinar, 547
Pupil, 632
  contraction of, 647

Pupil, dilatation of, 647
center for, 542
reflexes, 647
Purkinje's cells, 562
figures, 653
shadows, 676
Purkinje-Sanson's images, 673
Putamen, 548
Putrefaction in intestines, 347
Pyramids, 534
decussation of, 535

Racemose glands, 294
Ranvier, nodes of, 65
Reaction of degeneration, 474
Red corpuscles, 107
action of reagents on, 133
chemical composition of, 118
development of, 110
origin of, 110
varieties of, 110
nucleus, 546
Reflex action, 519
time of, 523
arc, 519
centers in medulla, 540
Reflexes, complex, 521
cutaneous, 528
inhibition of, 527
morbid, 527
muscle, 528
simple, 520
special centers for, 526
spinal, 524
tendon, 528
Refraction, 671
Refractory period, 172
phase, 465
Relaxation phase of muscle, 449
Remak's fibers, 66
ganglia, 175
Rennin, 303, 334
action of, 327, 337, 357
Reproductive organs, 679
of female, 683
of male, 679
Reserve air, 260, 285
Residual air, 260
Respiration, 243
changes in diameter of chest, during, 284
Respiration, effect of altitude on, 280
of, on circulation, 280
of various gases on, 279
of vitiated air on, 279
expiration, 256
influence of cutaneous nerves on, 288
of general sensory nerves on, 274, 288
of glosso-pharyngeal on, 274
of phrenic on, 289
of superior laryngeal on, 274
of vagus on, 273, 289
inspiration, 253
internal, 244
laboratory experiments in, 283
mechanism of, 253
nervous apparatus of, 272, 288
rhythm of, 258
special types of, 277
tissue, 244
volume of air breathed, 284
Respirations, number of, 262, 283
Respiratory apparatus, 244
elimination of carbon dioxide by, 271
nervous regulation of, 272
capacity, 260, 285
circumstances affecting, 261
center, 272, 542
automatic action of, 275
stimulation of, 275
changes in air breathed, 263
in the blood, 267
in the tissues, 270
interchange, 290
movements, 253
character of, 283
establishment of, at birth, 277
nervous mechanism of, 288
rate and character of, 287
recording of, 257, 283
relative time of, 258
of nostrils and glottis, 257
murmur, 259
muscles, force of, 262
pressure, 267, 285
quotient, 266
rate, 262, 283
rhythm, 258

Respiratory rhythm, action of stimuli on, 273
terms for quantity of air breathed, 259
Rete mucosum, 392
Reticular formation in medulla, 538
Reticulum, 8, 17
Retiform tissue, 35
Retina, 633
cones of, 636
inverted image on, 672
layers of, 634
localization in, 657
movement of pigment cells, 659
rods of, 636
Retinal image, duration of, 676
relation of size to distance, 676
Retinoscopy, 678
Rheoscopic frog, 470
Rhodopsin, 658
Rhythmical contractility, 170
Rhythmicity of arterial flow, 198
Ribs, movement of, in respiration, 255
Rigor mortis, 461
cause of, 461
heat, 462
order of occurrence, 462
water, 462
Rima glottidis, 245
Rolandic area, 583
Running, 479

