A text-book of histology and microscopic anatomy of the human body, including microscopic technique / by Ladislaus Szymonowicz ; translated and edited by John Bruce MacCallum.

Contributors

Szymonowicz, Ladislaus.
MacCallum, John Bruce, 1876-1906.

Publication/Creation

Philadelphia : Lea, [1902]

Persistent URL

https://wellcomecollection.org/works/hvs6r2rt

License and attribution

Conditions of use: it is possible this item is protected by copyright and/or related rights. You are free to use this item in any way that is permitted by the copyright and related rights legislation that applies to your use. For other uses you need to obtain permission from the rights-holder(s).

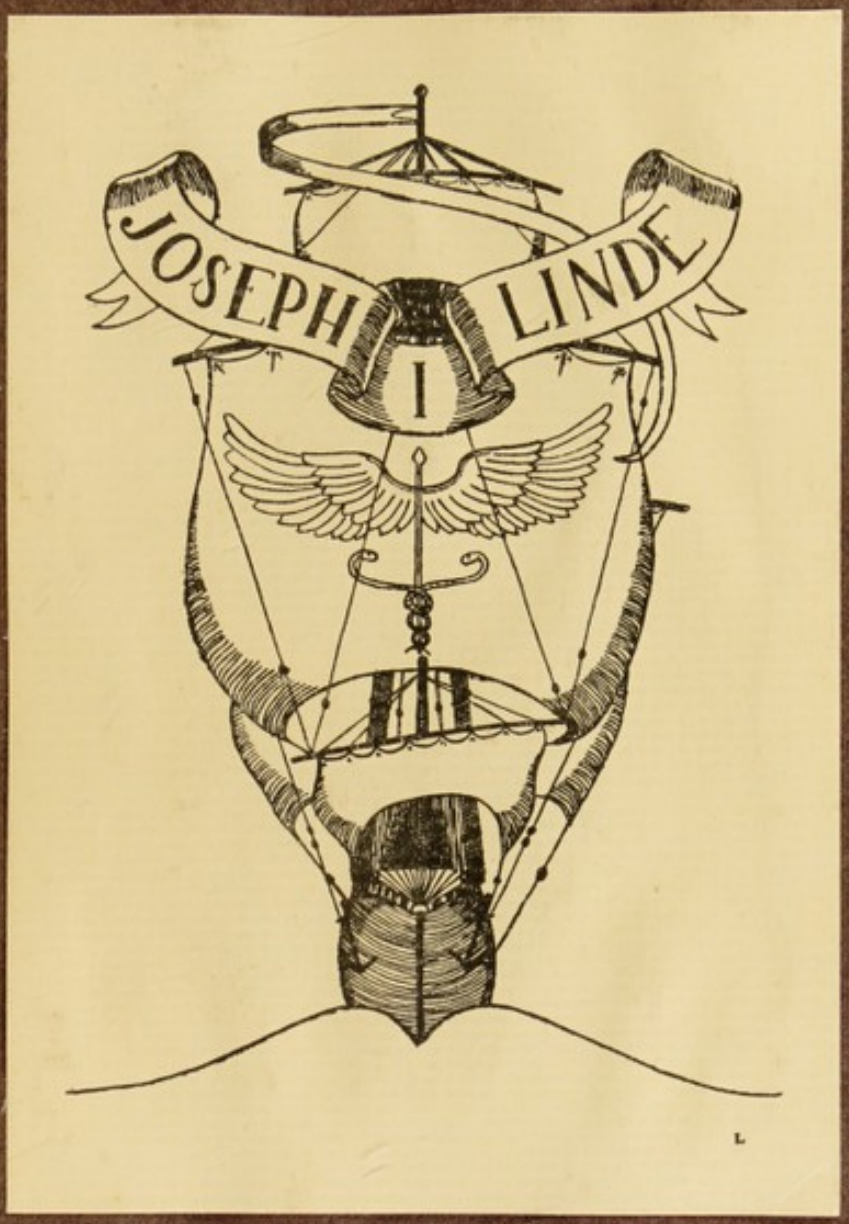
wellcome collection

Wellcome Collection
183 Euston Road
London NW1 2BE UK
T +44 (0)20 7611 8722
E library@wellcomecollection.org
https://wellcomecollection.org




22500024023

Med
K8271



DEPARTMENT OF
HISTORY OF MEDICINE
UNIVERSITY COLLEGE
LONDON

Joseph Irving Linde

A TEXT-BOOK

OF

HISTOLOGY

AND

MICROSCOPIC ANATOMY

OF THE

HUMAN BODY,

INCLUDING MICROSCOPIC TECHNIQUE.

BY

DR. LADISLAUS SZYMONOWICZ,

A. Ö. PROFESSOR OF HISTOLOGY AND EMBRYOLOGY IN THE UNIVERSITY OF LEMBERG.

TRANSLATED AND EDITED BY

JOHN BRUCE MacCALLUM, M. D.,

JOHNS HOPKINS UNIVERSITY, BALTIMORE.

ILLUSTRATED WITH 277 ENGRAVINGS, INCLUDING 57 PLATES IN COLORS AND MONOCHROME.



LEA BROTHERS & CO.,
PHILADELPHIA AND NEW YORK.

1902

Entered according to Act of Congress, in the year 1902, by

LEA BROTHERS & CO.,

In the Office of the Librarian of Congress, at Washington. All rights reserved.

14804 014

WELLCOME INSTITUTE LIBRARY

Coll.	WelMOmec
Coll.	
No.	QS

ELECTROTYPED BY
WESTCOTT & THOMSON, PHILADA.

PRESS OF
WILLIAM J. DORNAN, PHILADA.

PREFACE.

In the translation of this work and the preparation of an American edition an effort has been made to place at the command of English-speaking instructors and students a text-book which includes the best results of recent investigations. The spirit and characteristic features of the German original have been carefully retained, changes in text or illustration being made only where some definite advantage was to be attained. These changes have mostly resulted in enlargements. Thus ten of the German engravings have been replaced with thirty-five new ones, taken from various sources. These can be identified by the credits given in connection with the respective figures. Many additions have likewise been made in the text. I am especially indebted to Dr. Florence R. Sabin for a brief description of the medulla and midbrain.

Nearly all of the drawings which have been taken from the German edition were made by Dr. Baracz from material prepared by the author, who acknowledges the assistance also of Dr. Bochenek, Professor Browicz, and Dr. R. Krause.

It has been my object throughout to trace, as far as possible, the development of the organs and the histogenesis of the tissues, and it is hoped that the attention of instructors and students may be drawn to the importance of viewing Histology from this standpoint. I have endeavored, also, to emphasize the fact that in many organs it is possible to recognize structural units which are repeated in a definite way and bound together by a characteristic framework.

I am much indebted to Professor F. P. Mall for the kind interest he has taken in the preparation of this edition.

John Bruce MacCallum.

Baltimore, July, 1902.

Digitized by the Internet Archive
in 2016

https://archive.org/details/b28132154

CONTENTS.

PART I.

HISTOLOGY.

MICROSCOPIC ANATOMY OF CELLS AND TISSUES.

PAGE

A. THE CELL 18

Direct Division (Amitosis) 28

Indirect Division (Mitosis, Karyokinesis) 28

Process of Fertilization 32

B. THE TISSUES 35

I. Epithelial Tissue 37

Glandular Epithelium and Glands 46

Chorda Dorsalis 51

II. Supporting, Connecting, and Interstitial Tissues 52

1. Connective Tissue 53

(*a*) Embryonic Connective Tissue (Gelatinous, Mucoid Tissue) 53

(*b*) Areolar or Fibrillar Tissue 54

(*c*) White Fibrous Connective Tissue 63

(*d*) Elastic Connective Tissue 64

(*e*) Reticulum 65

(*f*) Fat 66

2. Cartilage 68

(*a*) Hyaline Cartilage 68

(*b*) Elastic Cartilage 72

(*c*) White Fibrous Cartilage 73

3. Bone 74

III. Muscle 80

1. Smooth Muscle 81

2. Heart Muscle 83

3. Voluntary Striated Muscle (Skeletal) 88

IV. Nervous Tissue 97

A. Nerve Cells 98

B. Nerve Fibres 104

V. Blood and Lymph 112

1. Blood 112

2. Lymph 120

PART II.

MICROSCOPIC ANATOMY OF THE ORGANS.

PAGE

I. CIRCULATORY SYSTEM 121
1. Blood Vascular System 122
(a) Capillaries 122
(b) Arteries 123
(c) Veins 127
(d) Heart 129
2. Lymphatic System 132
(a) Lymph-vessels 132
(b) Lymph Glands 133
(c) Peripheral Lymph Nodules 138
3. Spleen 138
4. Thymus 143
5. Thyroid Gland 144
6. Adrenal (Suprarenal Gland) 147
7. Pituitary Body (Hypophysis Cerebri) 152
8. Carotid Gland (Glomus Caroticum) 153
9. Coccygeal Gland (Glomus Coccygeum) 154

II. DIGESTIVE SYSTEM (ALIMENTARY TRACT) 154
A. Mouth Cavity 155
1. Mucous Membrane of the Mouth 155
2. The Teeth 156
Development of Teeth 161
3. The Tongue 164
4. The Tonsils 167
Development of Tonsils 169
5. Glands of the Mouth Cavity 170
B. Pharynx 177
C. Œsophagus 178
D. Stomach 180
E. Intestine 185
Blood-vessels, Lymph-vessels, and Nerves of Stomach and Intestine . 190
F. Pancreas 192
C. Liver 193
Gall Bladder 203
H. Peritoneum 205

III. RESPIRATORY SYSTEM 206
A. Larynx and Trachea 206
B. Bronchi and Lungs 206

IV. URINARY SYSTEM 212
A. Kidneys 212
Blood-vessels of the Kidney 217
B. Urinary Passages 221
(a) Kidney Calyces and Pelvis; Ureter, and Urinary Bladder . . . 221
(b) Urethra 223
(1) Male 223
(2) Female 223

PAGE

V. GENERATIVE (REPRODUCTIVE) SYSTEM 224
1. Male Sexual Organs 224
A. Testis 224
B. Spermatic Ducts 231
C. Accessory Glands of Male Sexual Organs 234
1. Prostate 234
2. Cowper's Glands 235
D. Penis 235
2. Female Sexual Organs 237
A. Ovary 237
B. Fallopian Tube 250
C. Uterus 251
Placenta 257
D. Vagina and External Female Genitals 262

VI. LOCOMOTOR SYSTEM 264
1. The Skeletal System 264
A. Bones 264
(*a*) Bone-marrow 265
(*b*) Joining together of Bones 267
(*c*) Development of Bones 268
(1) Development of Bone from Cartilage 268
(2) Development of Bone from Connective Tissue . . . 273
B. Cartilages 273
2. Muscular System 274
Development of Muscles 276

VII. NERVOUS SYSTEM 278
1. Central Nervous System 278
A. Spinal Cord 278
B. Medulla, Pons, and Midbrain 287
C. Cerebral Cortex 291
D. Cerebellum 293
E. Meninges 296
F. Blood-vessels of Central Nervous System 298
2. Peripheral Nervous System 299
A. Nerves 299
B. Ganglia 301
C. Nerve-endings 304
(1) Intra-epithelial Nerve-endings 305
(2) Nerve-endings in Connective Tissue 307
(3) Nerve-endings in Muscle 312
(*a*) Motor Nerve-endings 312
(*b*) Sensory Nerve-endings 314
(4) Nerve-endings in Nervous Tissue 316

VIII. SENSE ORGANS 318
1. The Skin—The Tactile Organ 318
(*a*) Outer Skin 318
(*b*) Hairs 322
(*c*) Nails 329

PAGE

(*d*) Glands of the Skin 331
Sebaceous Glands 331
Sweat Glands 333
(*e*) Vessels and Nerves of the Skin 335
(*f*) Mammary Gland 337
2. Visual Organ 340
(*a*) Eyeball 340
(1) Tunica Externa 340
(2) Tunica Media 343
(3) Tunica Interna 346
(4) Optic Nerve 354
(5) Lens 355
(6) Vitreous Body and Zonula Ciliaris 356
(7) Blood-vessels of the Eyeball 357
(8) Lymph Paths of the Eyeball 359
(9) Nerves of the Eyeball 360
(*b*) Protecting Organs of the Eye 361
(1) Eyelids and the Conjunctiva 361
(2) Lachrymal Apparatus 364
3. Auditory Organ 364
(*a*) Inner Ear 364
(1) Sacculus, Utriculus, and Semicircular Canals 365
(2) Cochlea 367
(3) Blood-vessels of the Membranous Labyrinth 373
(4) Lymph Paths in Labyrinth 375
(*b*) Middle Ear 375
(*c*) Outer Ear 376
4. Olfactory Organ 377
5. Organ of Taste 381

GENERAL MICROSCOPIC TECHNIQUE 383

1. The Microscope 383
2. The Preparation of Specimens for Microscopic Study 385
(*a*) Isolation and Teasing of Tissues 386
(*b*) Sectioning of Tissues 387
(*c*) Fixation of Tissues 387
(*d*) Hardening of Tissues 390
(*e*) Decalcification of Bone 390
(*f*) Infiltration of Tissue with Celloidin and Paraffin 391
(*g*) Staining 395
(*h*) Injecting 399

SPECIAL MICROSCOPIC TECHNIQUE 401

1. The Cell 401
2. Epithelial Tissue 402
3. Connective Tissue, Cartilage, and Bone 403
4. Muscle 405
5. Nervous Tissue 406
6. Blood 407

PAGE

7. Circulatory System 408
8. Digestive System 409
9. Organs of Respiration 410
10. Urinary and Reproductive Organs 410
11. Skeletal System 411
12. Nervous System 412
13. Skin 414
14. Eye 414
15. Ear and Nose 415

HISTOLOGY

AND

MICROSCOPICAL ANATOMY OF THE HUMAN BODY

PART I.

HISTOLOGY.

MICROSCOPICAL ANATOMY OF CELLS AND TISSUES.

Histology is the study of tissues (*ὁ ἱστός, τὸ ἵστιον*, tissue). It must therefore primarily treat of the cell as a tissue-element; then concern itself with the description of vegetable and animal tissues; and finally discuss the relations which the tissues bear to one another in all the organs. This last part of histology is also spoken of as *microscopical anatomy*.

Our text-book, which concerns itself only with the histology of man and the animal body, is divided into two parts: the first will treat of the animal cell and tissues; the second will make the reader acquainted with the microscopical structure of the organs.

Histology takes a prominent part among the biological sciences which have developed so greatly since the discovery of the cell in the year 1838. As early as the end of the seventeenth century there were more or less definitely expressed premonitions and suspicions that cells formed the elementary constituents of plants. Only in the year 1838, however, did the opinion that plants consist of cells gain general recognition after the publication of M. Schleiden. In the

next year, 1839, Schwann, encouraged by the findings of Schleiden, undertook investigations on animals, and found here also a cellular structure. These two investigators considered the cell a small vesicle containing a fluid in a definite membrane. Even at this early date they thought the cell membrane and nucleus to be very important, characteristic, and constant constituents of the cell. So it was discovered that both animal and vegetable organisms consist of very minute elements; and further, that all these more or less complicated structures take their origin from a single cell,—*i. e.*, the fertilized egg. Then it was shown that on the border land between the animal and vegetable kingdoms unicellular creatures exist which form a starting-point for both kingdoms. The original conception of the cell underwent great changes in the course of the following decade.

A number of years after this, when membraneless cells had been discovered, the cell membrane came to be considered as an unessential part of the cell. In the ground substance of many animal cells movements were observed, which were already known in plant cells. These evidences of life were studied, and the ground substance in animal and vegetable cells was called *protoplasm*.

A. THE CELL.

What is to-day known as a cell (cellula) is a small mass of protoplasm containing within it a nucleus. We must consider cells as elementary units; or, since they are the bearers of the life functions, as the units of life.

In reviewing the animal series, which is made up partly of organisms consisting of only a single cell (protozoa), partly of those containing a countless number of cells (metazoa), it is to be noted that the cells of the first class subserve simultaneously different functions, while we find in the second class much differentiated cells with very diverse functions. In the most highly developed organisms we find these differentiations and this division of labor so strongly marked that one kind of cell cannot take on the functions of another kind.

Here the cells are joined together only for certain functions: for example, to cover and serve as a protection, to separate, to absorb, to draw together, or to conduct impulses. In unicellular organisms, on the contrary, a cell is a complex of organs which serve different functions.

The essential constituents of the cell are

(*a*) the *protoplasm* and

(*b*) the *cell nucleus.*

The nucleus may in many cases disappear, especially if the cell begins to lose its vital activity.

Protoplasm is a morphological conception, and not a body capable of sharp definition chemically. By the term "protoplasm" is not to be understood a uniform substance with constant physical and chemical properties, but, on the contrary, a combination of various different chemical bodies joined with one another in a truly wonderful way; a substance which exhibits different physical, chemical, and biological properties (O. Hertwig). Protoplasm is semifluid, elastic, almost always colorless, and insoluble in water. It is not entirely homogeneous, but shows fine granules (*microsomes*) and fibrils which are contained in the homogeneous ground substance.

We may often observe that the cell consists at the periphery of a non-granular protoplasm (*hyaloplasm*), while in the inner part there is a granular protoplasm-mass (*granuloplasm*). These two parts of the cell are known also as *ectoplasm* and *endoplasm*, respectively.

The chemical composition of protoplasm is unknown, except that its essential and most important constituent belongs to the protein substances (albuminous bodies). Besides this, protoplasm contains globulin and albumin in small quantities, a large proportion of water, a recognizable quantity of different salts, and constantly changing products of metabolism, such as fats, cholesterin, lecithin, glycogen, sugar, etc. Living protoplasm always has an alkaline reaction.

Concerning the finer protoplasmic structure there are four different and opposing views (Fig. 1).

According to one view held at the present time by only a

very few investigators, protoplasm has no definite structure—*i. e.*, it is quite homogeneous.

The second is the *fibril network theory*, which considers the protoplasm as made up of a thread-like network and an interstitial substance. With regard to these strongly refractive fibrils different views are held. According to some authors (Flemming), they do not join with one another in any way; while according to others they combine to form a sort of net-

FIG. 1.

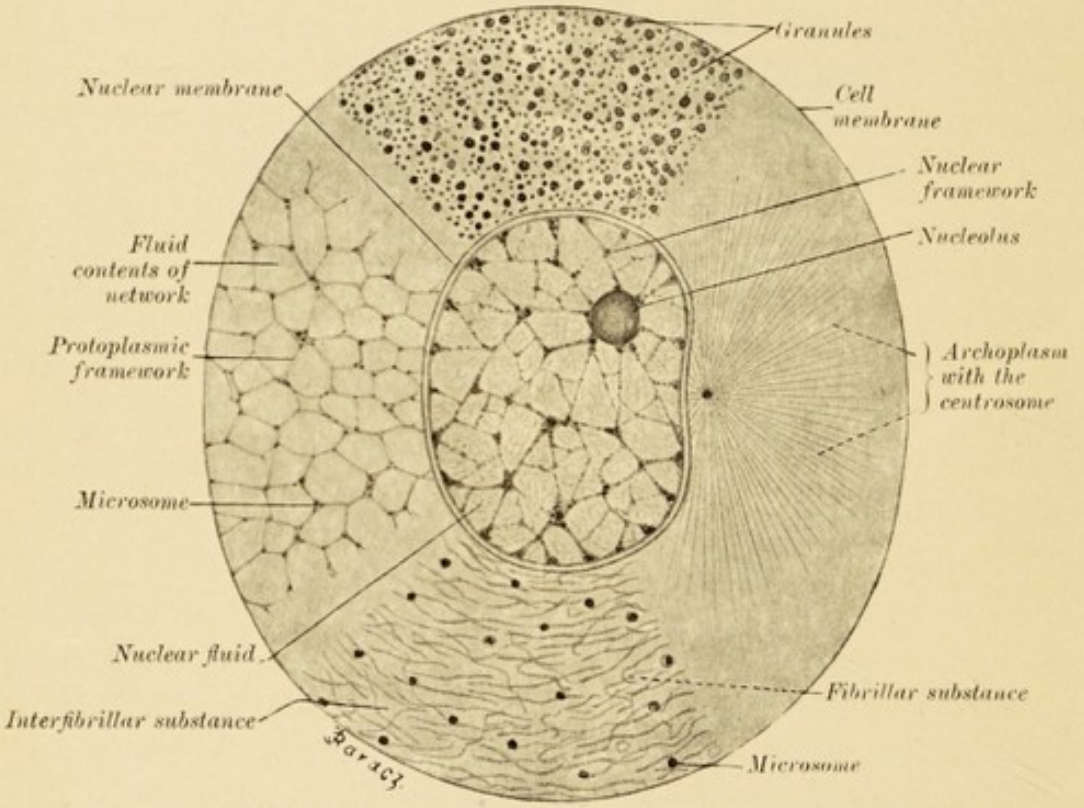


Diagram of a cell. The lower segment illustrates the fibrillar theory, the upper the granular theory, the left the foam theory. At the right the protoplasmic threads radiate from the centrosome. The nuclear network consists of nuclein, linin, and lantanin.

work, so that a sponge-like structure is formed (Heitzmann, Fromman, Leydig). The less refractive and more fluid interstitial substance separates the fibrils from one another. The latter form the so-called *filar-mass* or *mitom*, the former the *interfilar-mass* or *paramitom*. The fibrils occur in varying quantities in the cell, are of different lengths, and often are coiled. The interstitial substance often contains more or less numerous granules.

The third place is taken by the so-called *foam theory* (Bütschli); a protoplasmic network forms a number of spaces closed in on every side. All these spaces are filled with fluid. In the angles of the foam-work fine granules (microsomes) are contained.

Finally there exists the *granule theory* (Altmann) according to which the cells consist of fine granules which are distributed in the jelly-like intergranular substance. These granules Altmann claims to be the final elementary part of the cell, and calls them, as the bearers of life, *bioblasts*. According to this hypothesis, the granules play the principal rôle, and the intergranular substance only an accessory part. With regard to the meaning of these two constituents of the cell, the first three theories are quite opposed to the last. According to the former, the granules of the protoplasm play a more subordinate rôle. The intergranular substance of the granule theory is identical with the essential protoplasm of the other three theories.

In the protoplasm there are various substances not belonging to it, which we include under the name *protoplasmic* or *cellular inclusions*. To distinguish them from protoplasm, we call them *deutoplasm*. Their nature is not constant. They may be fat, carbohydrates, pigment granules, etc.

These protoplasmic-inclusions (deutoplasm) occur in some cases in such great quantity that the protoplasm itself becomes inconspicuous and forms only a kind of network for the reserve materials and secretion stored up there, as we may notice in many egg cells and goblet cells.

Fluid protoplasmic inclusions usually are present in spaces called *vacuoles*. These spaces are made visible by dissolving out the contents. For example, fat droplets may be dissolved in ether and the empty spaces left are plainly to be seen.

The form which a mass of protoplasm or a whole cell takes on may be various: spherical, cylindrical, flat, star-shaped, spindle-shaped, or fibrillar.

Cells vary in size from 3 μ[1] to that of a bird's egg (*e. g.*, an ostrich egg, which is a simple cell).

[1] μ = a micron = 0.001 mm.