Saccharose, 92
Sacculus, 618, 629
Saliva, 309
action of, on starch, 311, 312, 353
chemical composition of, 310, 352
function of, 310
properties of, 310
ptyalin in, 303, 310, 311
quantity of, 310
secretion of, center for, 305
mechanism of, 305
rate of, 310
Salivary digestion in stomach, 313
influence of acids and alkalies on, 354
of temperature on, 353
glands, 304
Salivary glands, changes in, during secretion, 308, 352
nerves of, 351
structure of, 304
secretion, 308
reflex, 351
Salts, absorption of, by intestines, 368
as foods, 300
bile, 341, 360
in the body, 93
tests for, 99
Sanson's images, 644
Saponification, 99, 337
Sarcode, 2
Sarcolemma, 59
Sarcoplasm, 61
Sarcostyles, 59
Sarcous elements of Bowman, 60
Scheiner's experiment, 673
Schwann, sheath of, 65
Sebaceous glands, 394
Secretin, 334, 345
influence on pancreatic secretion, 334, 358
Secreting glands, 293
production of heat by, 434
types of, 293
organs, types of, 292
Secretion, 291
circumstances influencing, 295
discharge of, 295
external, 291
internal, 291, 427, 431
organs and tissues of, 292
process of, 294
psychic, 355
true, 291
Segmentation, 692
Semicircular canals, 619, 628
Semilunar valves, 148
action of, 157
Seminal fluid, 682
Sensations, binaural, 627
common, 595
objective, 596
of color, 659
special, 596
subjective, 596
Sense, hearing, 614
muscular, 595, 603
of equilibrium, 628

Sense of pain, 602
of sight, 630
of smell, 609
of taste, 604
of temperature, 600
of touch, 597
organs, directions for experiments on, 669
perceptions, 597
Senses, the 595
special, 597
Sensorium, 596
Sensory areas of brain, 584
illusions, 596
impressions, 529
Serous membranes, 292
Serum, 102
agglutinative substances, 129
albumin, 81
blood, 102, 117
chemistry of, 139
composition of, 117
globulicidal action of, 128
globulin, 82
hemolytic action of, 128
precipitins of, 129
Seventh nerve, 554
Sharpey's fibers, 45
Sight, 630
Silicon, 94
Sixth nerve, 554
Size, estimation of, 668
Skein, 19
Skin, absorption from, 369
amount of carbon dioxide exhaled by, 396
excretion by, 407
excretory functions of, 391, 395
exhalation from, 396
functions of, 391, 397
glands of, 393
loss of heat from, 434
papillæ of, 392
respiratory functions of, 396
structure of, 391
Sleep, 590
Small intestine, digestion in, 345
mucosa of, 364
villi of, 364
Smell, center for, 585
sensation of, 670
Smell, sense of, 609
Soaps, 91
Sodium salts in the body, 94
Solidity, judgment of, 667
Somesthetic area of brain, 584
Somnambulism, 591
Sound, 622
Sounds, articulate, 488, 490
localization of, 626
of the heart, 158
pitch of, 625
Special centers in bulb, 540
sensations, 596
Speech, 480, 490
action of tongue in, 491
mouth in, 491
Spermatids, 679
Spermatocytes, 679
Spermatogonia, 679
Spermatozoa, 679, 680, 682
Spermin, 432
Spherical aberration, 648, 672
Sphygmogram, 206
Sphygmograph, 205
Sphygmomanometer, 194
Sphygmometer, 206
Spinal accessory nerve, 560
bulb, 534
centers, 525, 526
cord, 510
antero-lateral ascending tract, 516
descending tract, 516
arrangement of nerve cells in, 511
ascending degeneration of, 516
columns of, 514
comma tract of, 516
conduction in, 528
course of motor impulses in, 530
of sensory impulses in, 529
crossed pyramidal tract, 515
descending degeneration of, 515
direct cerebellar tract, 516
pyramidal tract, 515
functions of, 510, 513
Gowers' tract, 516