The second essential part of the cell is the nucleus. This is often invisible in the living cell when the nucleus and the protoplasm have the same refractive power. They react differently, however, to certain reagents. For example, acetic acid causes protoplasm to swell up and the nucleus to shrink.

The nucleus is usually spherical or oval; sometimes horseshoe-shaped, ring-shaped, or branched.

The nucleus often holds a definite relation to the size of the cell. For example, the nuclei of unripe egg cells are very large.

As a rule we find one nucleus in each cell. Often, however, there are more than one, and exceptionally their number may be as great as one hundred (*e. g.*, in the giant cells of bone-marrow). Such multinucleated cells are called *syncytium*.

The cell nucleus is not a simple structure. We are able to recognize in it at least two and often as many as six proteids which are chemically and microscopically different, namely:

1. Nuclein—chromatin;
2. Paranuclein—pyrenin;
3. Linin;
4. Lantanin;
5. Nuclear fluid (Kernsaft);
6. Amphipyrenin.

The first two seem to be essential elements of the nucleus.

1. *Chromatin* (*nuclein*) is the most characteristic constituent of the nucleus. It is demonstrated by its great capacity for taking up stains, and is distinguished from the other substances by the fact that it contains phosphoric acid. Chromatin occurs in the nucleus in the form of granules, fine threads, or as a network which forms the so-called *chromatin network*.

2. *Paranuclein* (*pyrenin*) occurs in the form of a small highly refractive sphere which forms the true *nucleolus*. These nucleoli are to be distinguished from chromatic enlargements formed in the angles of the nuclear network. Pyrenin is distinguished from chromatin mainly by physical properties. It does not swell in water, dilute alkaline solutions, lime-water, or salt solution. Chromatin, on the contrary, swells in such

solutions, and is dissolved in stronger solutions. The unchanged nucleolus becomes even plainer after such treatment. Nuclein is colored better in acid stains, while paranuclein takes up more readily basic stains, eosin, and fuchsin. In this way these two parts can be differentiated by the so-called *double staining*.

3. *Linin* takes part in the formation of the network or framework. It is not stained by the ordinary coloring materials, and forms the so-called achromatic constituent of the nucleus.

4. *Lantanin* occurs often in the linin in the form of fine granules, which may be stained by acid anilin dyes, as opposed to chromatin, which takes up only basic anilin-stains. Lantanin is therefore called *oxychromatin*, while chromatin is known as *basichromatin*.

5. *Nuclear fluid* (Kernsaft) fills out the spaces between the structures formed of nuclein, paranuclein, and linin.

6. *Amphipyrenin* is the substance which forms the nuclear membrane separating the nuclear space from the protoplasm. In large nuclei the nuclear membrane shows a plainly double contour. In chemical properties it is most nearly related to pyrenin.

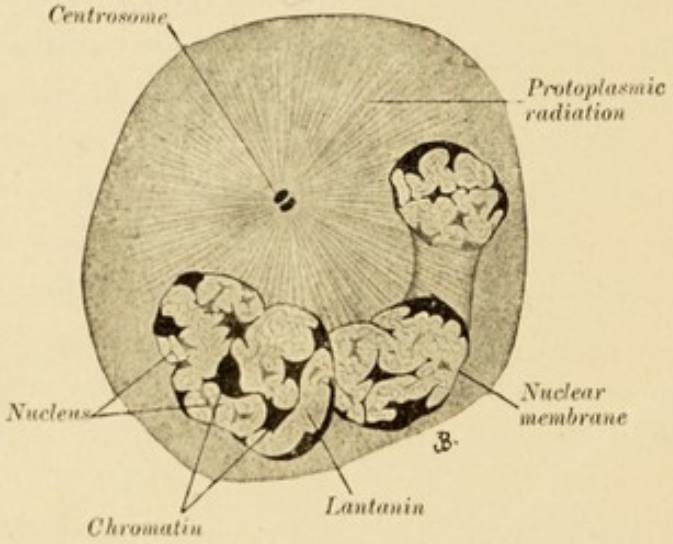
The nucleus may be simple or complicated in form. The most simple structure is seen in those nuclei which consist of quite compact nuclein bodies (*e. g.*, spermatozoa). In other cases the nucleus has a more open structure, the spaces in the nuclear network being filled with nuclear fluid. Such a nuclear network may in its simpler forms be made up only of chromatin; in other cases linin and lantinin are also present (Figs. 1 and 2). The resting nucleus may in certain cases appear as a vesicle surrounded by a nuclear membrane (amphipyrenin). In this is to be found a network of nuclein (chromatic) and linin (achromatic), in which granules of lantanin are scattered. It contains also a nucleolus (paranuclein) and a nuclear fluid.

The third but unessential constituent of the cell, the *cell skin* or *cell membrane*, may often be lacking in animal cells. If the superficial layer of the protoplasm is distinguished from the

remainder of the protoplasm lying more centrally, and is less dense, it is called *ectoplasm*. Such a cell contains no cell membrane, and is spoken of as *naked*. When we find a firm outer boundary for the cell, we call it *crusta* if there is no definite line of demarcation between it and the contained protoplasm. If, on the contrary, it is sharply marked off on its inner border, we have to do with a true cell membrane.

The cell membrane may surround the whole cell, in which case it is called *pellicula;* or it may cover only the free surface of the cell and is then known as *cuticula*.

FIG. 2.



Leucocyte from the spleen of *Proteus* (after Siedlocki). The centrosome appears in the form of two granules. The nuclear network is distinct.

The origin and manner of formation of the cell membrane are not known with certainty; for it is doubtful whether it is a secretion of the outer layer of the cell, or a modified, hardened part of the protoplasm itself.

Another cell constituent which has been the object of much attention in the last few years must not be passed over. This is the so-called *centrosome*. Most authors consider this structure an essential part of the cell (Figs. 1 and 2).

The centrosome occurs usually as one or two granules in the protoplasm, in the neighborhood of the nucleus, and may be contained in a hollowed part of it. Around the centrosome is often to be seen in the protoplasm a radiation which we call the

attraction sphere, *protoplasmic radiation*, or *archoplasm*. The significance and relations of the centrosome during the nuclear and cell division will be spoken of later.

We have considered above all the constituent parts of the cell at rest. It is necessary now to discuss briefly the living properties of the cell in so far as they can be studied by the direct help of the microscope.

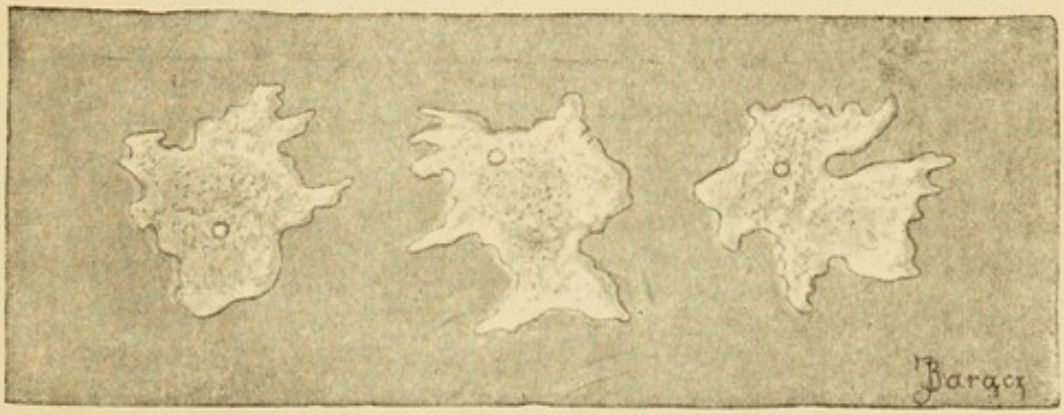
The reader may extend his information on this subject in more exhaustive works in which the cell is treated also from a physiological standpoint (O. Hertwig, Verworn, Bergh).

The different powers and properties of the cell we can group under:

1. Those of *motion*;
2. Those of *irritability*;
3. Those of *assimilation* and *excretion*;
4. Those of *reproduction*.

1. The first function which the cell can fulfil—*i. e.*, motility—seems to be dependent only on the protoplasm; for portions of this separated from the nucleus are capable of motion for some time. We may speak of various kinds of motion:

FIG. 3.



Lymph corpuscle of the frog, studied on a warm stage. The outline of the cell has been made at intervals of two minutes. One vacuole is to be seen. × 1500.

(*a*) *Amœboid movement* consists in the protrusion of processes (pseudopodia) by the protoplasm, which draw the rest of the cell after them. The pseudopodia may also be drawn back to the cell again. If we observe under the microscope such cells or unicellular organisms which have the property of

independent movement, we notice that they constantly change their form. This is seen most easily if we make outline sketches of the cell at short intervals and compare them (Fig. 3). This motility serves not only to change the location of the cell, but also to aid in the acquiring of nourishment. The pseudopodia surround the very fine foreign bodies with which they come in contact, draw them into the cell, and if they are digestible use them for the nourishment of the organism. Upon motility of this sort, a great proportion of the unicellular animals (*e. g.*, amœba) and many kinds of cells of higher animals (*e. g.*, white blood-corpuscles) are dependent.

(*b*) The second kind of motility, the so-called *ciliary movement*, is brought about by shorter or longer processes of the cell substance, the so-called *cilia* or *flagella*. It seems that this movement also is independent of the nucleus. Cilia are of a more permanent nature than pseudopodia. The latter may be pushed out or withdrawn, while the former are developed by a special differentiation of one part of the protoplasm and remain as they are, without changing as the cell moves.

(*c*) *Muscular contraction* is movement which is due to a special differentiation of the protoplasmic network, and serves to move not so much the cell itself, as the organism to which the cell belongs.

(*d*) We distinguish a twofold movement which is present in the protoplasm in the cell body: *circulation* and *rotation*. These movements are made visible to the eye in consequence of the fine granules present in the protoplasm, and are observed especially in plant cells, seldom in animal cells. If the granules move in one direction around under the cell membrane, we have to do with rotation. If, however, the movement is from the periphery to the centre in one part of the cell, and in the opposite direction in other parts, we have circulation. This occurs in all plant cells where the protoplasm contains vacuoles filled with fluid. In these cases strands of protoplasm connect the central perinuclear protoplasm with that at the periphery; and in these strands we often see two streams of granules flowing in opposite directions.

The passive movements which occur in living protoplasm and yet have nothing to do with the life phenomena of the elements moved must not be passed over. Such passive movements characterize the granules in protoplasm, which during rotation and circulation give the appearance of streams of particles moving in various directions. The so-called *Brownian molecular movement*, which may be observed both in living and in dead cells, also belongs to the passive movements. This consists of an indefinite oscillating (trembling) motion of the granules in the protoplasm which does not change the position of the granules to any extent. The nucleus does not possess the power of independent movement. It is, however, capable of change in shape, as, for example, when a cell is stretched, or forced through a small opening, the nucleus changes in form to correspond with its surroundings.

2. *Irritability* is the power of reaction to various stimuli. The stimulus may be mechanical, chemical, thermal, electrical, or due to light. In general it may be said that the stimulus causes an increase or a decrease of the phenomena of life. This depends on the strength and duration of the stimulus. Strong stimulation (*e. g.*, a temperature over 40° C.), causes death to most cells. Cells with active power of motion often move toward, or away from, the source of stimulation.

If the stimulation takes place by chemical means, we have to do with *chemotaxis* (*chemotropism*); and we must distinguish between *positive chemotaxis*, where the cell moves toward the source of stimulation, and *negative chemotaxis*, where the motion is in the opposite direction. With certain bacteria and infusoria there are appearances of chemotaxis under the influence of some chemical bodies (*e. g.*, oxygen, citric acid).

Similarly one may speak of *phototaxis* (*heliotropism*), *hydrotaxis* (*hydrotropism*), *thermotaxis*, *galvanotaxis*, etc. With regard to the last, certain organisms collect about the positive or negative pole on closing or opening a constant electrical current.

3. The processes of *assimilation* and *excretion* belong essentially to physiology. Certain details concerning these are spoken of in the discussion of the organs carrying on these functions.

4. *Reproduction* of the cell. For some time after the discovery of the cell as a unit in the formation of animal and plant organisms it was supposed that cells arose by growth from a formless germ substance, the so-called *cytoblastema*. A certain similarity was traced between this and the process of crystallization, wherein the cells were made to correspond with the crystals and the cytoblastema with the mother liquid. Thanks, however, to the observations and researches of Mohl, Nägeli, and others, the conception was arrived at that cells arise only by division directly from other cells, which fact Virchow expressed in these words, "Omnis cellula e cellula." Later, on the basis of further investigation, the conception was changed to "Omnis nucleus e nucleo." The increase of cells takes place by cell division, which may be of two kinds, distinguished by the behavior of the nucleus during division. We speak of a direct (*amitotic*) and an indirect (*mitotic*) division.

DIRECT DIVISION (AMITOSIS).

By direct division the nucleus is separated into two daughter nuclei by constriction, without any further important changes in its structure being manifest. This kind of division is not common, and seems in certain cases to be the result of abnormal processes; for often the nuclear division is not accompanied by a division of the cell. In this way multinucleated cells arise (*e. g.*, giant cells). There is ground for the belief that direct division is a process which no longer tends to the physiological increase of cells, but represents a degeneration (Flemming). We find amitotic division especially in the lower animals, more particularly in the protozoa; but it may occur also in higher animals, along with indirect division in many leucocytes, cartilage cells, decidual cells, surface epithelial cells of the urinary bladder, etc.

INDIRECT DIVISION (MITOSIS, KARYOKINESIS).

This division is characterized by a whole series of phenomena in the nucleus and protoplasm, while in consequence of a solu-

tion of the nuclear membrane a closer relation exists between the nuclear and protoplasmic structures. The most essential part of karyokinesis is the division of the chromatin of the mother cell into two quite equal parts for the daughter cells.

The chromatin divides itself into two equal parts, the so-called chromosomes. They may be loop-shaped, rod-shaped, or granular. Their numbers may be two, four, eight, sixteen, up to one hundred. The shape, as well as the number, of chromosomes is different, and is characteristic for cells of different animal species.

An exactly equal division of the chromatin takes place by a longitudinal splitting of the chromosomes.

In the protoplasm at the same time very important changes take place, namely, the division of the centrosome, and the arrangement of the protoplasm in radially disposed lines around the centrosome. The two parts of the centrosome move to the poles of the cell, and between them is formed the *central spindle* in the protoplasm. This is shown in Figs. 7 and 8.

The whole process of mitosis may be divided into five stages:

1. Prophase;
2. Mother star stage;
3. Metaphase—metakinesis;
4. Anaphase;
5. Telophase.

The *prophase* consists in the preparation of the resting nucleus for division. Inside the nucleus, the nuclear framework arranges itself in threads which are covered in the beginning with thickenings. These threads of different lengths become smooth on their surfaces and twisted, so that there is formed a coiled mass (Knäuel) (Figs. 4, *a*, 4, *b*, 5, 6).

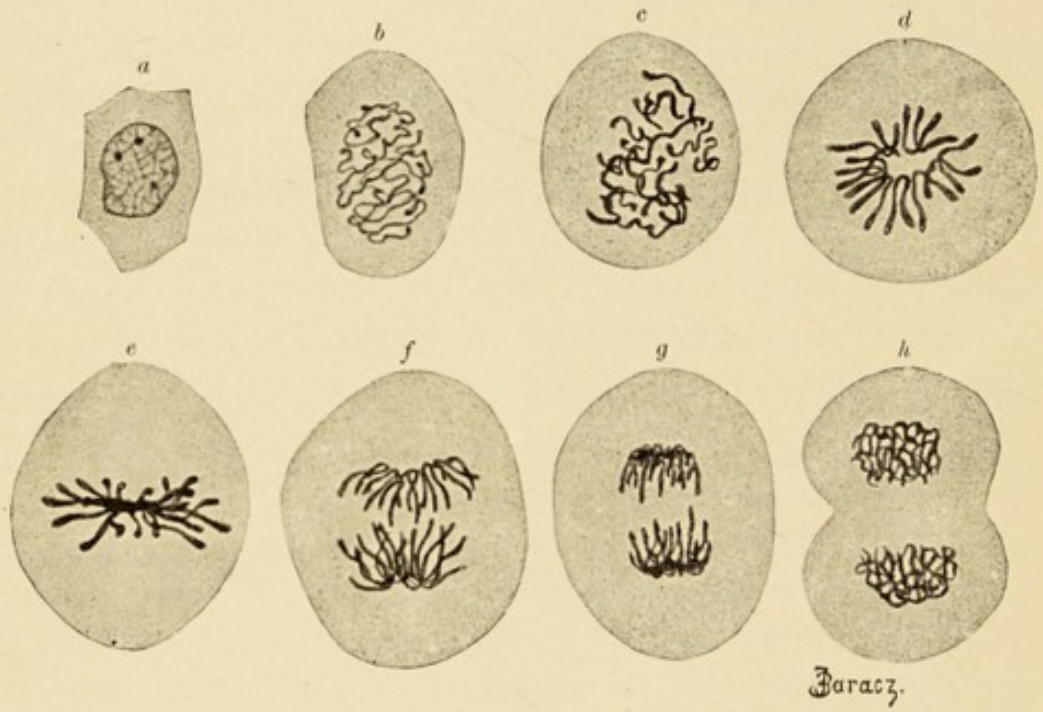
The originally rather thick coil or knot of chromatin threads becomes looser, and the chromosomes assume their characteristic forms of loops, rods, etc. (Fig. 4, *c*, Fig. 7).

The nucleolus always vanishes during the formation of the coil. The centrosome divides at the beginning of these changes into two parts, which are joined from the first by fine fibrils in

the protoplasm which are the beginning of the *central spindle*. This central spindle becomes larger the more the centrosomes advance toward the poles (Figs. 5–7).

The nuclear membrane undergoes solution and the chromosomes arrange themselves in the equatorial plane, giving rise to the *mother star* (*monaster*) (Figs. 4, *d*, 4, *e*, and 8). When the chromosomes are of the form of the letter U, the lower round part is directed toward the centre and the two arms of the loop approach the periphery of the cell. Looked at from above, the

FIG. 4.



Nuclear division in the epithelial cells of the cornea of the frog's larva. × 1400. (*a*) Epithelial cell with nucleus at rest. (*b*) Thick knot of chromatin threads. (*c*) Loose knot of chromatin threads. (*d*) Mother star (monaster) viewed from above. (*e*) Mother star viewed from the side. (*f*) Daughter star (diaster). (*g*) Anaphase. Daughter stars are moving toward the poles. (*h*) The daughter nuclei in the form of loose knots.

chromosomes so arranged have the appearance of a star (Fig. 4, *d*).

During this stage of the mother star the centrosomes proceed to the poles of the cell, and the striations or threads of the central spindle can be divided into three groups: (*a*) the fibres joining the chromosomes with the centrosomes (mantle fibres), (*b*) the central spindle fibres extending uninterruptedly from

pole to pole, and (*c*) the polar striation which extends over the whole cell with the exception of the part occupied by the mantle fibres and the central spindle. The polar radiation overlaps the equatorial zone in which the striations of the two halves of the cell cross.

At this period the *metaphase* begins by a longitudinal division of the chromosomes, so that each mother thread is divided into two daughter threads. If the chromosomes are in the form of loops, the daughter loops begin first to separate from one another at the curved apex and grow in opposite directions so as to approach the poles.

In this way there are formed from one mother star two daughter stars (*diaster*) (Figs. 4, *f*, 9). Between the daughter loops there extend connecting fibres which belong to the central spindle. In this stage of the diaster we observe that the polar striations no longer overlap the equatorial plane.

Following this comes the constriction of the cell body in the equatorial plane (Fig. 10). During the *anaphase* both daughter stars become changed into coiled masses. In the coils the typical structure of the resting nucleus again appears.

The threads of the coil show again an irregular surface with projections which join with one another. A nuclear membrane is formed, and finally the framework of the resting nucleus is built up, and the nucleolus appears. We notice that the anaphase is a reversal of the prophase. The last step in the division is the complete separation of the cell into two halves. During this separation the connecting fibres of the central spindle become drawn together in the equator, and at the same time there appear swellings in the fibres in this region. These swellings approach one another more closely, and there is formed between the daughter cells which are the product of the division the so-called *intermediate bodies* (Zwischenkörper) (Figs. 11 and 13). The fibres radiating from the intermediate bodies soon begin to be lost in the protoplasm, while the intermediate bodies themselves often remain a much longer time. After the division of the cell is completed the radiation disappears in most cases. After the end of the real mitosis one may distinguish a

stage of completion (*telophase*, M. Heidenhain) in which the centrosomes and daughter nuclei assume their normal appearance and position in the cells.

The epoch-making researches of late years (Flemming, M. Heidenhain, Boveri, van Beneden, C. Rabl, v. Kostanecki, etc.) throw clear lights on the mechanism of karyokinesis. These investigations show in the main that the achromatic part of the karyokinetic figures (radiations and centrosome) form a mechanical apparatus upon whose active movements the division of the chromosomes and of the whole cell body depends. The protoplasmic striations play in this an active rôle. Their central point of insertion forms the centrosome.

There arises, then, during karyokinesis under normal conditions two nuclei from one, and from each cell two cells. Only exceptionally and mainly under pathological conditions are many nuclei formed simultaneously by the division of one nucleus.

The multiplication of cells goes on during the whole life of the organism, so that those cells which under normal conditions must die, may be replaced.

The duration of life in the cell is variable. Its growth usually goes on as long as life lasts, and the original form of the cell is often much altered.

Death in the cell is recognized first in the nucleus. Certain changes occur which are spoken of collectively as *karyolysis* (*chromatolysis*, Flemming).

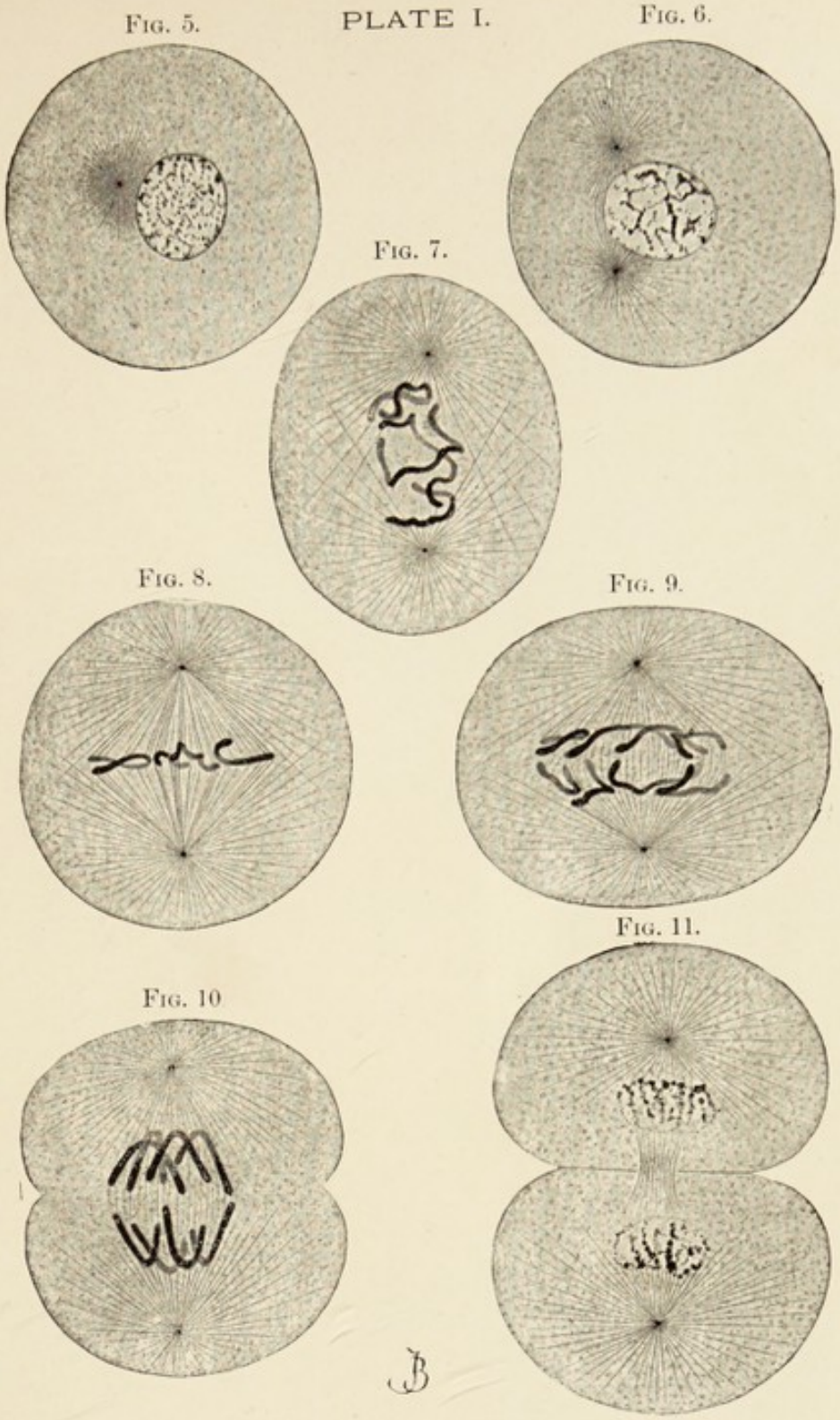
For a discussion of endogenous cell division and budding, see Cartilage and Bone-marrow.

PROCESS OF FERTILIZATION.

Division of the egg occurs always after fertilization (parthenogenesis excepted). The process of fertilization consists in the conjugation of the male cell (spermatozoon) with the female cell (egg). This leads to the division of the egg, and in consequence the formation of the embryo. This combination of the sexual cells takes place in such a way that the small and actively motile spermatozoon enters the large and non-motile egg.

Preceding the fertilization there occur in the egg certain

PLATE I.



Semidiagrammatic representation of the processes of cell and nuclear division in *Ascaris megalocephala*. (After Kostanecki.)

Fig. 5.—Resting cell.

Fig. 6.—Division of centrosome.

Fig. 7.—Prophase—centrosomes at the poles; radiation well developed; chromatin network broken up into four chromosomes.

Fig. 8.—Mother star stage (monaster); chromosomes arranged at the equator.

Fig. 9.—Metaphase; the longitudinally divided chromatin filaments moving toward the poles.

Fig. 10.—Anaphase; beginning of division of cell body.

Fig. 11.—Division of cell body almost completed; the central spindle shows the beginning of the intermediate bodies.

PLATE II.

Fig. 12.

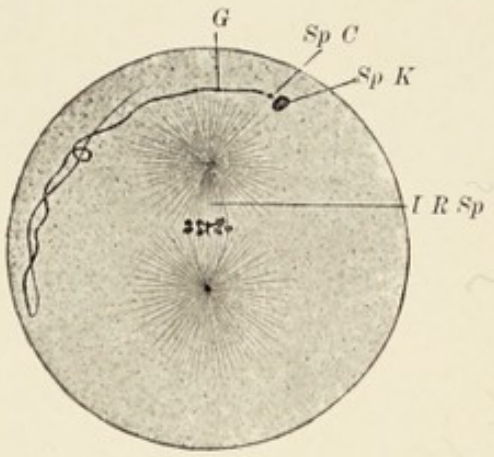


Fig. 13.

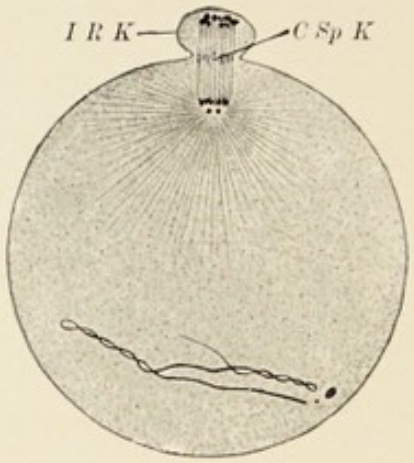


Fig. 14.

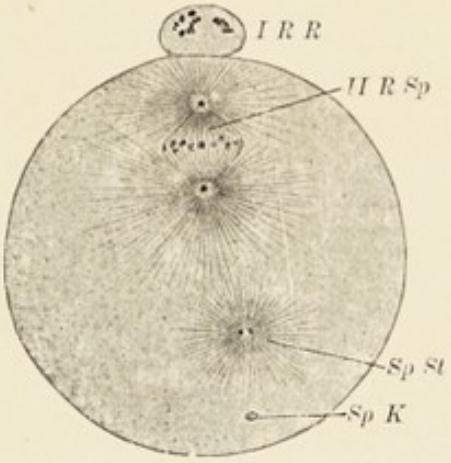
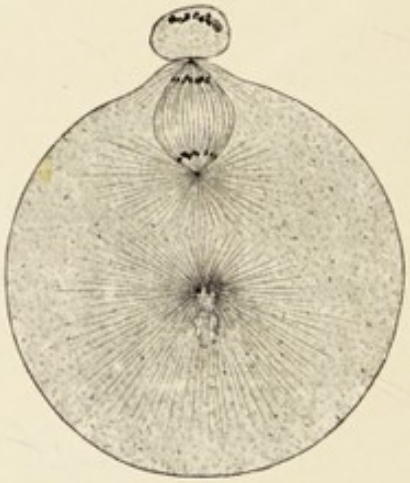


Fig. 15.



Stages in the fertilization of *Physa fontinalis*. (After Kostanecki and Wierzejski.)

Fig. 12.—Mother star stage passing into metakinesis for the formation of the first polar body. The spermatozoon is enclosed in the egg *in toto*.

Fig. 13.—Formation of first polar body; centrosome divided.

Fig. 14.—First polar body formed. Monaster stage for the formation of the second polar body. Sperm radiation is separated from the sperm nucleus.

Fig. 15.—Formation of the second polar body. Sperm radiation with two centrosomes near the vesicular sperm nucleus.

changes which are spoken of collectively as egg *ripening* or the *maturation* of the egg. These changes consist of the so-called *reduction of chromosomes.* The process of ripening may go on and be completed before the spermatozoon enters the egg or indeed approaches it. This is not the same in different animals. A similar reduction of chromosomes takes place in the spermatozoa, during their formation from the so-called spermatogonia, which will be discussed in its proper place. Here it is only necessary to say that the spermatozoon is a flagellated cell which possesses all the essential constituents of other cells. The anterior large part of the spermatozoon, the so-called head, represents the nucleus; the so-called intermediate or middle piece is the centrosome. The flagellum or tail represents the protoplasmic part of the cell.

The process of maturation and fertilization has been worked out in detail in a considerable number of animals. We shall describe this process as it occurs in *Physa fontinalis*, a mollusk, in which the clearness of the microscopical picture allows of exact observation of both processes in all their minuteness (Kostanecki and Wierzejski). Here the process of maturation does not take place until after the entrance of the spermatozoon into the egg; so that the so-called *extrusion* of both *polar bodies* occurs simultaneously with the first stages of the true process of fertilization.

The process of maturation consists of two unequal karyokinetic divisions of the egg cell, which have all the characteristics of the cell division described above (Fig. 12). The karyokinetic figure now moves toward the surface of the egg, and in consequence of the splitting of the chromosomes (metakinesis) the mother star is transformed into two daughter stars. A round elevation is formed on the surface of the egg, and this becomes occupied by one-half of the chromosomes and a centrosome with one-half of the central spindle (polar spindle). By the formation of an intermediate body the separation of the first polar body is completed (Fig. 13).

This same process is gone through again in the following way. When the first polar body is not entirely separated off

the centrosome left in the egg divides into two parts (Fig. 13). These centrosomes arrange themselves at the poles of the karyokinetic figure which is formed from the chromosomes remaining in the egg. The chromosomes do not split to form the diaster stage. They separate into two groups, giving rise to the two daughter stars, each of which contains one-half the number of chromosomes possessed by the mother star. The whole karyokinetic figure becomes situated under the surface of the egg, and a round mass of protoplasm projected from the surface receives one-half of the figure. Thus the extrusion of the second polar body takes place in a way quite similar to that of the first. This completes the process of maturation.

In consequence of this second division of the egg cell, the egg possesses only half as many chromosomes as other (somatic) cells of the animal body from which the egg proceeds. Also during the development of the spermatozoon a reduction of chromosomes takes place, so that the ripe sexual cells (the egg as well as the spermatozoon) contain only half the number of chromosomes possessed by somatic cells. Therefore their nuclei have really only half the value of other nuclei. By fertilization, in which there is a union of the two nuclei containing each one-half of the full number of chromosomes, the normal quantity is restored.

The process of fertilization—*i. e.*, the entrance of the spermatozoon into the egg—begins in many animals not until the extrusion of the second polar body. In the animal under consideration the fertilization process is already well advanced at the end of maturation; for the two processes go on together and begin at the same time. In *Physa* the whole spermatozoon as a rule enters the egg (Fig. 12). In other animals usually only the head and the middle piece gain entrance.

Since the function of the tail or flagellum is at an end after the entrance of the spermatozoon into the egg, it undergoes absorption. Around the centrosome of the spermatozoon—*i. e.*, the middle piece—a new radiation arises in the egg protoplasm (Figs. 13, 14). The radiation and the centrosome of the spermatozoon become more conspicuous at the expense of the

PLATE III.

FIG. 16.

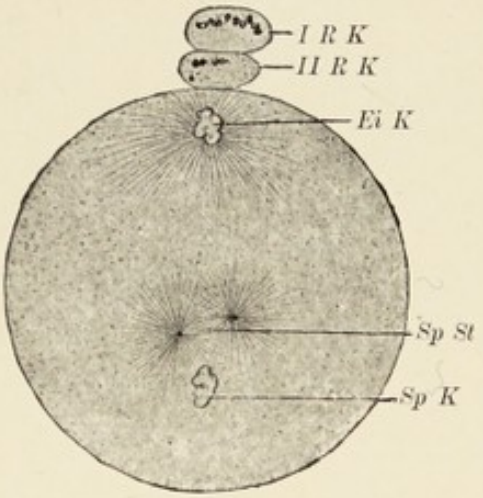


FIG. 17.

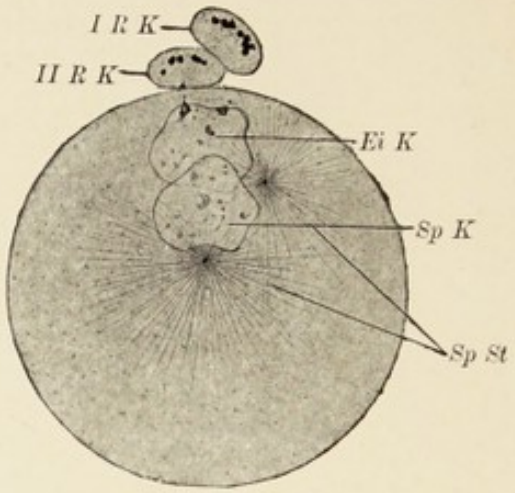


FIG. 18.

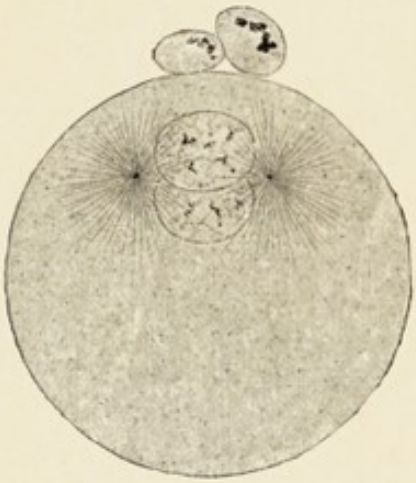


FIG. 19.

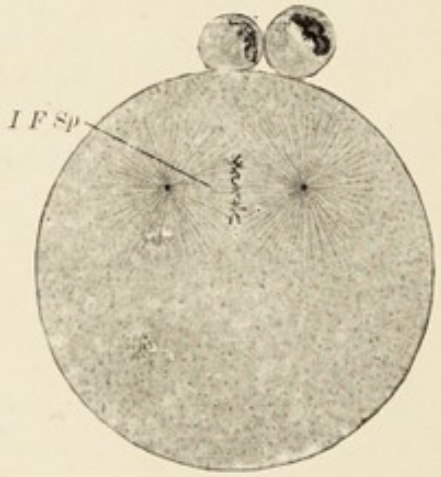


FIG. 16.—Two polar bodies above. Egg nucleus has become vesicular. Sperm radiation has increased in size.

FIG. 17.—Egg and sperm nuclei approach one another. The sperm radiation and the centrosomes move apart.

FIG. 18.—Egg and sperm nuclei closely approximated. The centrosomes arrange themselves on opposite sides.

FIG. 19.—The chromosomes of the egg and sperm nuclei form a monaster stage to give rise to two new cells.

C Sp K, central spindle.
Ei K, egg nucleus.
I F Sp, first spindle after fertilization.
G, tail of spermatozoon.
I R K, first polar body.
II R K, second polar body

I R Sp, first polar spindle.
II R Sp, second polar spindle.
Sp C, centrosome of spermatozoon.
Sp K, sperm nucleus.
Sp St, sperm radiation.

egg protoplasm. The sperm cell centrosome undergoes division, so that a central spindle is formed (Figs. 14–16).

At this stage of the fertilization the process of maturation is usually completed, and the egg nucleus has become vesicular (Fig. 16). The sperm nucleus now begins to swell and become also vesicular, and approaches the egg nucleus. The sperm centrosome and central spindle at the same time become closely related to the sperm nucleus (Figs. 15, 16). Both nuclei become larger, and as they approach one another the radiation of the egg centrosome becomes less conspicuous. The sperm radiation becomes more and more prominent, spreading over the whole cell. Finally the egg radiation vanishes, since the functions of the protoplasmic striations, as well as of the egg centrosome, are after the extrusion of the two polar bodies ended (Figs. 16, 17).

The radiation arising from the spermatozoon enters into combination with the nuclear framework and the last chromosomes of the egg nucleus. At this moment the process of fertilization as such is completed. Both nuclei undergo the first stages of indirect division and give rise to a mother star (Figs. 18, 19).

The further process is not different from the ordinary mitotic division. This karyokinetic figure should form nuclei, of which each contains an equal number of male and female nuclear segments. The number of chromosomes in the fertilized egg equals the sum of the chromosomes of the ripe egg and those of the spermatozoon—that is, the original full number of chromosomes which is characteristic of the somatic cells of the animal.

B. THE TISSUES.

The lowest animal organisms (protozoa) are unicellular structures. Since there is only one cell, this must carry out all the life functions. More highly developed animals are made up of many cells (metazoa), which all arise by a division of one single cell—*i. e.*, the fertilized egg. These cells are quite similar in their early embryonic state; and there is an almost spherical,

many angled form characteristic for embryonic cells. As development goes on, the cells become constantly more unlike one another—*i. e.*, a *differentiation* sets in. In such a multicellular organism the differentiated cells no longer subserve all the life functions, as is the case with unicellular animals. There are cells capable of performing only certain duties. We see here the principle of *division of labor*. These cells differentiated in certain directions, combined to perform certain functions, and arranged according to certain laws, form the tissues. By a tissue we understand a complex of cells definitely arranged, differentiated in a definite direction, and combined to carry out a definite activity.

Tissues consist not only of cells, but also of cell products, which we group under the term *intercellular substance*. This is sometimes a secretion of the cells, and sometimes a product formed by a change in the superficial part of the cell protoplasm. It is wanting in quite early embryonic tissues and is built up in time by the cells.

The various tissues unite in manifold ways to form organs—*i. e.*, bodies of a definite internal structure, and a constant external form, which serve a special physiological function. Only exceptionally does an organ consist exclusively of one tissue, as, for example, the lens of the eye. Usually many, often all of the tissues are used in the building up of the organ, —*e. g.*, the intestine, the skin, etc.

The classification of tissues is one of the most difficult problems in histology. It cannot be made on a purely morphological basis; for not only the form, but also the development and chemical properties of the tissue must be considered. The separation of tissues into groups according to their development and origin is not satisfactory, since the same tissue may arise in more than one way. The most generally accepted classification of tissues is the following:

1. Epithelial (and glandular) tissue;
2. Supporting and interstitial tissue;
3. Muscular tissue;
4. Nerve tissue.

I. EPITHELIAL TISSUE.

Epithelium is made up entirely of closely approximated cells consisting of cell protoplasm and nucleus. The intercellular substance is reduced to a minimum, and is seen only as a cement substance joining the cells with one another. A true cell membrane is usually wanting, only a slightly denser outer sheath being present in the protoplasm. The classification of epithelial tissue depends largely upon the function which it has to fill. It covers the outer surface of the body, and lines the body spaces. In addition to this, epithelial tissue has the power of secretion and absorption, and in such a case it is called glandular epithelium (glandular tissue). Finally it is in some instances capable of receiving certain stimuli from the outer world, and transmitting them to the nervous tissue. Such a tissue forms the so-called *sensory epithelium.*

FIG. 20.

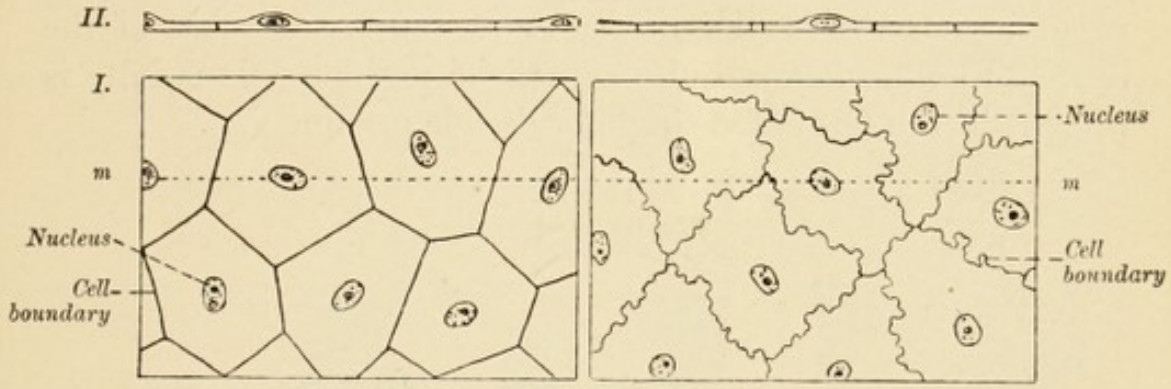
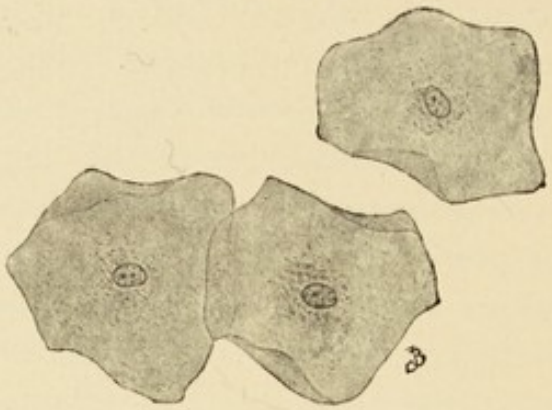


Diagram of flat epithelium. I. Seen from above. II. Seen from the side after transverse section on the line *m*: (*a*) cell boundaries as straight lines; (*b*) cell boundaries as wavy lines.

With regard to the form of the cells, epithelium may be *flat* or *cylindrical.* Flat epithelium consists of more or less regularly polygonal cells, whose depth is very inconsiderable in comparison with the other two dimensions. Looked at on the surface, the cell boundaries are made up of straight or zigzag lines. The spherical or oval nucleus lies usually more or less in the middle of the cell. Figure 20 shows the flat epithelium viewed from above and from the side. We notice that the cell in the neighborhood of the nucleus contains more protoplasm and is thicker at this point (Figs. 20, 21).

In cylindrical epithelium, on the contrary, the height exceeds the two other dimensions of the cell. The cells of cylindrical epithelium have the form of more or less long polygonal prisms or pyramids. The nucleus may be in the

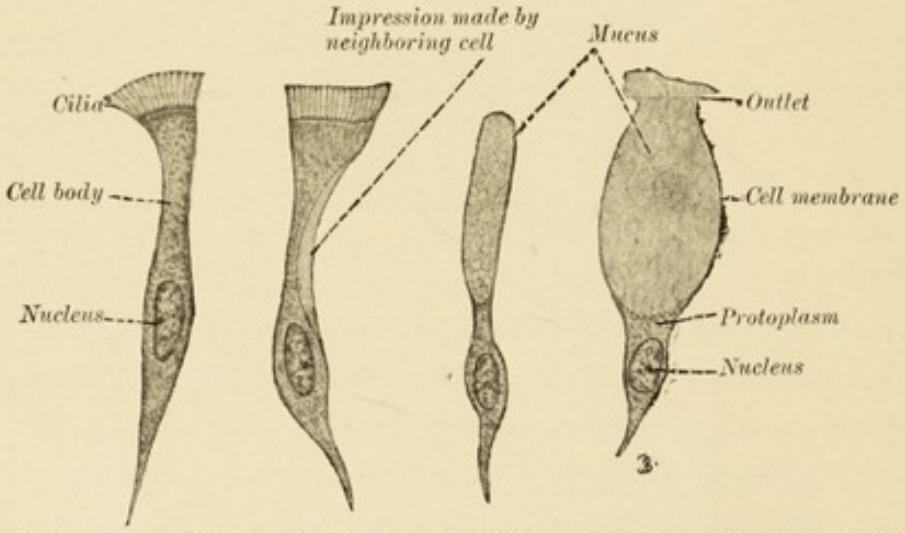
FIG. 21.



Flat epithelial cells isolated from the oral mucous membrane of man. × 375.

middle or at either end of the cell. The centrosome lies in the protoplasm between the nucleus and the free surface of the cell, and holds often a quite superficial position. It usually is present in the form of a single or double granule.

FIG. 22.



Two ciliated cells and two goblet cells isolated from the frog's œsophagus. × 520.

Between the flat and the higher epithelial cells there are *transition forms.* When all three dimensions are equal, we call them *cubical* epithelial cells.

Cylindrical epithelium may undergo certain modifications.

If during life it bears on the free surface moving hairs (cilia, flagella), we call it *ciliated* or *flagellated* epithelium (Fig. 22). There is sometimes on the free surface of the cell a more or less definite refractive border showing striations at right angles to the surface. These cells are called cylindrical cells with a cuticular border. Finally, if the upper part of the cell is changed into mucus, so that this region of the cell is dilated in the form of a goblet, we have to do with the so-called *goblet cells* (Fig. 22).