Spinal cord, hemisection of, 531
intrinsic cells in, 513
irradiation of impulses in, 521
Lissauer's tract, 516
peculiarities of different regions, 519
postero-lateral column, 516
postero-marginal zone, 516
postero-median column, 516
reflex action in, 519, 524
reticular formation, 513
tracts of, 514
weight of, 574
nerve-roots, functions of, 523
nerves, 516
anterior roots, 517, 523
course of fibers, 517
posterior roots, 518, 523
reflexes, 524
Spirem, 19
Spleen, vascular nerves for, 224
Spongioplasm, 8, 17
Staircase contractions, 455
Stammering, 491
Starch, 91
action of amylopsin on, 337
of ptyalin on, 311, 312, 353
chemical reactions of, 98
hydrolysis of, 98
Starvation, 420
death from, 420
effect on body temperature, 421
symptoms of, 420, 421
Steapsin, 303, 334, 337
Stercobilin, 90, 342
Stereoscope, 667
Stethograph, 258
Stethometer, 257
Stimuli, forms of, 442
maximal, 454
minimal, 454
Stokes' fluid, 121
Stomach, 316
absorption from, 362
action of pylorus, 328
blood-vessels of, 319
changes in glands during secretion, 320
digestion in, 313, 316
gases in, 349
Stomach, glands of, 316
lymphatics of, 319
movements of, 327
nerves of, 316
nervous control of movements of, 329
secretion in, 320
structure of, 316
vascular nerves for, 224
Stomata, 25
Strabismus, 550
Stratum granulosum, 392
lucidum, 392
Malpighii, 392
Striated muscle, 58
development of, 62
Submaxillary gland, action of atropine on, 306
paralytic secretion of, 306
secretion of, 306
Substantia nigra, 545, 546
Succus entericus, 344
Sucking, center for, 542
Sudoriferous glands, 393
Sugar, test for, in urine, 403
Sulphates, 94
tests for, 94
Sulphur in proteids, 89
Sulphuretted hydrogen, effect of breathing, 279
Sulphuric acid in urine, 384
Sulphurous acid, effect of breathing, 279
Summation, 459
of stimuli, 521
Superior laryngeal nerve in respiration, 274
Supplemental air, 260
Suprarenal capsules, 428
active principle of, 430
functions of, 428
internal secretion, 431
nerves of, 428
relation to Addison's disease, 429, 431
extract, 430
Swallowing, 313
Sweat, 395
centers, 543
chemical composition of, 395
glands, 393

Sweat, influence of nervous system on secretion of, 397, 399
Sympathetic ganglia, functions and structure, 591, 594
nervous system, 591
functions, 594
organization and distribution, 591
Synapsis, 520
Synovial membranes, 292
Systole of heart, 154, 156

Tactile corpuscles, 74, 599
of Meissner, 74
menisques, 75
Taste, 604
after-, 608
buds, 605
center, 587
influence of fifth nerve on, 553
seat of, 604, 607
sensation of, 670
varieties of, 607
Taurin, 341
Teeth, 50
dentine of, 52
development of, 54
enamel of, 53
ivory of, 52
permanent, 51
structure of, 51
temporary, 50
Tegmentum, 544, 545, 546
Telophase, 20
Temperature, body, 433
dissipation of, 435
influence of extreme heat and cold on, 436
regulation of, 434
sense of, 600, 669
variations in, 433
influence of, on muscular contraction, 456
Tenth nerve, 558
Testes, 679
relation to metabolism, 432
Tetanometer, 499
Tetanus, 459, 499
Thermogenic centers, 439
Third nerve, 549
Thoracic viscera, vascular nerves for, 222
Thorax, respiratory changes in diameter, 284
Thrombin, 105
Thrombocytes, 115
Thrombogen, 106
Thrombokinase, 106, 139
Thyroid gland, 427
accessory, 428
functions of, 428
Tidal air, 259, 285
Tissues, connective, 31
elementary, 22
epithelial, 22
interchange of gases in, 272
muscular, 56
nervous, 64
Tone, of artery, 212
of muscle, 172, 525
Tongue, 604
action of, in speech, 491
papillæ of, 606
Tonicity of heart muscle, 172
Tooth-pulp, 51
Touch corpuscles, 599
sense of, 597, 669
acuteness of, 599
Tract of Gowers, 516
of Lissauer, 516
Traube-Hering curves, 216
Treppe, phenomenon of, 497
Trigeminus nerve, 551
functions of, 552
Triolein, 90
Tripalmitin, 90
Tristearin, 90
Trochlearis nerve, 550
Trommer's test, 403
Trunk, vascular nerves for, 225
Trypsin, 303, 335
action of, 336
Tubular glands, 293
Tubuli seminiferi, 679
uriniferi, 372
Twelfth nerve, 560
Tympanum, 615