In ciliated cells certain details can be made out which are not always visible and whose study is attended with great difficulties. The cilia must be recognized as hair-like processes of the cell protoplasm which possess the power of moving uniformly and in one direction. Often such cilia are seen to be made up of several parts which are singly or doubly, strongly or weakly refractive.

This complicated structure can be made out in the schematic representation of the ciliated cell of *Anodonta* shown in Fig. 23. Here the cells are covered by a cuticle. Directly under this there is a row of so-called *basal granules*, which, according to the latest investigations (v. Lenhossék), are to be considered as centrosomes. The cilia pass through the cuticula and form in this a series of thickenings in the form of granules (Fig. 23). In the cell itself we find often in the protoplasm a series of threads which begin at the basal granules, run toward the nucleus, and make up the fibrillar structure of the protoplasm.

Fig. 23.

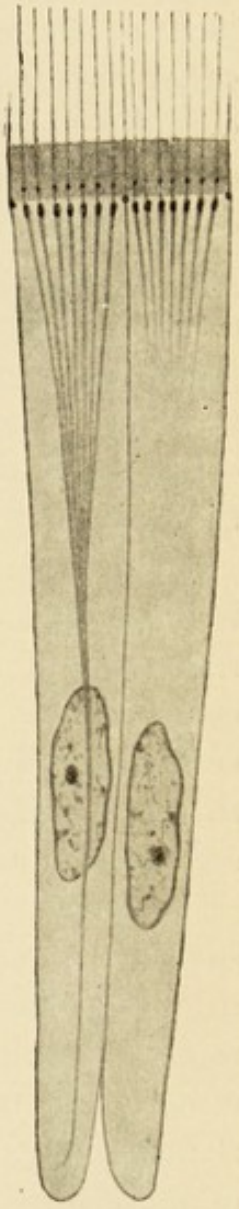


Diagram of ciliated epithelial cells. (After Apáthy).

These fibres, basal granules, and cilia are joined with one another in a continuous whole.

The theories concerning the function of this fibrillar structure are vague and unsatisfactory. According to one view, the nucleus controls the activity of the cilia by means of the fibres extending from it to the surface. This is not tenable, because parts of the cell containing no nucleus still retain their power of ciliary movement for a considerable time. Other authors consider these fibres to be intracellular nerve-endings. Still others ascribe to the basal granules the power of causing the ciliary movement. It is probable that, in common with the protoplasmic network of every cell, the fibrillar structure possesses the power of contracting. This contraction would take place mainly in the direction of the strongest fibrils, as it does in muscular tissue. And their action upon the cilia might be compared with the action of the muscles which move hairs in the skin.

The cuticular border plainly seen in the intestinal epithelium is a product of the cells. The striation is, according to the researches of R. Heidenhain, due to the entrance of fine processes of the cell body into the homogeneous cuticle, and a consequent change in the refractive index of different parts of this mass. These processes may be drawn back into the cell, and in such an instance the striation disappears (see Intestines).

During activity the glandular epithelium shows on its free surface a layer of fine rods, such as is seen in the convoluted tubules of the kidney. This may occur in cylindrical as well as cubical epithelial cells. There may also be often a longitudinal striation at the basal end, which extends more or less into the cell body. These two kinds of differentiation will be spoken of more fully in treating of the salivary glands.

According to the arrangement of the cells in epithelial tissue we have: (*a*) simple epithelium—*i. e.*, consisting of only one layer; and (*b*) stratified epithelium, consisting of many layers. This division, together with the form of the cells, gives rise to the following classification:

(*a*) Simple (one layer) epithelium:

(α) Simple flat epithelium (epithelium of the lung alveoli, the lining of the vessels, the pleural and peritoneal cavities, the pericardium, the joint cavities, the tendon sheaths, etc.);

(β) Simple cubical epithelium (epithelium of the small bronchi, some parts of the kidney tubules, the thyroid gland, the ducts of many glands, etc.); ciliated cubical epithelium is found in the oviduct, uterus, and fine bronchi);

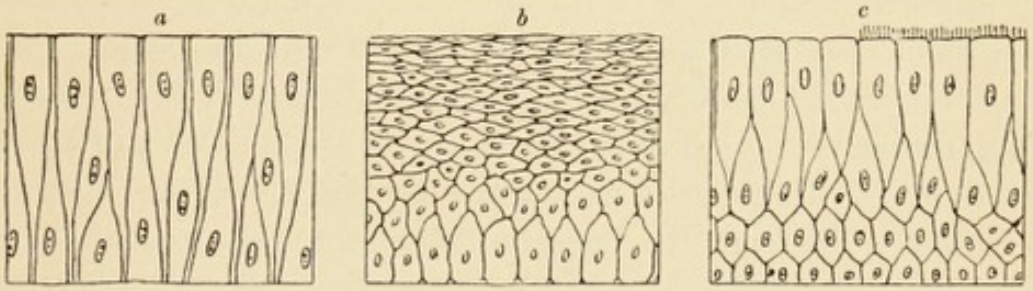
(γ) Simple cylindrical epithelium (epithelium of many large gland ducts, in the intestinal canal, etc.).

(b) Stratified epithelium (Fig. 24):

(α) Stratified flat epithelium or pavement epithelium. The superficial layers consist of flat cells (*e. g.*, epithelium of the cornea, the mouth cavity, the œsophagus, the skin, etc.);

(β) Stratified columnar epithelium. The most superficial layer consists of columnar cells, the deepest layer of cubical or polyhedral cells (*e. g.*, in the ureter, the urinary bladder, etc.). This is known also as transitional epithelium. The same sort of epithelium, possessing also cilia, is found in the larynx, trachea, large bronchi, vas deferens, epididymis, etc.

FIG. 24.



Diagrams of epithelium: (a) nuclei at various levels; (b) stratified pavement epithelium; (c) stratified cylindrical epithelium, ciliated at the right.

An epithelium may consist of elements which are not all of the same morphological significance. One often sees simple cylindrical cells, ciliated cells, goblet cells, and cells with a striated border in close association.

As a transition stage between simple and stratified epithelium, we have an epithelium in which the same cell reaches the outer surface and also rests on the connective tissue at the base of the epithelium (Fig. 24, a). The nuclei, which in typical

simple epithelium are usually all at one level, are here placed at various depths from the surface. Such cells usually bear cilia on their free surface, as, for example, in the larynx, etc.

Stratified epithelium may have cylindrical cells at the base and transition forms above this, until at the surface the cells are flat. This is known as stratified flat epithelium or pavement epithelium (Fig. 24), and is characteristic of the epidermis, the mouth cavity, the œsophagus, the vagina, etc. In the epidermis the cells of the superficial layers lose their nuclei and at the same time undergo a chemical change, the so-called *cornification* (see Skin).

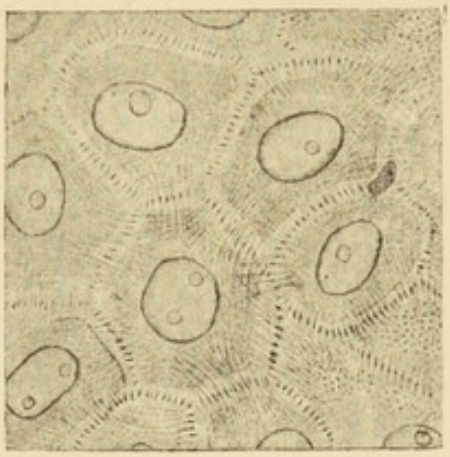
Stratified epithelium may consist also of a layer of columnar cells on the surface, with or without cilia, and below this transitional forms, until a row of cubical or polyhedral cells at the base is reached (Fig. 24, *c*). Such an epithelium may be called a *stratified cylindrical epithelium.* We find it in the main ducts of many glands.

Epithelial cells are joined together, as we have already said, by means of a cement substance, which occurs usually only in very small quantity between the cells. It is recognized always in tissues treated by silver nitrate. If the epithelium be submerged in a weak (0.1–1.5 per cent.) solution, the cement substance enters into some sort of a combination with the reagent, which under the action of sunlight becomes dark brown or black. The surfaces of the cells which the cement substance connects are often quite smooth, but show sometimes inequalities and depressions due to the pressure exerted by the cells on one another. This is seen in the epithelium of the mouth cavity (Fig. 21) and the urinary bladder.

In the line of the cement substance there is often seen a number of rod-shaped bodies connecting the two adjacent cells. These form the so-called intercellular bridges, and can readily be seen, for example, in the deeper layers of the epidermis. Where the cells are isolated, the rods stand out from the surface and give rise to the term *prickle cells.* The prickles or rods are essentially connecting bridges passing through the cement substance from one cell to the other. They are plainly processes

of the cell protoplasm, and, by special methods of staining, it is sometimes possible to follow them from one cell through another into a third (Fig. 25). Between the intercellular bridges there are spaces filled with intercellular substance. These spaces can be injected from the lymph-vessels, and are therefore supposed

FIG. 25.



From a section through the stratified pavement epithelium of the human epidermis. × 700. Some cells of the stratum spinosum are bound together by protoplasmic bridges.

to have the functions of lymph spaces. This would supply the nourishing fluids which the lack of other vessels in the epidermis makes necessary.

Epithelium possesses, as a rule, neither blood- nor lymph-vessels. Only in a few places have capillary branches in the epithelium been described definitely (auditory organ—Retzius, mucous membrane of the gums in *amphibia*—Maurer, etc.). Nerves, on the other hand, are abundant.

The flat epithelium of blood-vessels and lymph-vessels, as well as the epithelium covering the serous membranes, shows in certain places holes, the so-called *stomata* or *stigmata*. These are fine openings in the cement substance sufficiently large to admit white blood-corpuscles. According to some authors (Arnold) these structures are not preformed, but are the result of stretching.

Changes may take place in the protoplasm of the cell due to pathological processes, and give rise to appearances not at all characteristic of the normal cell. The more common of these are, the formation of vacuoles, the fatty degeneration in which

small fat globules are present throughout the cell, and the so-called cloudy swelling in which the protoplasm loses its translucency and becomes filled with small granules. Cells also may become swollen, so that they lose entirely their characteristic appearance; or, on the other hand, especially in hardened specimens, cells may be much shrunken. Certain special degenerations in blood cells will be spoken of in discussing blood.

Other special changes in the cell may be mentioned, such as cornification (skin, hair, nail), calcification (enamel), mucoid change (mucous glands), and fatty change (sebaceous glands, milk glands). The changes undergone by the respiratory epithelium of the lungs and the epithelium forming the lens of the eye will be discussed later. Finally, we must not overlook the fact that epithelial cells may contain granules of pigment, as, for example, the *pigment epithelium* of the retina, the hairs, and the lower cells of the epidermis in darkly colored races.

Between the cells of stratified epithelium we meet with nerve-endings in the form of freely terminating axis-cylinders. More will be said of this subject later. There occur also cells of a connective-tissue nature which have wandered up from lower levels. These may or may not contain pigment granules, and appear usually as stellate, much-branched structures. Finally, we find also white blood-corpuscles which have wandered in between the epithelial cells.

Histogenesis of Epithelium.

In the beginning, epithelial tissue has the form of a membrane which consists of only a single layer of cells. This may remain as it is or become thickened by an increase of its elements. In the latter case, by the numerical increase of cells, the new elements either are pushed in between the old ones, all the cells lying on the connective-tissue sheath; or the new cells form many layers, cutting off the old cells from their connection with the connective tissue. In the first case we have epithelium in which the nuclei are at different levels; in the second, the many-layered or stratified epithelium.

With further development the epithelial tissue may change superficially, giving rise to such epidermal structures as hairs, nails, claws, talons, the papillæ filiformes of the tongue, etc.; or it may be modified and grow in the deeper layers and give rise to glands. The superficial layers of a stratified epithelium which are worn away by use are replaced by cells from the deeper layers produced by mitotic division.

At the place where the epithelium comes in contact with the connective tissue, there is usually to be seen a bright refractive line, which forms a boundary between the tissues. This fine structureless membrane is called the *basal membrane*. It cannot be said with certainty whether it is a product of the epithelial cells or of the connective tissue. In certain cases when two epithelial layers lie upon one another and are separated by a refractive boundary line, there is no doubt that this basal membrane is derived from the epithelium.

The flat epithelium which arises from the middle germinal layer and clothes the joint spaces, the serous surfaces of the pleural and peritoneal cavities, the tendon sheaths, and the blood- and lymph-vessels, was for a long time considered as belonging to a separate group of cells known as *endothelium*. These cells were classed with connective tissue, because they have a certain similarity to the flat cells which line small spaces and lacunæ in connective tissue; and also because connective tissue is derived likewise from the middle germinal layer. In order to make the classification definite, it is best to regard these cells as *epithelial cells of mesoblastic origin*, so that there will be no middle group formed between epithelium and connective tissue. The main reasons for classifying these cells with epithelial tissues are the characteristic arrangement of the cells to form membranes, the small quantity of intercellular substance, and the absence of any properties which would stand in the way of their being so grouped. At the same time it must be noticed that often no sharp line can be drawn between connective-tissue cells arranged like epithelium and the simple flat epithelium itself.

Glandular Epithelium and Glands.

Glands consist almost exclusively of epithelial tissue. In every case the most important—*i. e.*, the secreting—elements are epithelial cells. We must therefore speak here in connection with epithelial tissues of the structure and classification of glands.

Glandular epithelium is one possessing a secretory function. By secretion we mean the production and elimination of materials which are not to be used directly in the building up of the body. These products may be made use of by the organism, in which case the process is called *secretion.* If, however, the materials eliminated are waste products, and of no value to the body, the process is one of *excretion.* If the latter are retained by the organism, they may be a menace to its welfare. These glandular functions may be carried out by a single cell, in which instance we have a *unicellular gland;* or there may be many cells combined to form what is known as a *multicellular* or *true gland.*

As an example of unicellular glands, we have the so-called goblet cells, which were described especially as a modification of the cylindrical epithelial cell. They produce mucus from their protoplasm (Fig. 22), and consist of two parts: a lower plasmatic portion, containing the nucleus; and the upper part near the surface of the epithelium, consisting of mucus. If this is present in large quantities, the upper part of the cell becomes dilated or swollen, so that the whole may with some truth be compared with a goblet. The basal part of the cell usually remains thin, and often is drawn to a point. Even ciliated epithelium, or that with a striated border, is capable of producing mucus and giving rise to goblet cells. The change always begins in the free end of the cell by the production of small bright globules, which increase in size, flow together, and finally leave only a small quantity of unchanged protoplasm as a sort of framework to hold the mucus. At the same time there is formed on the surface a cell membrane which prevents the escape of the secretion. The nucleus finally is crowded

into the basal end of the cell, together with a small mass of protoplasm surrounding it.

When the cell is filled to the utmost with mucus the outer cell membrane breaks, and through the opening the secretion escapes to the outside, while the cell suffers a considerable reduction in size, and, as it were, collapses. Usually we find goblet cells scattered here and there singly between other cylindrical epithelial cells. They are capable of undergoing many times the changes described, always reassuming their original cylindrical form, until they finally die or degenerate.

Goblet cells are distributed widely in the animal organism. Especially do we find them in the epithelium of the respiratory tract (trachea, bronchi) and in the intestinal tract (stomach, small and large intestines). In the mucous glands we find cells containing large quantities of mucus, and representing specific gland cells.

We now pass on to the true glands, which consist of a few or innumerable gland cells. They form a definite whole which is bound together by connective tissue. The gland cells are arranged beside one another to form a glandular surface, from which the secretion is poured into the gland lumen bounded by such surfaces. The lumen usually is surrounded by many cells; only exceptionally (liver) is it formed by two cells.

Often only the deeper lying part of the gland secretes, and is called the *gland body*, while the parts lying near the outer surface have nothing to do with this activity or play only the subordinate rôle of conveying the products to the outside—*i. e.*, they form the *ducts* of the gland. Rarely the duct is absent, and then the gland secretes throughout its whole extent.

The arrangement of the glandular elements gives to the gland a definite form; and according to this and to the shape of the lumen we make a morphological classification of glands. They may be in the form of simple cylindrical tubes (*tubuli*), or in that of spherical or oval sacs (*alveoli*). These form the *tubular* and *alveolar* glands, respectively. We further divide these two groups according as they consist of one or many tubuli or

alveoli, into simple and compound tubular or alveolar glands (Fig. 26).

In tubular glands the simple tubule always ends blindly, and may be coiled and form a *coil gland;* or it divides dichotomously and forms a *simple branched tubular* gland. A compound tubular gland consists of several tubules which divide and may

FIG. 26.

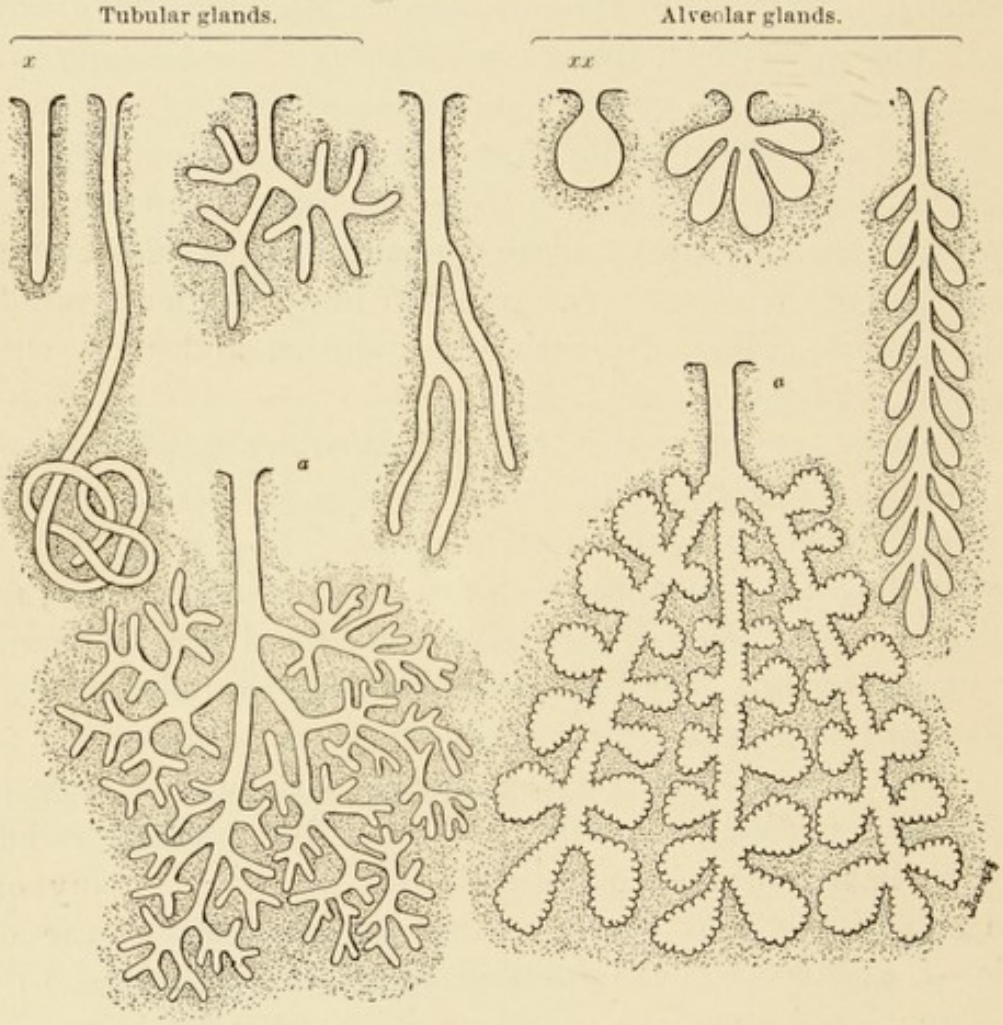


Diagram of various forms of glands: *a*, duct; *x*, simple tubule; *xx*, simple alveolus.

become convoluted. Each of these possesses a duct which opens into the main duct of the gland. In compound glands the duct divides, while in the simple glands this is not the case. In simple glands there may be a division of the secreting gland body, giving rise to a *simple branched* gland.

The branches of tubular glands may anastomose with one another (*e. g.*, in the kidney). Indeed, the anastomosis may be

so great that a net-like structure results. This is known as a net-like or *reticular tubular* gland (liver). Most of the glands of the body are tubular. We distinguish the following:

(*a*) *Simple unbranched tubular* glands: fundus glands, glands of Lieberkühn, and the coil glands.

(*b*) *Simple branched tubular* glands: pyloric glands, Brunner's glands, small serous and mucous glands of the oral cavity, uterine glands.

(*c*) *Compound tubular* glands: salivary glands, lachrymal glands, kidneys, testes, liver, Cowper's and Bartholini's glands, and the prostate body.

Similarly we distinguish between simple and compound alveolar glands. The simple ones may be branched or unbranched. Branched glands consist of many alveoli, combined to form an alveolar system, and opening into a duct. If many of such systems join to form a gland, we have to do with a compound alveolar gland. Here, as in compound tubular glands, many ducts open into a main duct. These may be put down as follows:

(*a*) *Unbranched simple alveolar* glands: small sebaceous glands.

(*b*) *Branched alveolar* glands: large sebaceous glands, and the Meibomian glands.

(*c*) *Compound alveolar* glands: lungs, and mammary glands.

Some authors speak of a transition form, the so-called *tubulo-alveolar glands*. They claim that such glands as the salivary glands have alveolar dilatations at the end of the tubuli.

Some glands possess no duct, as this has in the course of development been closed. Such glands get rid of their secretion in two ways. In the ovary, for example, the egg cell bursts out from the Graafian follicle and comes to the outside world. This is a so-called *dehiscent* gland. Other glands without a duct, such as the thyroid, adrenal, hypophysis, pass their secretion into the blood which flows through them. This is what is known as *internal* secretion. Certain glands have both an external and an internal secretion, the functions of the

two products being entirely different (*e. g.*, the liver, the pancreas, and the testes). For a fuller discussion of internal secretion and its great influence in the general economy, the reader is referred to works on physiology, to which this subject truly belongs.

Glands may also be classified according to their products into those secreting cells (ovary, and sebaceous glands), and those secreting fluids. The glands of the first class either cast out whole cells, or the cells break and their contents are secreted, the cell going to pieces and forming a part of the secretion. To this class belong the sebaceous glands, mammary glands, testes, ovaries, and large sweat glands. Those of the second class secrete a material from cells which do not disintegrate, but retain the power of producing this secretion many times. A sharp line of distinction cannot be drawn between these two classes, for cells secreting fluids may also under other circumstances be wholly or partially cast off themselves.

We shall now consider certain elements which go to make up glands in general. At the outer side the cells of the glandular epithelium usually are bounded by a fine membrane (membrana propria or m. basilaris). This usually shows no details of structure, and it is doubtful whether it is a product of the cells or whether it is of connective-tissue origin. In some cases it contains flat stellate cells which surround the gland body like a basket, and join together by processes. These are called *basket cells.*

Many authors consider the membrana propria to be made up of connective-tissue elements; others have found in it contractile muscle elements which have the power of drawing together and pressing the secretion out of the gland.

Compound glands are divided usually by means of strands of connective tissue into lobules; from each of which a duct emerges to pass into the main duct. Outside the membrana propria blood- and lymph-vessels and nerves are present in the connective tissue. Also we find in some glands typical smooth muscle fibres under the membrana propria. Often around the

larger ducts there is a quite strongly developed layer of smooth muscle.

Glands are among the most richly vascular tissues. The blood-vessels divide into fine capillaries, which surround the tubuli or alveoli, and run along the basal ends of the gland cells. The blood flowing to the gland carries with it materials used in the formation of the secretion, the gland cells being between the blood-vessels and the lumen. The constituents of the secretion may be directly taken up from the blood; but usually they are the result of specific metabolic changes in the gland cells, some materials being, however, supplied by the blood. Also the secretion may have partly one and partly the other origin.

In some glands the secretion proceeds to the lumen not only from the surface of the cells, but also through fine canals, the so-called *secretory capillaries*, it is carried in all directions (see Salivary Glands and Stomach). These secretory capillaries, which anastomose freely with one another to form a sort of network, open finally into the gland lumen.

The materials which are secreted internally are taken up by the blood and carried to the parts of the body in which they are used.

The varied appearances met with in gland cells (granular, vacuolated, striated, etc.) are due in large part to the kind of secretion present. This may be equally varied, such as mucus, bile, urine, gastric juice, ferments, sugar, etc. Likewise the appearance of the secretory cell changes according to its degree of activity. There may be various stages of functional activity shown at the same time in the cells of a tubule or alveolus. Some are filled with materials which they are about to secrete, while others are shrunken and empty on account of having discharged their products.

Chorda Dorsalis.

The tissue of the chorda dorsalis occupies an uncertain position in the classification. This structure is present only in the embryonic life of higher vertebrates, and is made up of

tissue which, judging from its origin and chemical properties, is related to epithelium. On the other hand, the fact that it may be transformed into cartilage would seem to bring it nearer to the connective tissues.

II. SUPPORTING, CONNECTING, AND INTERSTITIAL TISSUE.

This group is made up of tissues whose function it is to form the supporting framework for the organs and for the body; to join together the units which make up the organs; and to fill up the spaces between such units and organs.

A general characteristic of these tissues is the presence of a large quantity of intercellular or ground substance, so that the cellular elements are often inconspicuous. The connecting substances are distributed throughout the whole body, and are classified mainly with regard to physical and chemical differences in the intercellular substances. We distinguish: 1, connective tissue; 2, cartilage; and 3, bone.

Usually these tissues can plainly be distinguished from one another. They are grouped together: because they are closely related both ontogenetically and phylogenetically; because when they are near one another there is often no sharp line to be drawn between them; and because they are capable of replacing one another. So we see, for example, that the skeleton in the different classes of animals may consist of soft connective tissue, of cartilage, or of bone. Similarly the sclera in higher animals is a connective-tissue structure, while in some fishes it is bony or cartilaginous. Also it is well known that bone may develop from cartilage, and that cartilage may develop connective-tissue fibres in its substance. All of these tissues are of mesodermal origin—*i. e.*, they arise from the middle germinal layer (*mesoderm*).

These tissues begin to develop from the so-called *embryonic cellular* tissue. This consists of round or polygonal cells with, in the beginning, no ground substance. Later the cells change their form and become spindle-shaped, or, by the formation of anastomosing processes, stellate. At this time the cells lie in a semifluid intercellular substance, which is certainly a product

of the cells themselves. At first this is homogeneous, but in further development formed elements appear in the form of fibres. After certain changes in the cellular elements and the ground substance a form is reached which belongs to one of the three main groups of connective tissues described above.

In the spaces of the intercellular substance there lie various kinds of cells, whose function it is to nourish the intercellular substance. The nutritive fluids pass through the ground substance from one cell to another; and when the ground substance is of firm consistency there are special paths or canals formed.

1. Connective Tissue.

To this group belong those tissues whose intercellular substance (also called ground substance) is not especially firm, and contains mucin, collagen, or elastin. We may distinguish several kinds—

(*a*) Embryonic connective tissue.
(*b*) Areolar or fibrillar tissue:
  (1) Intercellular substance:
    (*α*) White connective-tissue fibrils;
    (*β*) Elastic fibrils;
    (*γ*) Ground substance.
  (2) Cells:
    (*α*) Fixed cells;
    (*β*) Granular cells;
    (*γ*) Wandering cells.
(*c*) White fibrous tissue.
(*d*) Yellow elastic tissue.
(*e*) Reticulum.
(*f*) Fat tissue.

(*a*) *Embryonic connective tissue* (gelatinous tissue, mucoid tissue) consists of round or stellate cells which are joined by processes, between which there is a large quantity of mucus- (mucin-) holding interstitial substance (Fig. 27). Mucin may be recognized by treatment with acetic acid, with which it forms a granular precipitate. In young embryos the intercellular substance is homogeneous, while in older embryos connective-

tissue fibrils begin to be formed. This gelatinous tissue is found in the umbilical cord, and also in the embryonic cutis. It is not to be considered as a separate kind of tissue, but only as an early stage in the development of the true fibrillar connective tissue. A similar tissue is present in the vitreous humor of

FIG. 27.



Embryonic connective tissue from the subcutaneous layer of the skin of a three and a half day old chick. × 640. Two karyokinetic figures are seen.

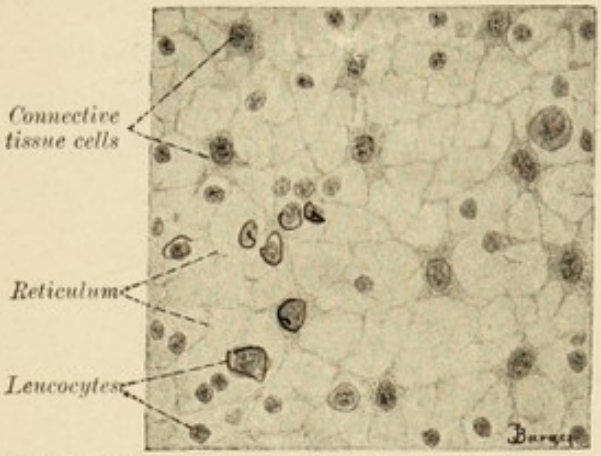
the eye, where, however, the homogeneous semifluid ground substance is very abundant and the cells have in large part disappeared.

(*b*) *Areolar or Fibrillar Connective Tissue.*—The intercellular substance contains formed elements of two different kinds: the white connective-tissue fibrils, and the elastic fibres. There are also cells of various kinds present (Fig. 29).

(1) *Intercellular Substance.*—(*a*) The *white connective-tissue fibrils* consist of collagen—*i. e.*, when boiled they yield gelatin (glutin). These fibres run always in bundles (Fig. 30), and when they are present in large quantities are known as *white fibrous*

tissue (see below). These bundles are joined together by a cement substance, which is soluble in lime-water, baryta-water, or in a saturated aqueous solution of picric acid. The fibrils themselves never divide but the bundles may branch dichoto-

FIG. 28.



Reticulum of cat's lymph gland, showing leucocytes and connective-tissue cells in its meshes. × 430.

mously. The fibrils swell in acetic acid, and in solutions of sodium and potassium hydroxide, and are dissolved by boiling in dilute acids or in dilute potash. In pepsin they are digested easily, in pancreatin not.

FIG. 29.

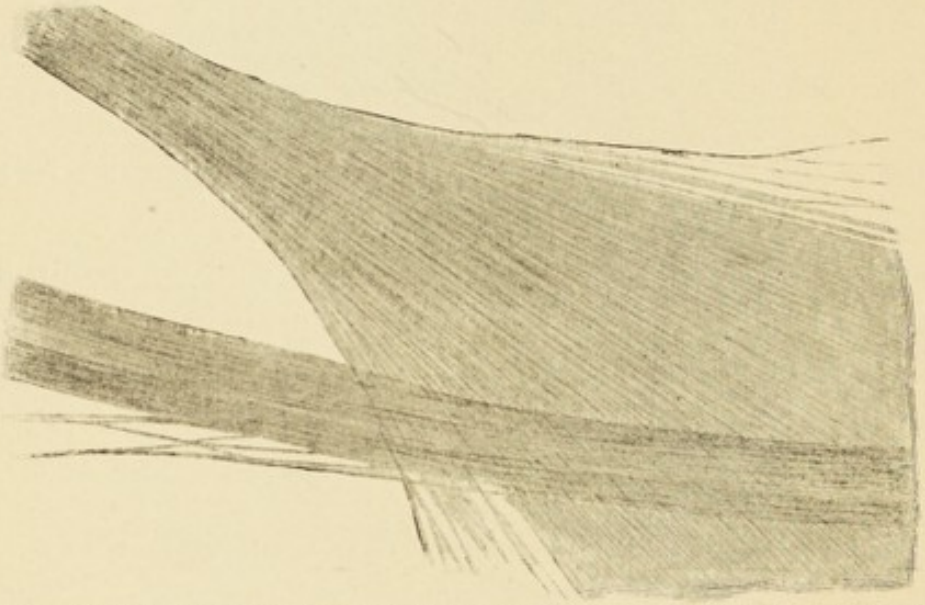


Areolar connective tissue from the subcutis of a rat. × 300.

(β) *Elastic fibres* are found in areolar tissue in smaller quantities than the fibrils of the white fibrous tissue. They may be of different thicknesses, but always run singly without forming bundles. They often divide dichotomously (Fig. 29)

and anastomose with one another to form a network. They are characterized by being highly refractive and elastic. If we act upon white fibrous tissue with acetic acid or alkalies, the fibrils swell up, and on this uniform background the twisted or spiral course of the elastic fibres is often brought out with great distinctness, for the latter are not affected by these reagents. The *elastin* of which the elastic fibres consist is characterized in general by a resistance to ordinary reagents. Acids and alkalies do not affect it. Digestion in pepsin and boiling in water and dilute acids or alkalies are all resisted. It

FIG. 30.



White connective-tissue fibrils from a tendon of the mouse, treated with picric acid and teased out with needles. × 800.

digests, however, in pancreatin. When a great many of these elastic fibres occur together, we speak of them as *elastic tissue* (see below).

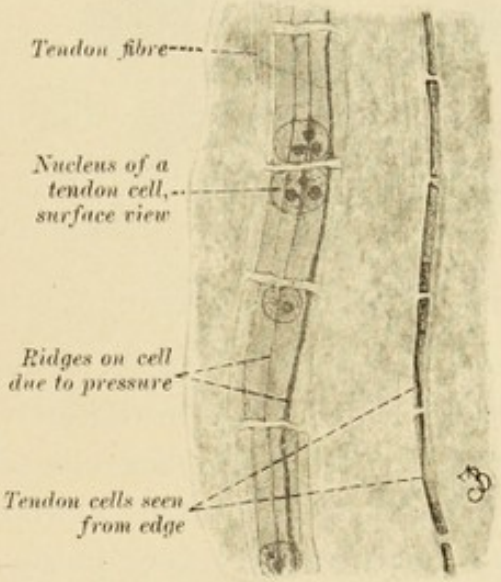
(γ) The ground substance in which these fibres are laid down is quite homogeneous, and in definitely developed connective tissue is present in very small quantities.

(2) *Cells.*—In the ground substance between the fibres we find a considerable number of cells. Two main sorts can be distinguished, namely, the *fixed connective-tissue cells*, which have no power of motion, and the *wandering cells*, which can move from one place to another. This division is not definite, because

fixed cells sometimes become motile, and wandering cells fixed. They may therefore be classified in three groups on a morphological basis. There are (α) fixed or true connective-tissue cells, (β) granular cells, (γ) wandering cells.

(α) *Fixed* or *true connective-tissue cells* are always flat, usually polygonal cells, which may possess processes and have the appearance of stellate or spindle-like cells (Fig. 29). This last form is found usually in young connective tissue. Looked at from the side, they are like long, thin spindles. The border of the cell is often very thin. In the neighborhood of the nucleus

FIG. 31.



Piece of tendon from tail of white mouse. Between the bundles of connective-tissue fibrils are cells arranged in rows. Some are seen in surface view, and others in optical section. × 400.

is an accumulation of finely granular protoplasm, which makes the cell thicker at that place. Where they are pressed upon by the fibres of the intercellular substance the cells sometimes show ridges and markings. Often the cells lie in rows on the bundles of fibres (*e. g.*, in tendon) (Fig. 31), where they are disposed longitudinally. The cells may surround the bundles and form more or less complete sheaths for them. By the separation of these cells the isolation of connective-tissue bundles by the action of acetic acid can be explained. On the swelling up of connective-tissue fibres the sheaths formed of connective-tissue

cells become broken. In certain places there are cells which surround the bundles and offer a great resistance to the pressure. The bundles here swell up between bands of cells and leave constrictions where the cells remain intact.

In some pigmented parts of the body (skin, eye) the protoplasm of the fixed connective-tissue cells contains brown, black (melanin), or other colored granules. These are the so-called *pigment cells* (Fig. 32). Pigment granules are insoluble

FIG. 32.



Pigment cell from the skin of a young salamander. × 200.

in water, alcohol, ether, and dilute acids. They dissolve in alkalies and lose their color in chlorine-water. They are a product of the protoplasm formed from materials taken up from the blood. Pigment cells often are found abundantly in the skin of lower animals, where they are very large and stellate, and have the power of moving themselves by means of processes. These movements are supposed by some to be under the influence of the nervous system, and nerve-endings have been recognized in the cells (Leydig, Ballowitz, Eberth, and Gunge).

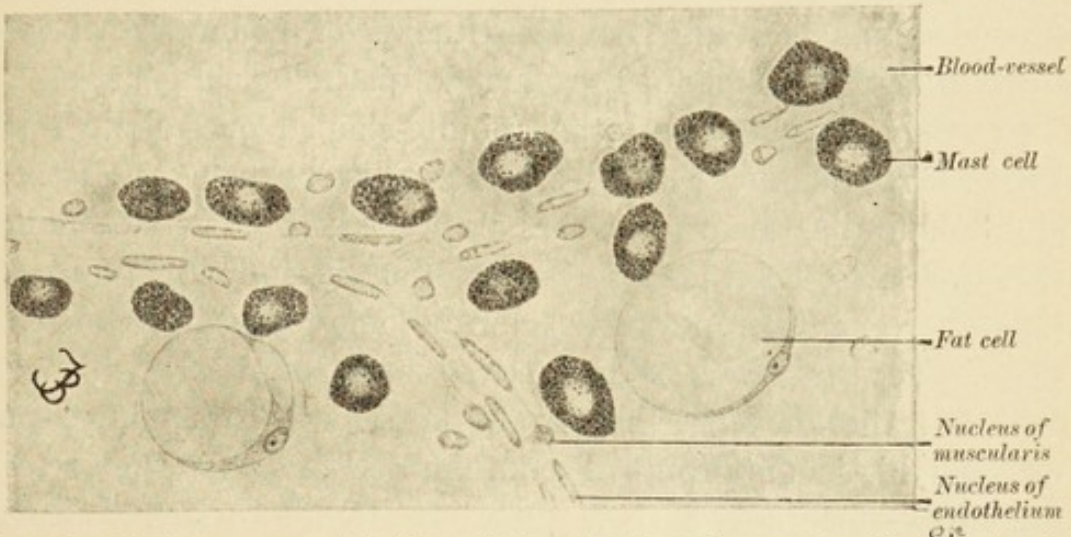
Fixed connective-tissue cells may also develop within their protoplasm fine fat globules, which flow together to a large droplet and give rise to the so-called *fat cells* or *signet-ring* cells (Fig. 33). When a great many of these cells gather together, they are spoken of as *fatty tissue* or *fat* (see below).

(β) *Granular Cells:*

1. Plasma cells;
2. Mast cells of Ehrlich;
3. Clasmatocytes of Ranvier.

1. *Plasma Cells* (Unna).—These are cells of variable form, whose protoplasm stains characteristically in polychrome methylene-blue. They are found especially in the neighborhood of small blood-vessels. Two varieties usually are recognized: small plasma cells, which are similar in many ways to the ordinary lymphocytes, and large plasma cells. According to most authors, plasma cells arise from lymphocytes and later on become fixed connective-tissue cells.

FIG. 33.



From the subcutaneous connective tissue of the rat. Along the vessel are found mast cells and two fat cells. × 540.

2. *Mast cells* may assume all the forms of plasma cells. The protoplasm is filled with round refractive granules which have a special affinity for basic aniline dyes. The granules take a deeper color than the rest of the tissue, and often assume quite a different color (metachromatic staining). Dahlia-violet stains the mast cells a characteristic reddish tint, while the other parts of the tissue are colored only faintly. The nuclei, on the other hand, take up stains only slightly, so that the nucleus-holding portion of the cell appears pale (Fig. 33). The nucleus may often be invisible if the darkly stained granules form a layer covering it. The term "Mastzellen," which was proposed by Ehrlich because, according to his idea, these cells appeared under the influence of better nourishment, is somewhat inappropriate, for they are found often in senile and atrophic tissues.

They seem to be in no way connected with the general nutritive condition of the animal. It is interesting to note that they have been found in equal abundance in bats before and after the winter sleep (Ballowitz). Like plasma cells, the mast cells are found usually in the neighborhood of blood-vessels. They are found also under epithelial surfaces, in the smooth muscles, mammary gland, and testicle. Many authors claim that the two are identical, and the differences in staining reaction they consider to be dependent on a chemical or functional condition. Some trace their origin from leucocytes; others assert that they are true elements and essential constituents of connective tissue; still others regard them as products of pathological change.

3. *Clasmatocytes* are large spindle-shaped or stellate cells, with long, irregular processes, which may be torn or cast off and be found as separate masses near the cell. Ranvier claims that they arise from leucocytes, and that in inflammation of a tissue, for example, they may again become leucocytes and form pus. They stain well with methyl-violet 5 B.

Truly there is little known, and nothing with certainty, concerning this whole group of granular cells. Up to the present time their origin and their function are by no means clearly understood, nor, indeed, do we know in what relation the three kinds of cells stand to one another.

(*c*) *Wandering cells* (Fig. 29) are really not connective-tissue cells, but leucocytes which by "diapedesis" have wandered through the walls of the smaller blood-vessels into the surrounding connective tissue. They are not characteristic for connective tissue, since they are found also (*e. g.*) in epithelium; but they occur in greater quantities in the former than in any other tissue. They possess the power of amœboid movement, and wander freely between the constituents of other tissues.

Wandering cells may undergo division in the connective tissue and increase there. They have, in common with leucocytes, the power of taking up certain materials (*e. g.*, bacteria), which they either assimilate or render innocuous to the organism—*i. e.*, they play the part of *phagocytes* (Metchnikow).

It has been observed that young fixed cells which arise from

the division of old ones may acquire the power of amœboid movement and become wandering cells. It is known also that wandering cells may lose their motility and be transformed into fixed connective-tissue cells. Both these considerations play an important rôle in the formation of pus in an inflammatory process.

Wandering cells may contain pigment granules in their protoplasm and form motile *pigment* cells.

The relative number of these different cells in the connective tissue is very variable, and is dependent on conditions which are not well understood.

In describing the *development of fibrillar connective tissue*, we must consider not only the origin of its constituents, but also the relation which exists genetically between the cellular elements and the intercellular substance. Connective tissue arises, as has been mentioned, from the mesoderm, and passes through the stage of gelatinous or mucoid tissue. The changes which the cells undergo in the formation of mucoid tissue have already been spoken of. The whole connective tissue at first consists of cells, and the mucin-containing ground substance which develops between the cells is a product or secretion of these. The solution of the problem as to the formation of the two kinds of fibres is difficult. According to most authorities, the fibres are of cellular origin; according to others, they are intercellular structures. Schwann considers that the fibres are formed by a stretching out and elongation of the cell body and a disappearance of the nucleus. Lebert and Robin modify Schwann's conception slightly, and regard the bundles of connective tissue as derived from the protoplasm by a process of division; so that the cell loses its individuality as such, and becomes changed into one or more fibres. According to Virchow's theory, on the contrary, the cells have nothing to do with the formation of the fibres; these arise in the hitherto homogeneous ground substance. Merkel, v. Ebner, and others also adhere to this theory. Finally, other authors (Schulze, Flemming, Mall, Spuler) regard the fibres as a derivation of the peripheral part of the cell protoplasm—*i. e.*, the exoplasm.

In support of Schwann's theory is the fact that fibrillar connective tissue contains a decreasing number of cells as age advances, while at the same time the fibres increase largely. But it is certain that the decrease in cells is only a relative one. As the organism grows more space is left for the intercellular substance, and in older connective tissue cells become apparently less numerous. This theory, in the light of later investigations, has lost its adherents. It is to be noted that between the cellular and intercellular theories there is no essential difference. The ground substance is a product of the cells, which exercise a nutritive and formative influence on the intercellular substance and regulate all processes going on therein. In other words, the cells are the only elements playing an active rôle in the tissue. According to the cellular theory, the cells form the fibres directly; while according to Virchow's view, the fibres arise indirectly from the cells which have first formed intercellular substance. In this intercellular substance a differentiation takes place under the influence of cells. One may take up a position half-way between these two theories. Flemming states this as follows: "There is formed in the peripheral part of the cell a fibrillar layer; this layer becomes intercellular substance, increases in quantity, and may produce new fibrils as long as it grows." He believes that "the intercellular substance is not dead or inert, but is a material produced from the cells by a chemical and structural modification, and is capable for a long time of producing fibrils." This has been confirmed by the work of Mall.

With regard to the *formation of elastic fibres* there are also two hypotheses. Some regard them as intercellular; others, as intracellular in origin. The old idea that the nucleus or the whole cell is transformed into elastic fibres is without foundation. Mainly on the ground of investigations of the development of elastic cartilage has it been determined that the elastic fibres arise entirely in the hyaline ground substance, and have only an indirect relation to the cartilage cells (Müller, v. Kölliker, Ranvier, Mall). According to Mall, they appear as delicate fibrils in the ground substance midway between the

cells. In the later stages in the development of the arytenoid cartilage there appear small granules which increase in size to form the elastic granules of Ranvier. These do not form elastic fibrils. O. Hertwig and Bubnoff hold that elastic fibres are a product of the superficial layers of the cell protoplasm. Kurkow claims that the fibres are formed in the protoplasm immediately surrounding the nucleus, and that the nucleus influences this formation.

Fibrillar connective tissue may, according to the arrangement of the fibril bundles and the density of the tissue, be classified as: 1, loose or unformed; 2, dense or formed connective tissue.

1. In the first group the fibres form a loose network in which cells of various kinds lie. This contains often large or small groups of fat cells. It is distributed over the whole body, and partly fills up the spaces between organs or their parts. It also holds these organs or parts of organs together, as is plainly seen in many parts of the body.

2. In the second group the fibril bundles have a firm combination and a regular arrangement. They may cross one another at various angles, as, *e. g.*, in the skin, the mucous membranes, the periosteum, perichondrium, in the capsules of many organs, etc.; or they may be arranged in definite directions, and form firm strands and membranes. In the latter case all the fibril bundles may run in one direction (*e. g.*, in tendons), or they may form flat sheaths whose fibres usually run at right angles, as, *e. g.*, in fascia and the cornea.

In this way we have three kinds of connective tissue which are merely modifications of fibrillar tissue, namely, white fibrous tissue, elastic tissue, and fat tissue.

(*c*) *White fibrous connective tissue* (Fig. 30) is merely a tissue in which regularly arranged fibres of the sort described as white connective-tissue fibres are the main constituents. It is found most abundantly in tendons and fasciæ, but is to be seen in smaller quantities in almost every part of the body. It has the chemical properties described in speaking of the white fibrils, and owes its name to its white appearance in the fresh condition,

and to the fact that one can separate it into long white fibres which are quite tough and strong. This tissue always contains a small number of elastic fibres and various connective-tissue cells.