Unorganized ferments, 301, and see *Enzymes*
Unstriped muscle, 57

Urea, 380
amount in tissues of body, 381
antecedents of, 412
determination of, 402
formation of, 381, 411
preparation of, 401
properties of, 380
quantity excreted, 382
Ureters, 377
Uric acid, 382, 402
condition of, in urine, 382
formation of, 413
properties of, 382
tests for, 402
Urinary bladder, 377
Urine, 377
abnormal constituents of, 403
albumin in, 385, 403
ammonia in, 383
analysis of, 399
average daily quantity of constituents, 379
chlorides in, 385, 400
creatinin in, 383, 402
cystin in, 385
dextrose in, 385, 403, 404
discharge of, 390
diuretics, action of, 389
excretion by, 407
of, experiments on, 386
factors affecting secretion of, 386
filtration theory of secretion, 386
general properties of, 377
hippuric acid in, 383, 413
method of excretion of, 386
mucus in, 384
nitrogenous substances in, 380
occasional constituents of, 385
oxalic acid in, 385
phosphates in, 384, 401
pigments in, 383, 402
quantity of, 377, 399
reaction of, 378, 399
relation of blood pressure to secretion of, 398
saline matter in, 384
secretion of, theories of, 386
solids of, 400
specific gravity of, 379, 399
sugar in, 403, 404
sulphates in, 384, 400
Urine, urea in, 380, 401
uric acid in, 382, 402
variations in quantity of constituents, 379
in specific gravity, 379
Uriniferous tubules, 372
Urobilin, 90, 342, 383, 402
Urochrome, 90, 383
Uroerythrin, 90, 384
Uromelanin, 384
Uterus, 686
Utriculus, 618, 629

Vagina, 687
Vagus nerve, 558
effects of section, 560
functions of, 560
relation to deglutition, 315
to gastric secretion, 321
to heart's action, 179
to respiration, 273, 289
Valves of heart, 148
action of, 156
of veins, 154
Vas deferens, 680
Vasoconstrictor activity, 219
center, 214
nerves, 213, 219, 226
reflexes, 215
Vasodilator activity, 219
center, 218
nerves, 217, 219
reflexes, 218
Vasomotor centers, 543
changes, 241
nerves, 211, 220
tone, 214
Veins, 152
blood pressure in, 195
structure of, 152
valves of, 154
vasoconstrictor nerves in, 226
Venous flow, 202
velocity of, 203
Ventilation, 279
Ventricles of heart, action of, 155
Vesico-spinal center, 526
Vesiculæ seminales, 680
Vesicular breathing, 259
Vicq d'Azyr, bundle of, 547
Villi, 361