(*d*) *Elastic connective tissue* is the name given to a tissue which is made up in large part of elastic fibrils. It is known also as *yellow elastic tissue*, on account of its bright-yellow color when it is seen in large quantities, as, *e. g.*, in the ligamentum nuchæ of an ox, where the elastic fibres are so abundant that white fibrils can hardly be distinguished among them. This tissue may be a part of an organ (*e. g.*, in the blood-vessels), or it may make up a whole organ by itself, as in the ligamentum nuchæ and ligamentum intercrurale. The thickness of elastic fibres varies considerably from a fraction of a μ to more than 10 μ. They often cross and form a network with meshes of large size. The fibres have a considerable degree of elasticity, and are usually cylindrical and arranged often in bands. If such flat bands fuse with one another, there is formed an elastic membrane, which may present small openings or windows, from which is derived the name of the *fenestrated membrane*, which is present in medium-sized arteries (see below).

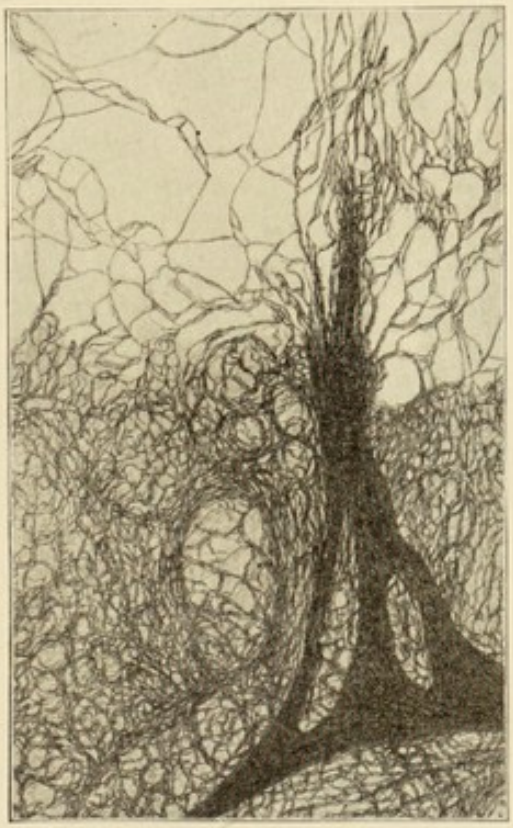
When elastic tissue is boiled in concentrated HCl, it disintegrates in such a way that the fibrils are partially dissolved. According to Mall, the interior of the fibril dissolves first and leaves a membrane intact. This is called the *membrane of Schwalbe*. Sometimes a fibrillar structure can be made out in these membranes, indicating that they are probably made up of more than one substance. The interior of the fibre stains intensely with magenta, while the membrane remains uncolored.

The fenestrated membrane of Henle may be isolated, according to Mall, by boiling in acetic acid or potassium hydroxide. The characteristic openings are found in a stained preparation to be covered with a delicate membrane. It is thus made up of three layers, an upper and a lower transparent membrane, in which there are no openings, and a middle layer, which may be colored deeply with magenta, and in which there are open spaces. The two colorless layers correspond with the mem-

brane of the fibre, and the central layer with its interior. For a detailed discussion of the reactions of elastic tissue the reader is referred to Mall's work.

(*e*) *Reticulum.*—This is the name given by Mall to a tissue making up the framework of many glands and organs. It is found usually in the form of a network of interlacing fibres which are in no way connected with the connective-tissue cells. Since this tissue can be distinguished from elastic tissue and white fibrous connective tissue by means of its chemical properties, it must be considered by itself.

FIG. 34.



Reticulum from lymph gland of dog, stained with acid fuchsin and picric acid (Mall). × 150.

Reticulum is separated from yellow elastic tissue by the fact that it is not digested by pancreatin; and from white fibrous tissue by its greater power of resisting the action of various reagents. White fibrous tissue dissolves in boiling HCl (0.5 per cent.) in one minute, while reticulum in the same solution remains intact for eighteen minutes (Mall). A similar resistance is found in treatment with a solution of KOH. This resistance, however,

is apparently somewhat variable, for Mall has found in the spleen two varieties of reticulum, one more and the other less capable of withstanding the action of acids and alkalies. On boiling, reticulum yields a small quantity of gelatin and a residue of *reticulin*. The latter is a compound related to elastin and gelatin. The gelatin obtained in this way is derived probably from white fibrous tissue mixed with the reticulum, as it is impossible to obtain the latter absolutely pure.

The reticulum of a lymph gland is shown in Fig. 34. The lymphoid cells in this specimen have been shaken out, leaving only the framework of the gland.

Reticulum is distributed widely throughout the body, and has been demonstrated in many organs. In the liver it is identical with what Oppel has described as "Gitterfasern." In the lymph gland, spleen, adrenal, intestine, lung, the capsules of many organs, the testis, and the thyroid, reticulum has been observed. Bone, cartilage, and the entire nervous system contain no reticulum. In the pancreas, thymus, and heart there is probably very little.

(*f*) *Fat tissue* may, as mentioned above, be present anywhere in loose connective tissue. It appears in groups of cells of the kind spoken of as signet-ring cells.

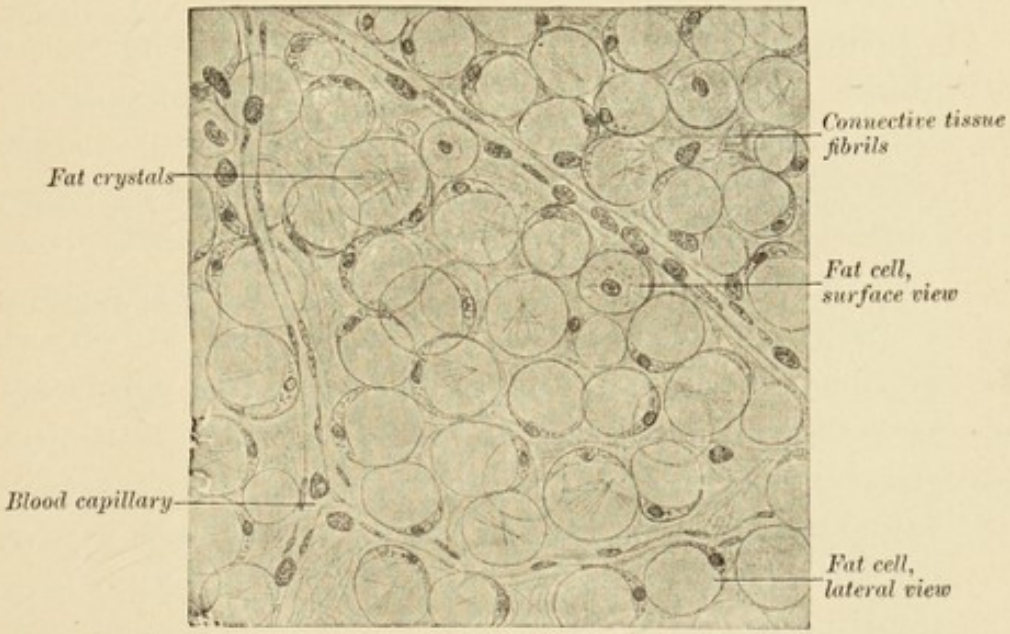
Whether in the *development of fat* specific cells are concerned, is not definitely known. The majority of authors state that it can be formed from any fixed connective-tissue cells. Others claim that it is only plasma cells, or cells resembling these that have the power of collecting fat droplets within their protoplasm.

The very beginning of fat tissue, the so-called *primitive organ of the fat lobule* (v. Kölliker), or the *fat germinal layer* (Toldt), appears in the form of grayish-red masses, which consist in each case of round membraneless cells with clear protoplasm, in which under certain conditions fat is formed. This process begins with the appearance in the protoplasm of fine small highly refractive globules of fat which flow together. By means of certain reactions (perosmic acid, which turns the fat black; Sudan III., which stains it red, and cyanin, blue) we

are able to recognize the smallest droplets of fat. The large globule which is formed by the coalescence of the smaller droplets increases in size until it fills nearly the whole cell. The nucleus with the small quantity of protoplasm that remains is pushed to the periphery of the cell, which is now known as a *signet-ring cell* (Figs. 33, 35). The cell membrane thickens and holds the fat within it, thus preventing the fat globules from running together. The cell membrane can easily be seen in fat treated with alcohol, ether, chloroform, or ethereal oils. By the accummulation of fat the cells may become as large as 130 μ in diameter. Fresh fat is usually yellow or orange in color, but is of different tints in different animals.

After death groups of needle-like crystals form in the cells. These consist of palmitic and stearic acids, the so-called *margarin crystals* (Fig. 35).

FIG. 35.



Fat from the subcutaneous layer of the skin of a white mouse. × 200.

Fat is arranged characteristically in round lobules separated from one another by fibrillar connective tissue, which forms a capsule for each lobule. In the lobule, however, between the cells we find only very few fibril bundles. Thus fat is merely a modified fibrillar connective tissue, in which the cells are changed specifically, and the fibrils subserve a subordinate func-

tion. It is characterized by a rich vascular supply. Each lobule contains a closed blood vascular system. An artery enters each lobule, and breaks up into a thick capillary network, which gives origin usually to two veins. This is the first we have seen of the so-called blood vascular units, of which much will be said later on. The fat, as will be observed, is made up of many lobules, which, as far as the blood-supply is concerned, are all units in themselves.

For many interesting points in connection with fatty degeneration in cells, and the relation of fat production to food, the reader is referred to works on pathology and physiology.

2. Cartilage.

Cartilage is distinguished from the connective tissues by the hard consistency of its ground substance and the characteristic appearance of the cells. It forms a transition between connective tissue and bone.

On boiling, cartilage gives chondrin, which is not identical with glutin. For the properties and chemical composition of this the reader is referred to works on physiological chemistry.

The surface of cartilage is, with the exception of places where it lies directly on the bone or forms articular surfaces, covered by a sheath of fibrillar connective tissue, the *perichondrium*. This contains the blood-vessels, and thus plays an important part in the nourishment, the growth, and new formation of cartilage. According to the different character of the intercellular substance, we distinguish three kinds of cartilages:

(*a*) Hyaline cartilage;
(*b*) Elastic cartilage;
(*c*) Fibrous cartilage.

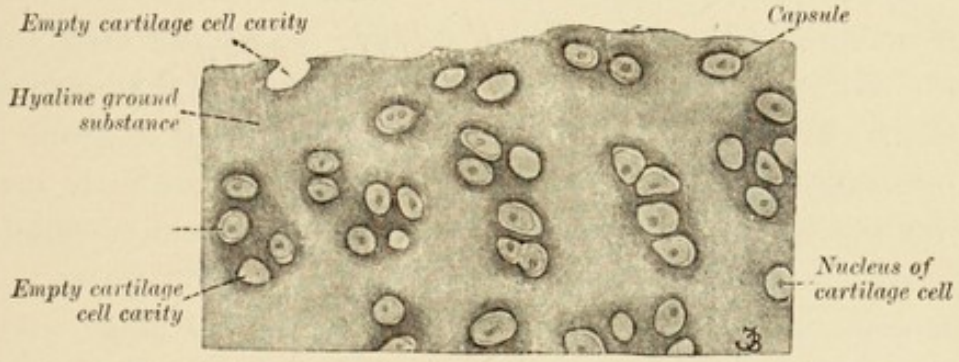
The cells of these three kinds of cartilage are in general similar. We shall therefore describe the cells of hyaline cartilage only.

(*a*) *Hyaline Cartilage.*—The *cells* are round or oval, and often arranged in groups (Fig. 36). When they lie near one another they are pressed together, so that adjacent sides are flattened. The protoplasm is finely granular, and contains in

the middle of the cell a large clear vesicular nucleus with a distinct nuclear membrane, and one or more nucleoli. There are seldom found two nuclei in one cell. Often the protoplasm contains fat and glycogen droplets. The presence of the first is easily demonstrated by perosmic acid, which turns the fat black. The second may be shown by treatment with iodine solution, which stains the glycogen brownish red. Pigment granules are seldom found in cartilage.

In the more superficial layers the cells are usually more flattened, spindle-shaped, and smaller than the cells of the deeper layers. They are on the outer surface arranged in parallel rows. In some animals the cell body sends out processes, and has a stellate appearance like a bone cell. This is seen mainly

FIG. 36.



Hyaline cartilage. From a section through the thyroid cartilage of the cat. × 190.

in the lower animals (cephalopods, selachians), and only in a few places in some mammals. It is noticed also in pathological new formations (endochondromata). Cartilage cells vary from 3 to 30 μ in diameter. They increase usually by indirect division, but direct division has also been observed.

The *ground substance* in the cartilage of higher animals is very abundant. If we examine a thin section of fresh hyaline cartilage, we notice that the ground substance appears quite homogeneous and structureless, and contains the so-called *cartilage spaces.* Some time after death, however, and in cartilage treated with reagents (*e. g.*, water), the cells shrink and between them and the boundaries of the spaces there appears an empty area which allows the outlines of the cells to be plainly made

out. The form of the cells corresponds accurately with that of the spaces. In the preparation of the section the cells often fall out, leaving the spaces empty. The part of the ground substance immediately around the cell is highly refractive and has a special affinity for certain stains. This is the so-called *cartilage capsule*, and forms a boundary for the cartilage spaces, containing the cells. The cells have in the beginning definite cell membranes, which become thicker and firmer, and give rise to the intercellular substance. The ground substance, then, is a differentiated product of the cell protoplasm, and the most lately formed ground substance is nearest the cells. The capsule shows often a concentric marking.

Inside the capsule there are often seen two cells, the result of a division. Each of these cells forms a new capsule around itself, which fuses with the capsule of the mother cell. As many as four or eight cells may be seen in one capsule, forming a cell group or family. These are separated only by a homogeneous thin wall. There is in the formation of so large a group an absorption of the inner layers of the capsule, in order to make room for the cells. Such cell division inside a firm capsule we call *endogenous cell formation.*

The *growth of cartilage* takes place by an increase in the number of cells and a further differentiation of new ground substance. These two processes we call *interstitial growth.* On the surface the increase of cartilage takes place by the so-called *appositional growth*, by which new layers of cartilage are formed from the perichondrium. The interstitial growth takes place mainly in young cartilage.

The *capsules* are stained deeply, as above mentioned, by such dyes as color mucin, while the rest of the ground substance remains unstained. The capsule possesses also a great resistance to the action of chromic acid and hydrochloric acid. By maceration in these fluids the ground substance is dissolved and the cartilage capsules remain for a time unchanged.

That the ground substance is only apparently structureless can be shown by the action of certain reagents (*e. g.*, potassium permanganate, 10 per cent. salt solution, trypsin, baryta-

an lime-water). In such preparations we see that it contains fibrils, running usually in parallel lines and only exceptionally crossing one another. That they are not seen in the living tissue is due to the fact that their refractive index is nearly equal to that of the substance in which they live. The reagents cause changes which make the difference between them greater. Viewed with polarized light also, the fibrils may be demonstrated.

It is to be assumed that the metabolism in cartilage is not active, because in higher animals there is only exceptionally any vascular supply to the tissue, and no visible canal system can be made out in which nourishing fluids could circulate. In lower animals, however, canals can readily be recognized without the use of reagents. These join the cartilage spaces with one another, and form a system by which nourishing materials may pass from one part of the tissue to another. Certain authors (Spina, Budge, Wolters, etc.) have demonstrated canals by means of special staining methods. These methods, however, involve the use of materials (*e. g.*, water, alcohol, ether, etc.) which cause shrinkage of cartilage, and it is possible that the results obtained are artifacts. Similarly it is difficult to say what parts take up the staining materials. It is possible that the fibrils present in the ground substance act as paths for the conduction of fluids from one part to another. In spite of numerous recent investigations on the subject, the problems concerning canals in cartilage are still unsolved.

Cartilage possesses usually no blood-vessels. Only rarely, and in places where active growth or ossification is going on, are they present. The connective tissue and wandering cells accompanying the vessels are known as the *cartilage marrow.*

The *perichondrium* consists of white connective-tissue fibrils, with only a very few elastic fibrils. These are arranged in bundles which cross in different directions. The superficial layers of cartilage usually pass over without sharp boundaries into the perichondrium. This contains blood-vessels which, under such conditions as are mentioned above, may grow into the cartilage. During appositional growth the connective-tissue

fibrils of the perichondrium change into the ground substance of the cartilage and the connective-tissue cells into cartilage cells. The ground substance undergoes, in age, senile changes, such as the so-called *asbestos change*, calcification, and bone formation.

The first change, which may be recognized by the naked eye, produces in the cartilage areas which have somewhat the appearance of asbestos. The process usually begins in the ground substance by a production of fibres arranged in parallel lines. These have nothing to do with the essential fibrillar structure of the ground substance. They appear first at a distance from the capsules, and proceed on every side toward these, which also in time suffer change. They spread slowly over the whole cartilage, and give it a white appearance. The fibres do not swell up in acetic acid, but dissolve in dilute solutions of sodium hydroxide and on boiling.

Calcification, on the other hand, begins with the deposition of granules of calcium carbonate in the ground substance in the neighborhood of the capsules. This spreads throughout the ground substance, and appears white in reflected light and black in transmitted light. The granules dissolve in hydrochloric acid, giving rise to bubbles of carbon dioxide. This change takes place especially in the laryngeal, tracheal, and costal cartilages, which become in consequence opaque and hard.

Ossification of cartilage takes place as age advances. Its first stage is marked by an ingrowth of blood-vessels from the perichondrium (see Bone Development).

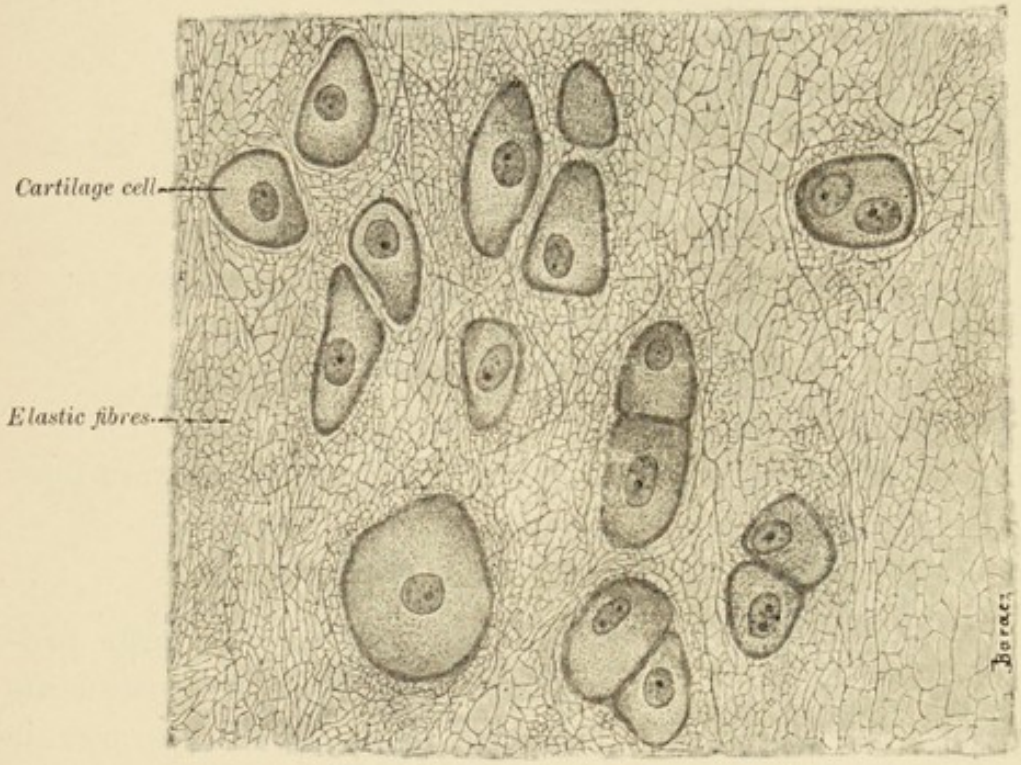
Hyaline cartilage is found temporarily in embryos in places where bone is to be formed. Permanently it occurs in the epiphyses and the joint cartilages. Also, it forms a large part of the laryngeal, tracheal, and bronchial cartilages. It is found in the nose, the ribs, and in all symphyses and synchondroses.

(*b*) *Elastic Cartilage.*—Here the ground substance contains a greater or smaller number of elastic fibres, which vary greatly in thickness and show a marked tendency to branch and form

networks (Fig. 37). By means of specific staining reactions the elastic fibres can plainly be demonstrated. They give to the fresh cartilage a less transparent appearance, and cause it to have a slightly yellow color, by which it may be distinguished by the naked eye from hyaline cartilage. The elastic fibres pass over into the perichondrium at the border of the cartilage.

The development of elastic fibres in cartilage has been spoken of in describing their origin in connective tissue.

FIG. 37.



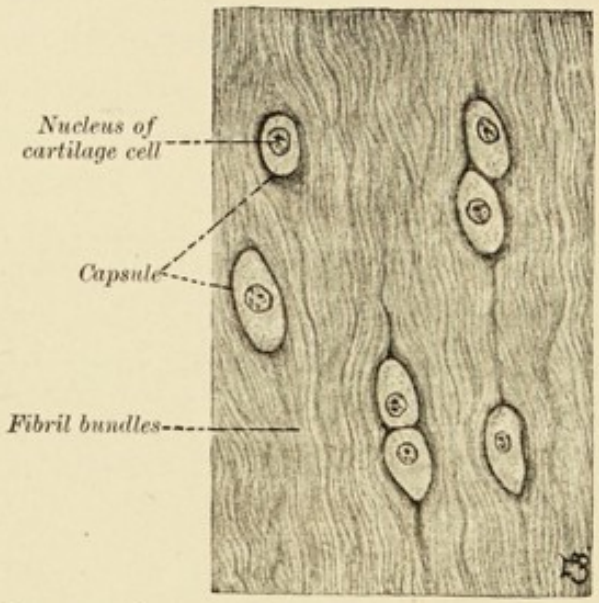
Elastic cartilage from the human ear. × 570.

Elastic cartilage is found in the outer ear, in the Eustachian tube, and the sesamoid cartilages. It is found also in portions of the laryngeal cartilages; the epiglottis, processus vocales of the arytænoid cartilages, the cuneiform and corniculate cartilages.

(*c*) *White Fibrous Cartilage.*—Here we find in a small quantity of ground substance bundles of collagen-producing fibrils, which are arranged in parallel and slightly wavy lines. The homogeneous ground substance is very small in quantity and usually reduced to only that which forms the capsules around the cells. The cells themselves are not numerous, and have a

tendency to arrange themselves in groups (Fig. 38). This cartilage occurs in the nucleus gelatinosus of the intervertebral ligaments, in the symphysis ossium pubis, in the interarticular

FIG. 38.



Fibrous cartilage from the ligamentum teres femoris of a dog. × 570.

cartilages, and in the place of insertion of the ligamentum teres femoris.

3. Bone.

Like other supporting tissues, bone possesses a large proportion of intercellular substance. The mineral constituents (calcium salts), which are connected closely with the organic parts known as *ossein*, produce the characteristic hardness of bone.

By so-called decalcification we are able to dissolve away all the calcium salts and leave only the organic framework which shows the structure of bone completely. On the other hand, we can, by heating the bone (calcination), destroy the organic constituents, and leave a skeleton which consists of salts and likewise presents an exact picture of the bone structure. In this way it is possible to study the finer architecture of bone equally well in decalcified or in dried specimens.

We distinguish *compact* and *spongy* bone substance, the former being dense and firm, the latter resembling the skeleton

PLATE IV.

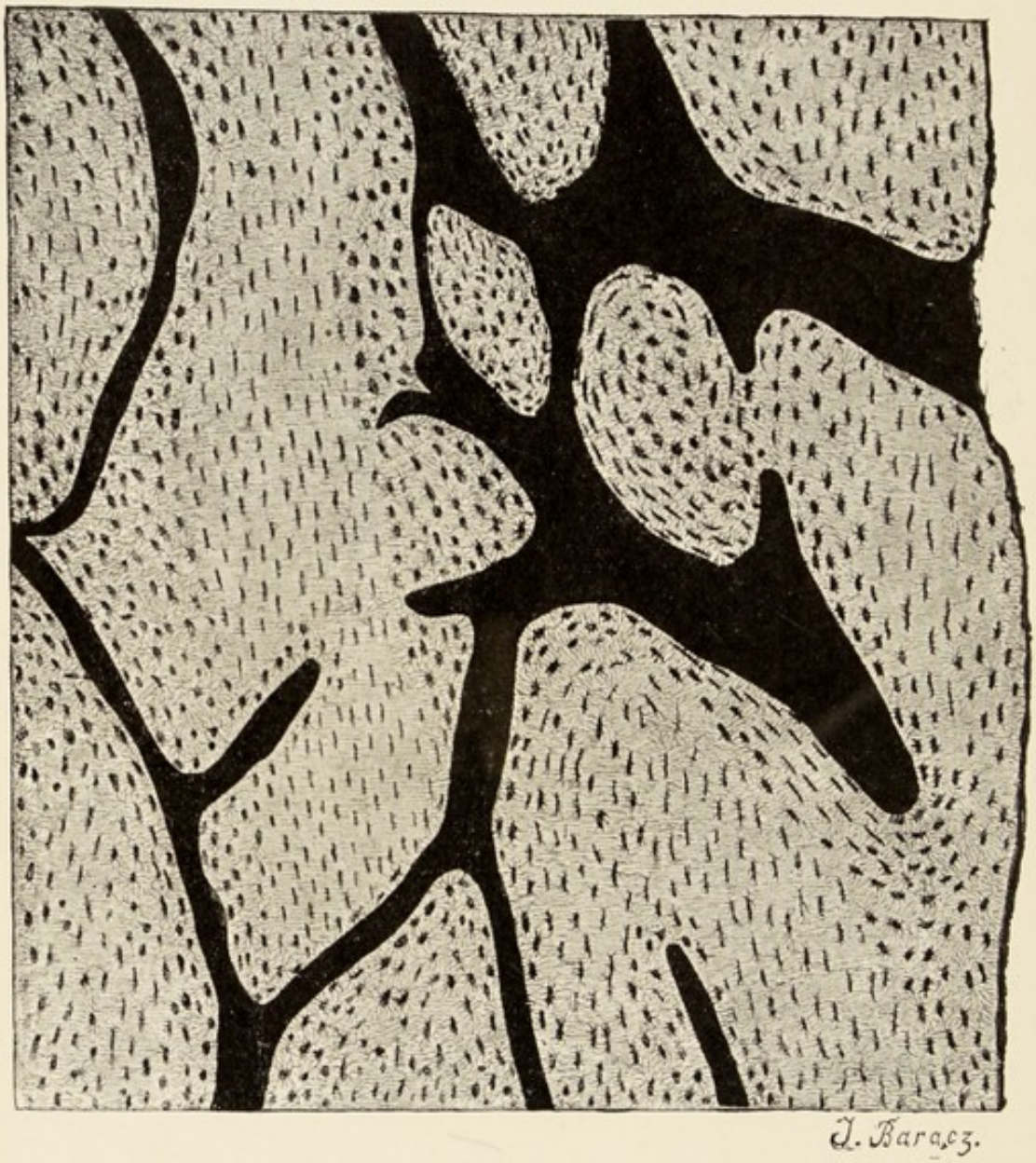


FIG. 39.—From a ground longitudinal section through the diaphysis of the human ulna. All canals are filled with pigment, which is here black. Haversian canals are cut longitudinally. × 90.

PLATE V.

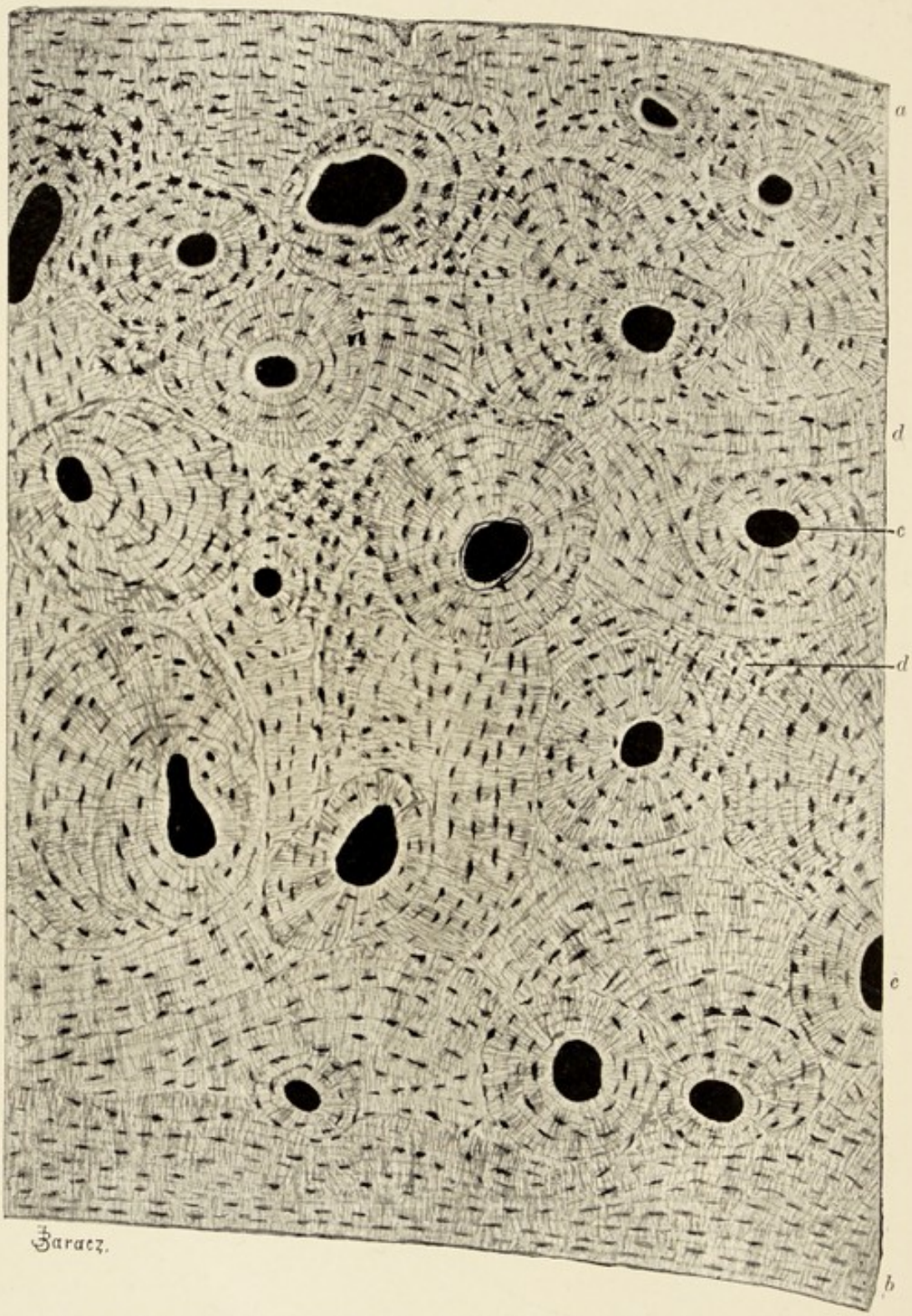


FIG. 40.—From a ground cross-section of the diaphysis of the human metatarsus: (*a*) outer ground lamellæ; (*b*) inner ground lamellæ; (*c*) Haversian lamellæ; (*d*) interstitial lamellæ. All canals and bone cavities are filled with coloring-matter and appear black. × 90.

of a sponge. The diaphyses of long bones as well as the outer parts of small and flat bones consist of compact bone substance, while the epiphyses of long bones and the middle of short and flat bones are made up of spongy bone.

If we examine a longitudinal section of a bone which has been for some time macerated, we observe with low magnification broad canals which run more or less parallel to the longitudinal axis (Fig. 39). These are connected by transverse canals, and form altogether a complete canal system. These so-called *Haversian canals* are in macerated bone empty, because the blood-vessels which they contain in life have been dissolved by the macerating fluids.

Everywhere in the ground substance there are spaces, the so-called *bone lacunæ*, in which before maceration the *bone cells* are contained. These are arranged in rows which are more or less parallel with the Haversian canals.

On examination of a cross-section of bone (Fig. 40), we notice that the Haversian canals are round and the transverse canals are cut longitudinally. Around the Haversian canals the bone lacunæ are arranged in concentric rows. With higher magnification the ground substance is seen to be made up of lamellæ lying in groups at various angles to one another. In compact bone we may distinguish several kinds of lamellæ:

1. Special lamellæ of the Haversian systems, or *Haversian lamellæ*, are those arranged concentrically around the Haversian canals. All those lying about one Haversian canal make up what is known as an *Haversian system of lamellæ*. The number of lamellæ in a system may vary from three to twenty or more, although it is usually from eight to fifteen.

2. *Interstitial* or *intermediary lamellæ* are those which fill up the spaces between adjacent Haversian systems. These are divided into *real* interstitial lamellæ, which are formed from the periosteum and run in the same direction as the outer ground lamellæ; and *false* interstitial lamellæ, which are merely remains of Haversian systems that have been destroyed (see Skeletal System).

3. *Outer ground lamellæ* form the outer layers of the bone, and are situated directly under the periosteum.

4. *Inner ground lamellæ* form the boundaries of the medullary cavity and are arranged concentrically around it.

The outer ground lamellæ are in places pierced by canals which carry blood-vessels from the periosteum. These are known as *Volkmann's canals.*

All these systems of lamellæ are joined with one another by a cement substance. If this is abundant, it forms the so-called *cement lines* of v. Ebner, which separate the adjacent systems (Figs. 41 and 42).

The structure of the intercellular substance (ground substance) is fibrillar. These fibrils, which are capable of producing gelatin, are joined into bundles by means of homogeneous interfibrillar cement substance. The bundles are joined in turn by interfascicular cement substance. The fibril bundles run parallel to one another and make up the lamellæ. These are often so arranged that the bundles of adjacent lamellæ lie at right angles to one another. An example of this is shown in a cross-section of the compact substance of a long bone (Fig. 41). The longitudinal fibril bundles are cut transversely, while those in the adjacent lamellæ running concentrically are cut longitudinally. On examination with polarized light it is found that the bundles which are cut longitudinally are doubly refractive, while those that run concentrically around the Haversian canal are singly refractive. Thus in the crossing of Nicol's prisms the former appear black and the latter light (Figs. 41 and 42).

This lamellated intercellular substance is found in all adult bones. The ground substance with coarser fibres is found mainly in embryos or only in special places in adults (*e. g.*, in the points of insertion of tendons).

In the intercellular substance we find bundles of connective-tissue fibrils which are quite independent of the lamellar fibrils. They pass through the lamellæ from the periosteum transversely or diagonally (Fig. 41). These are known as *Sharpey's fibres*, and remain only partially or not at all calcified. They

are found in the outer ground lamellæ and in the true interstitial lamellæ—*i. e.*, in all lamellæ which are formed from the

FIG. 41.

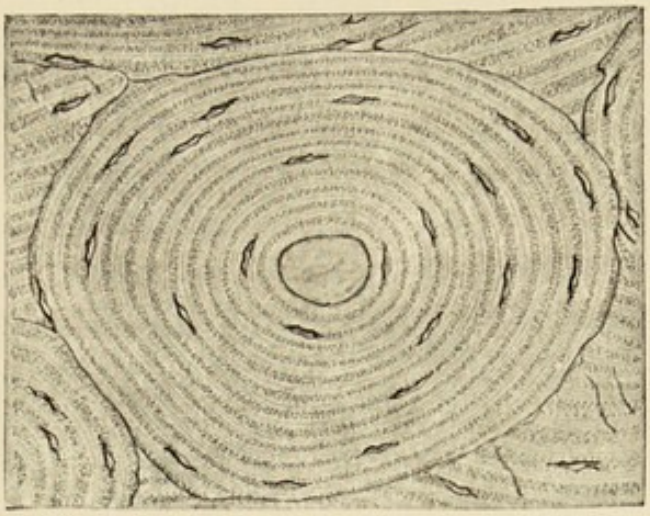
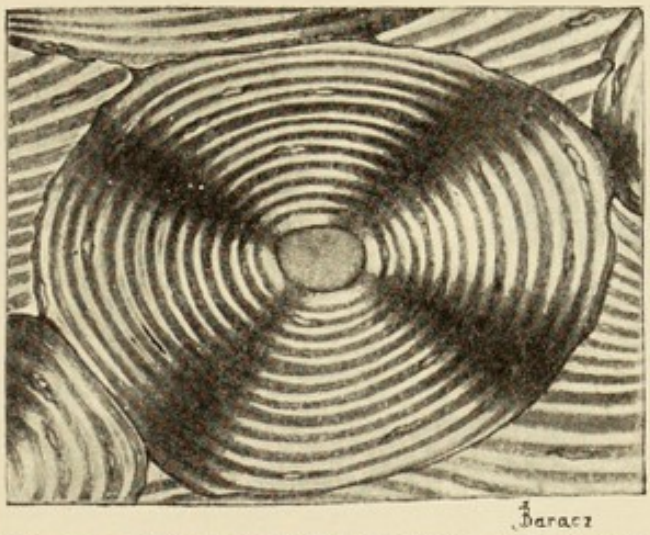


FIG. 42.



FIGS. 41, 42.—Ground cross-section through the diaphysis of the human ulna viewed with polarized light. × 170.

The entire Haversian lamellar system, together with the neighboring interstitial and Haversian lamellæ, is shown. In the centre is the Haversian canal. Around this are lamellæ which contain bone spaces. Between the adjacent systems are to be seen cement lines. The dark diagonal lines at the lower right side of Fig. 41 represent Sharpey's fibres.

Fig. 41, with uncrossed ; Fig. 42, with crossed Nicol's prisms.

The dark cross in Fig. 42 is an appearance caused by the polarization.

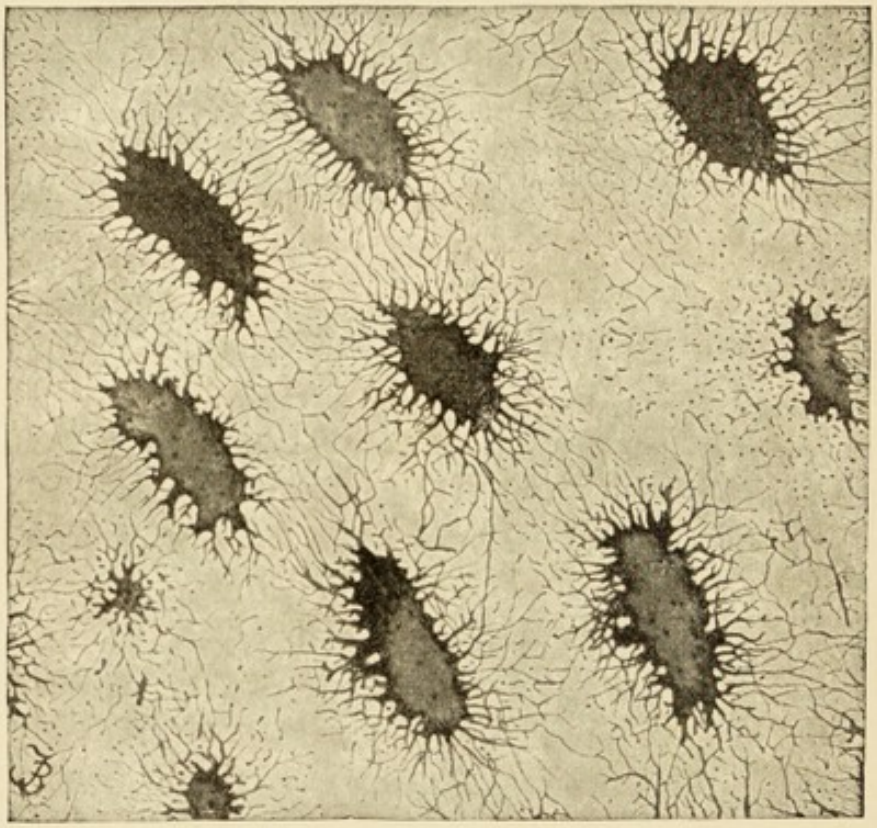
periosteum. We find them also in large quantities in the lamellæ containing coarse fibres, spoken of above.

The uncalcified Sharpey's fibres are destroyed in macerating fluids, and also in dried specimens. From the periosteum there

often run elastic fibres to the lamellated bone substance. These may combine with the Sharpey's fibres or remain independent.

In the intercellular substance there are small spaces (13–31 μ long, 6–15 μ wide, 4–9 μ deep). These *bone lacunæ* or *bone cavities* (formerly incorrectly called bone corpuscles) lie, as a rule, among the longitudinally disposed lamellar fibres. Their shape is variable, and is dependent on the direction of the section studied. They possess numerous very fine processes, the

FIG. 43.

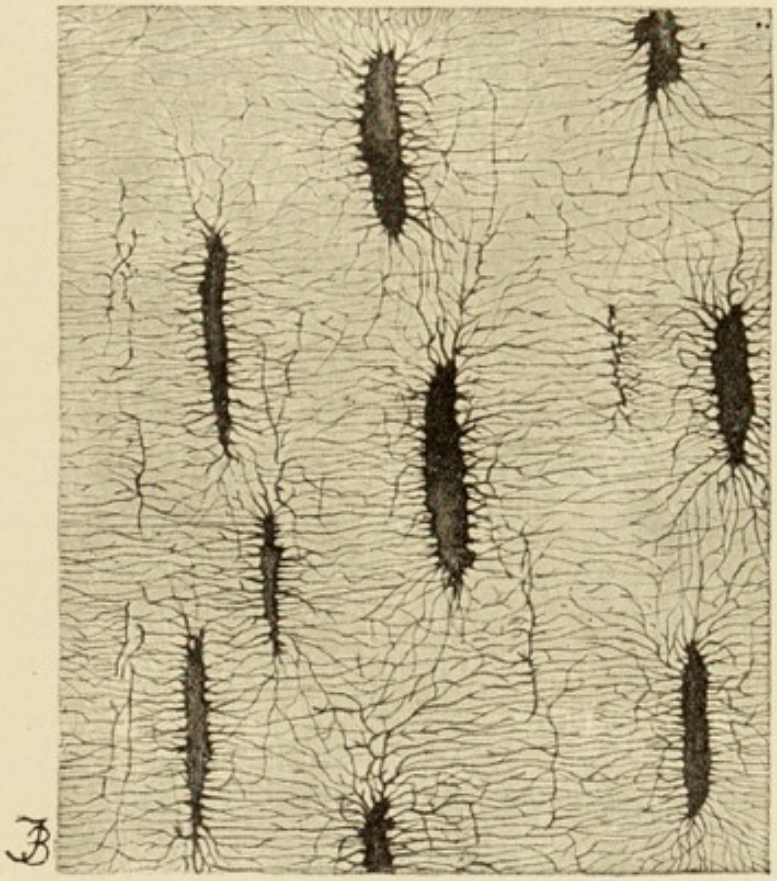


From a section through the bone of a roebuck. The bone cavities are seen from above, and are filled with coloring-matter. In places small dots are visible, which represent the cross-sections of bone canaliculi. × 850.

so-called primitive tubules or *bone canaliculi*, by means of which not only adjacent, but also distant lacunæ, are placed in communication with one another. The lacunæ lying near Haversian canals, the medullary cavity, or the surface of the bone, send canaliculi which enter the canals or the medullary cavity, or open out under the periosteum at the surface of the bone. In this way there is an anastomosis not only between all the

bone lacunæ, but also between these and all the cavities which carry nourishing material in the bone. This whole canal system can be demonstrated by filling it with colored materials (Figs. 43 and 44). The part of the ground substance immediately surrounding the lacunæ is more resistant toward reagents than elsewhere. By the action of concentrated acids, a preparation showing merely the canal system can be obtained, for the whole intercellular substance, with the exception of a

FIG. 44.



From a section through the bone of a roebuck. The bone cavities are seen from the side. × 850.

very thin layer lining the cavities, is dissolved. If a section is cut so that the lacunæ can be looked into from above, small openings can be seen which represent the mouths of the small canals or processes (Fig. 43).

In these lacunæ lie the *bone cells.* These are membraneless cells, each of which fills the whole cavity. Their form corresponds with the cavities in which they are situated. In prepa-

rations made by treatment with strong acids, the cells are usually shrunken away from the walls of the cavities. They are stellate, sending out processes into the bone canaliculi. In the lower animals the processes of neighboring cells anastomose, and also during the development of higher vertebrates the cells join with one another in the canaliculi. It is, however, certain that in adult individuals of the higher animals and man there is no such cell combination.

Spongy bone substance has a quite similar minute structure, as has been described for compact bone. Its ground substance has a fibrillar structure and contains bone lacunæ. There are, however, no Haversian canals and no lamellar systems. The layer masses of this tissue show a lamellar structure, of which the lamellæ lie parallel to the broad surface of the mass.

Other subjects in this connection, such as the vascularization and development of bone, are treated of in the section on the Skeletal System.

III. MUSCLE.

This tissue is characterized by a marked contractility of the protoplasm. The power of contracting on stimulation from without is possessed by all protoplasm to a certain degree, but in muscle the contraction takes place mainly in one axis of the cell. According as the contraction is under the control of the will or not, we distinguish *voluntary* and *involuntary* muscle tissue. This is a physiological classification, but there are structural differences which allow the same division to be used histologically. It is, however, perhaps better to divide the tissues into groups on an entirely histological basis, speaking of: 1, *smooth muscle;* 2, *heart muscle;* and 3, *voluntary striated muscle.*

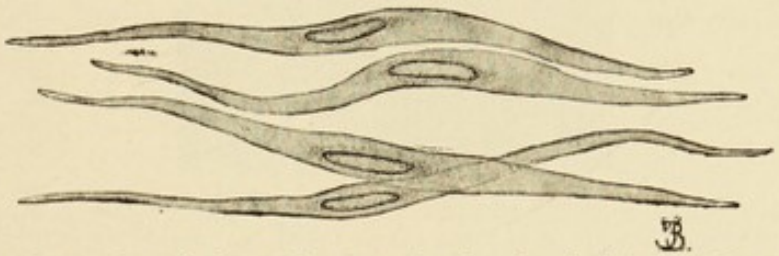
All muscle cells contain one or more nuclei and protoplasm with a more or less highly differentiated structure. There may or may not be a cell membrane, and the cells are united by only a small quantity of cement substance. In the protoplasm there are usually to be found fibrils which may be regarded as differentiations in one direction of the primitive network of

the protoplasm. They are associated with the power of contractility possessed by the cells.