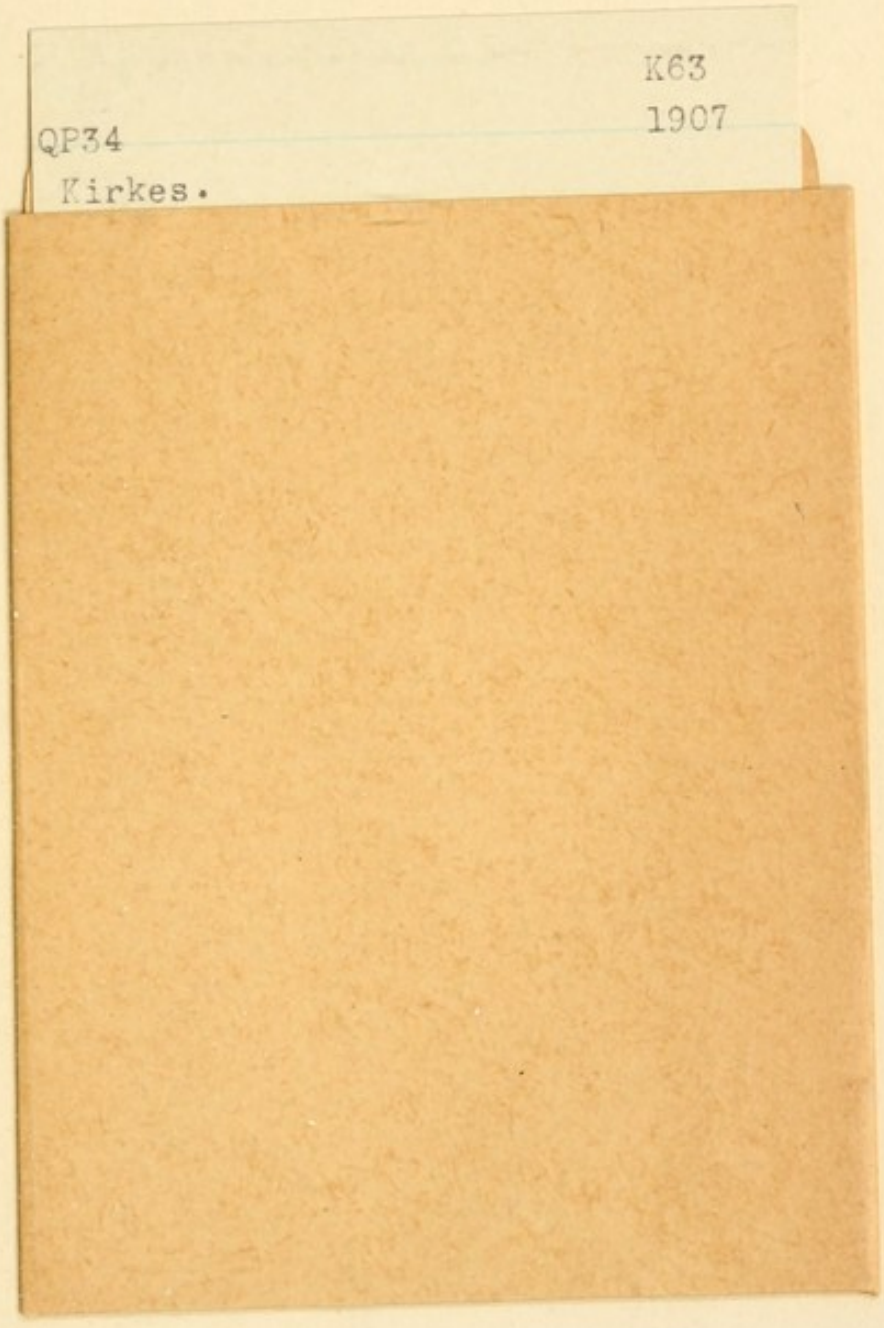
Visceral sensations, 529
Vision, accommodation of, 642, 645
binocular, 664
field of, 657
limits of, 660, 672, 677
localization of, 657
mechanism of accommodation, 645
range of distinct, 645
Visual acuity, 678
center, 585
judgments, 667
purple, 658
sensations, 652
after-images, 654
intensity of, 654
sense, 630
Vital capacity, 260, 285
phenomena, 1
Vitellin, 86
Vitiated air, effects of, 279
Vocal cords, 245, 480
movements of, 486
Voice, 480
difference between male and female, 488, 489
in singing and speaking, 488
production of, 479
quality of, 489
Voice, vocal range of, 488
Vomiting, 330
action of abdominal muscles, 330
of diaphragm, 330
of pylorus, 330
center for, 331
nervous mechanism of, 331
Vowels, 490

WALKING, 475
Wallerian degeneration, 506, 515
Water, 95
absorption of, in intestines, 368
amount excreted, 396, 407
in expired air, 266
in the body, 95
as food, 300
rigor, 462
Weyl's reaction, 402
White fibrous tissue, 33
development of, 36
Wreath, 19

XANTHO-PROTEIC reaction, 96

YELLOW elastic tissue, 33
development of, 36

ZYMOGENS, 302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