1. Smooth Muscle.

This tissue consists of spindle-shaped cells, usually 50–200 μ long and 4–7 μ thick (Fig. 45). In the pregnant uterus they may be as much as 500 μ in length. They do not possess a true cell membrane. In the middle of the cell, at its thickest

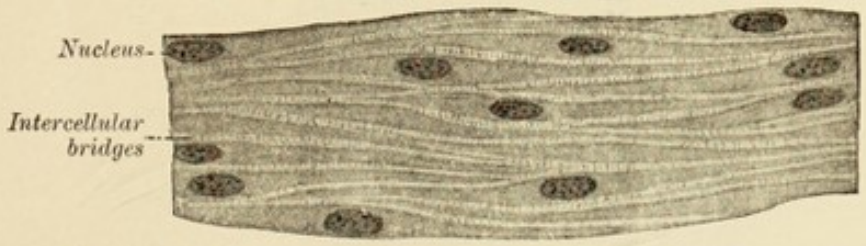
Fig. 45.



Four smooth muscle cells from the stomach of a frog, isolated in 33 per cent. KOH. In the centre of each cell lies an oval nucleus, at either end of which there is a collection of granular protoplasm. × 400.

part, there is an oval rod-shaped nucleus, rounded at the ends and containing one or more nucleoli. The nucleus is surrounded at both ends by granular protoplasm. In the protoplasm there can be made out a number of fibrils running longitudinally. These are seen more distinctly in the

Fig. 46.



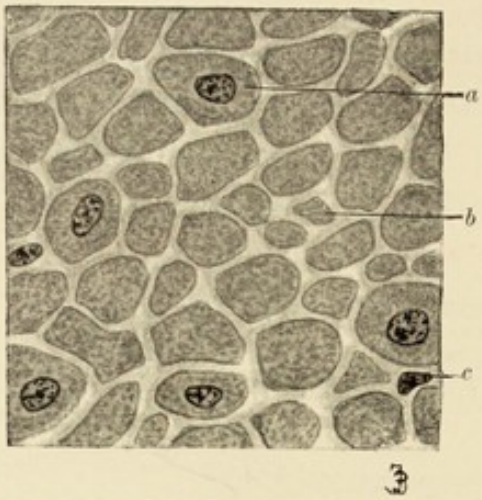
Longitudinal section of the muscle layer of a dog's large intestine. × 530.

lower animals. The differentiated fibrils are doubly refractive, and lie in the undifferentiated *sarcoplasm*.

The smooth muscle cells usually lie close together in groups, which may be combined to form definite layers, as is seen on the muscular coats of the intestine. In cross-section the cells appear as polygonal or round areas of unequal size, on account

of the fact that the section passes through different parts of the spindle-shaped cells (Fig. 47). The smaller areas contain no nucleus, because they are sections of the small ends of the cells.

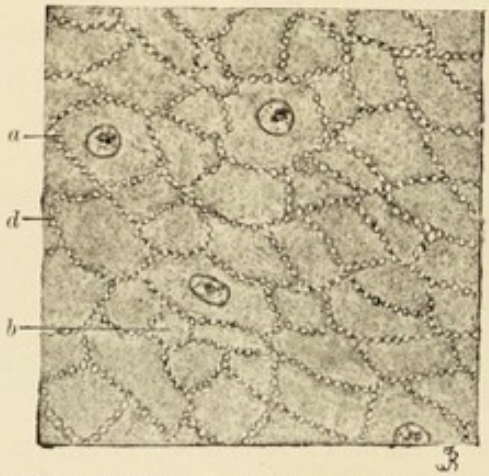
FIG. 47.



Cross-section of smooth muscle from a dog's large intestine. *a*, cell cut at level of nucleus; *b*, cell cut near the end; *c*, nucleus of connective-tissue cell. × 800.

The cells are joined together by a small quantity of cement substance. Intercellular bridges are also often to be made out passing across the cement substance (Figs. 46 and 48) (Kultschitzsky, Barfurth). The presence of protoplasmic bridges in smooth muscle is doubted by other authors (Schaffer, J.). The cells may be separated by maceration in dilute solutions of potassium or sodium hydroxide. Between the groups of cells are found blood-vessels and nerves imbedded in connective tissue.

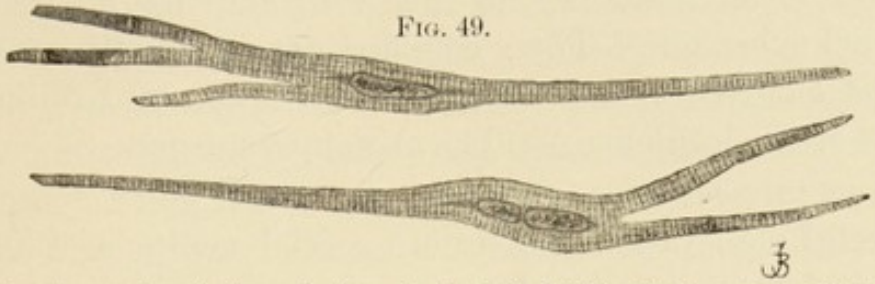
FIG. 48.



Cross-section of smooth muscle of a dog's large intestine, showing intercellular bridges. *a*, cell cut at level of nucleus; *b*, cell cut near the end; *d*, intercellular bridges. × 800.

This tissue is found in the walls of the alimentary tract, in the respiratory, urinary, and sexual organs, in the vessel walls, in many glands, and in the skin.

FIG. 49.

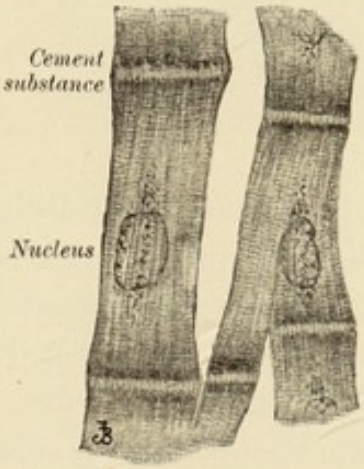


Two heart muscle cells from the frog, isolated in KOH. In the upper cell one nucleus is to be seen, in the lower cell two. At the ends of the nuclei the granular sarcoplasm is collected. × 700.

2. Heart Muscle.

This has a place midway between smooth muscle and voluntary striated muscle. It might be called involuntary striated muscle. In higher animals it consists of short rhomboidal or cylindrical cells joined together end to end by means of a cement substance, which may be dissolved in alkalies and nitric acid. The cells usually are branched, as shown in Fig. 50.

FIG. 50.



From a longitudinal section through human heart muscle. Two entire cells are to be seen. The right one branches. × 500.

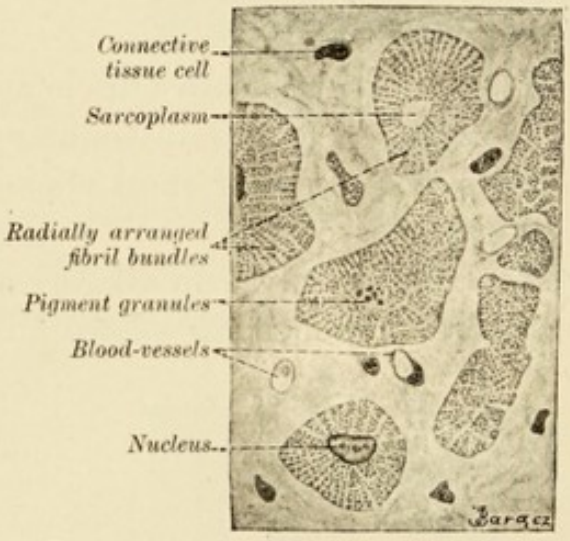
They possess no cell membrane. In the middle of the cell there is usually one nucleus, although there may be as many as three or four. This nucleus is oval, vesicular, and surrounded by a mass of undifferentiated protoplasm, in which there is

found more or less granular brown pigment. This pigment increases with age (Fig. 51).

The cell substance shows darkly stained columns, which run parallel to the long axis of the cell, and are separated by unstained substance. These columns are commonly spoken of as *fibril bundles*, and correspond with what v. Kölliker has called "Muskelsäulchen." The unstained substance is generally known as *sarcoplasm*.

Careful observation and certain special methods of staining reveal a definite relation between these two parts of the cell (J. B. MacCallum). The fibril bundles are striated like those of

FIG. 51.



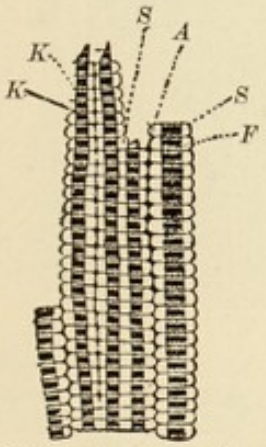
From a cross-section through human heart muscle. × 800.

voluntary muscle, showing alternating light and dark bands. In the centre of the light band is a narrow deeply staining striation, known as *Krause's membrane* (Zwischenscheibe of German writers). The broader dark band is called *Brücke's line*, of doubly refractive substance (Querscheibe). In thin sections, especially those stained by Kolossow's method, the Krause's membranes are seen to belong to the sarcoplasm as well as to the fibril bundles. This is shown in Fig. 52. The sarcoplasm is divided into distinct disks by membranes, which horizontally are continuous with the Krause's membranes of the fibril bundles. There may be more than one of these disks between two adjacent fibril bundles (Fig. 52, A), and at the

centre of the cell the perinuclear sarcoplasm is made up entirely of these disks.

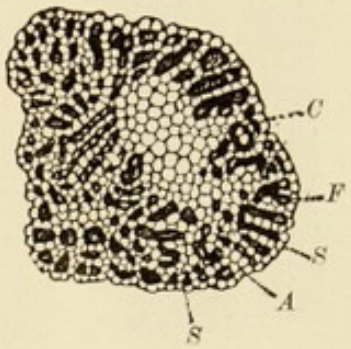
Seen in transverse section (Figs. 51 and 53), the cell consists of darkly staining masses which are cross-sections of the fibril bundles. These are band-shaped and radially arranged at the periphery of the cell, and are smaller and columnar nearer the centre. Between these there are definite disks of unstained substance. From this it will be seen that the cell protoplasm contains a network which consists of the fibril bundles and the membranes surrounding the disks of sarcoplasm. The mem-

FIG. 52.



Longitudinal section of adult human heart muscle. *S*, sarcoplasmic disks; *F*, fibril bundle; *K*, Krause's membrane. (MacCallum.)

FIG. 53.



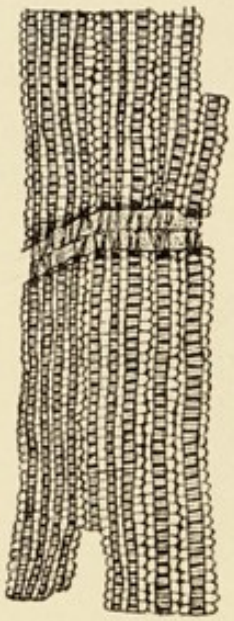
Cross-section of adult human heart muscle. The section is through a part of the cell either above or below the nucleus. *C*, central sarcoplasm mass, *S*, sarcoplasmic disk; *F*, fibril bundle. (MacCallum.)

branes join with the fibril bundles at the lines known as Krause's membranes, and the whole forms a continuous network.

With regard to the manner in which heart muscle cells in the higher mammals are joined together, two appearances commonly met with must be mentioned. In some cases, especially where there is a certain degree of œdema in the muscle, the fibril bundles present a row of thickenings on each side of the cement line. These form what Przewoski termed the *stratum granulosum terminale* (Fig. 54). From each of these thickenings one or more fine filaments pass across the cement line to meet those from the opposite cell. The two series of filaments meet at a delicate line in the centre of the cement line. The

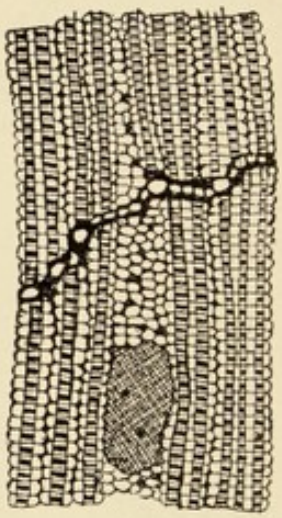
latter line was not observed by Przewoski. In some preparations this structure cannot be made out. Instead of it, there is a cement line having the characteristic step-like course. This in osmic acid preparations shows the appearance always described as caused by protoplasmic bridges (Fig. 55).

FIG. 54.



Longitudinal section of adult human heart muscle, showing the junction of two cells. (MacCallum.)

FIG. 55.



Longitudinal section of heart muscle from an adult dog, showing protoplasmic bridges between two cells. (MacCallum.)

In the lower vertebrates the structure of heart muscle differs in many essentials from that of man and the higher mammals. In fishes the cells are small and spindle-shaped, and possess fibril bundles only around the periphery. In amphibians and reptiles the cells are still spindle-shaped and sometimes branched, but the fibril bundles are more conspicuous (Fig. 49). In birds the heart muscle cell is large and contains many fibril bundles. It is differentiated very much more highly than the heart cell of the lower classes of vertebrates. It is a fact worthy of notice that the heart muscle cells of cold-blooded animals are of much more primitive type than those of warm-blooded animals.

Histogenesis of Heart Muscle.

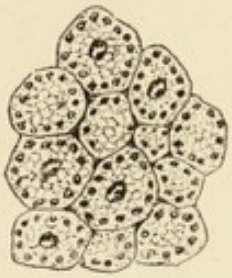
In early embryos (*e. g.*, pigs' embryos 10–12 mm. long) the heart muscle is made up of small spindle-shaped cells lying close together. In cross-section they are round and contain an oval nucleus. The cell protoplasm contains a more or less regular network (Fig. 56). No fibril bundles are present.

FIG. 56.



Cross-section of heart muscle cells of a pig's embryo 12 mm. long. (MacCallum.)

FIG. 57.



Cross-section of heart muscle cells of a pig's embryo 25 mm. long. (MacCallum.)

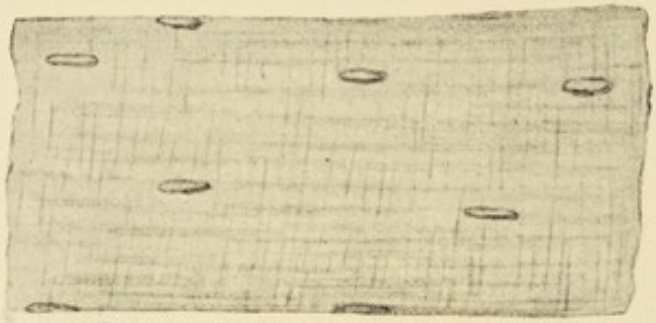
In somewhat older embryos (25 mm.) the cells are still spindle-shaped. Around their periphery is seen a row of dark masses, which are the cross-sections of newly formed fibril bundles (Fig. 57). These are merely an accumulation of the substance of the primitive network to form longitudinal fibril bundles. In embryos 40 mm. long fibril bundles are present not only around the periphery, but are also scattered here and there in the more central parts of the cell. In pigs 70 mm. in length the cells are no longer spindle-shaped, and have all the characteristics of adult cells.

It is apparent, then, that the continuous network spoken of in the adult fibre made up of the fibril bundles and the membranes bounding the disks of sarcoplasm, is developed directly by a process of differentiation from the primitive protoplasmic network of the embryonic cell. The gradual acquirement of special powers of contractility is due to the progressive development of the network of contractile substance present in the beginning.

3. Voluntary Striated Muscle (Skeletal).

This tissue is made up of the most highly differentiated of all muscle cells. They are long fibres, possessing a sarcolemma or cell membrane, many nuclei, and a protoplasm containing fibrils with a double striation (Fig. 58). Each cell is

FIG. 58.



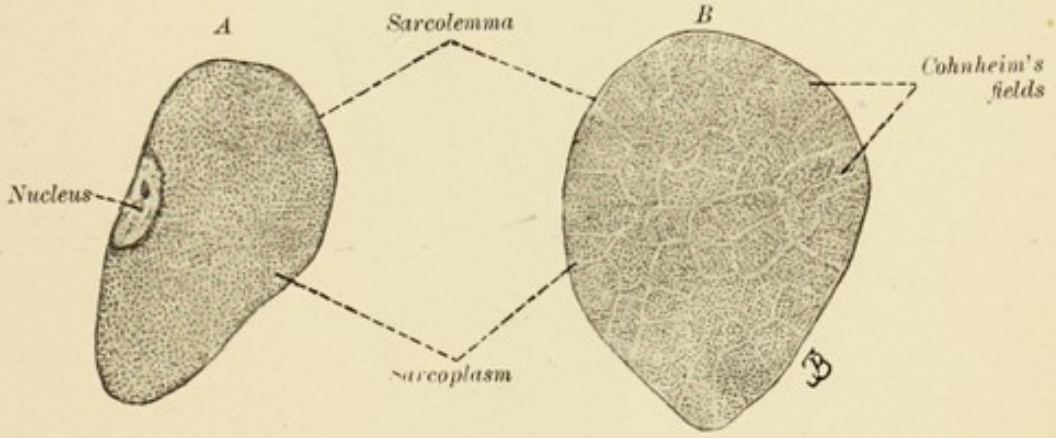
Part of voluntary muscle fibre of frog.

what is known as a *syncytium*—*i. e.*, the nucleus has divided many times without corresponding division of the cell. They may be as long as 10 cm., and in small muscles may extend their entire length. The diameter of the cells varies from 30 to 60 μ. In old animals the fibres are larger than in young. When the ending of a fibre is found, it is seen to be conical or round. Often the ends are branched or forked, as in the muscle fibres of the tongue.

The cross-striation is due to striæ which are present in the longitudinally disposed fibrils (Fig. 60). These can be seen in the fresh muscle. The fibril bundles are made up of what are called *primitive fibrils*. These are differentiated parts of the protoplasm, and have to do with the power of contraction possessed by the cell. A small part of the protoplasm remains unchanged, the so-called *sarcoplasm*. The arrangement of the fibrils may be variable, as seen in a cross-section. They may form polygonal bundles, which are known in cross-section as *Cohnheim's fields* (Fig. 59). These correspond to what v. Kölliker has termed Muskelsäulchen in heart muscle. They are separated by more or less sarcoplasm, which appears as a bright network, in whose meshes the fibril bundles or Cohnheim's fields are situated. The distinctness of the striations

depends somewhat on the amount of sarcoplasm present. A thin layer of sarcoplasm is usually present under the sarcolemma. Some authors who regard this as the inner sheath of the sarcolemma call it the *endolemma* and the outer sheath the *epilemma*. In the sarcoplasm under the sarcolemma there lie oval nuclei, arranged with their long axes parallel to the long axis of the cell. They are found sometimes in the middle of the fibre, between the primitive fibrils (*e. g.*, in amphibia), but most often are present under the sarcolemma (Fig. 59). In some animals (*e. g.*, the rabbit) we find muscles of two kinds: the so-called *red muscle* cells, which contain much sarcoplasm

FIG. 59.



Cross-section of voluntary striated muscle fibres of a rabbit. In *A* the primitive fibrils are equally distributed; in *B* they are grouped into Cohnheim's fields. The fine dots are transverse sections of primitive fibrils. × 1000.

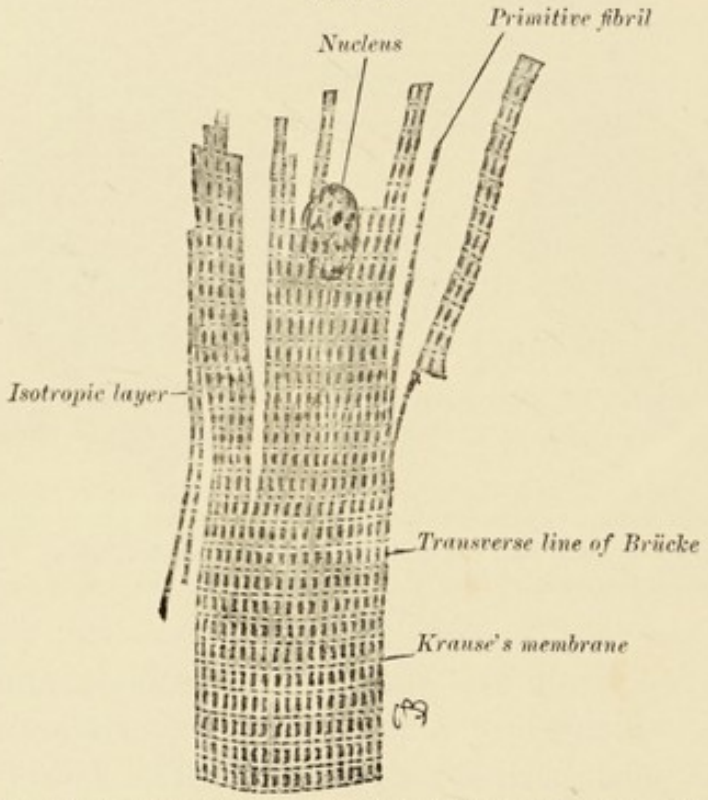
and possess nuclei in the interior of the cell; and the *white muscle* cells, which show a more distinct striation, less sarcoplasm, and nuclei peripherally placed. The more sarcoplasm a cell has, the more slowly will it contract and the longer it will function without tiring. In many vertebrates, and in man also, the muscles are almost exclusively of the red muscle type; some muscles, however, the so-called *mixed muscles*, possess both red and white fibres.

Every fully developed voluntary muscle fibre in the higher vertebrates is surrounded by a *sarcolemma*. This is a thin, homogeneous, structureless membrane, which under normal conditions is so closely approximated to the contents of the cell that

it cannot be made out. On treatment of the tissue with water, however, the osmosis lifts the sarcolemma up so that it can be plainly seen. Also in torn, twisted, or teased cells, where the contents of the fibre have been extruded, it can be seen. It is absent in the muscle of some lower animals.

The striation of the muscle fibre is due to changes in the physical properties of parts of the fibrils, in consequence of which some portions have a different refractive index and stain differently from others. The appearance changes also on high and low focussing. What appears light in high focus becomes

FIG. 60.



Piece of muscle fibre of the frog, broken up into fibrils. × 650.

dark on focussing to a deeper level. The following description is made from low focussing: We notice with high magnification alternating light and dark bands on the fibrils. These are of about equal thickness. The dark bands, the so-called Brücke's lines (*Q*), are doubly refractive—*i. e.*, they appear light in polarized light with crossed Nicol's prisms (anisotropic). The bright bands, on the contrary, are singly refractive, are isotropic, and appear dark in polarized light.

It is to be observed also that there are other lines dividing these bands, so that each is bisected. The light band (isotropic) possesses in its centre a thin, very dark, doubly refractive line, the so-called Krause's membrane (*Z*), which was described first by Amici. In the dark band we find usually a light line—*i. e.*, it refracts light less strongly that the rest of the anisotropic substance. This is the so-called *Hensen's line* (*h*).

FIG. 61.

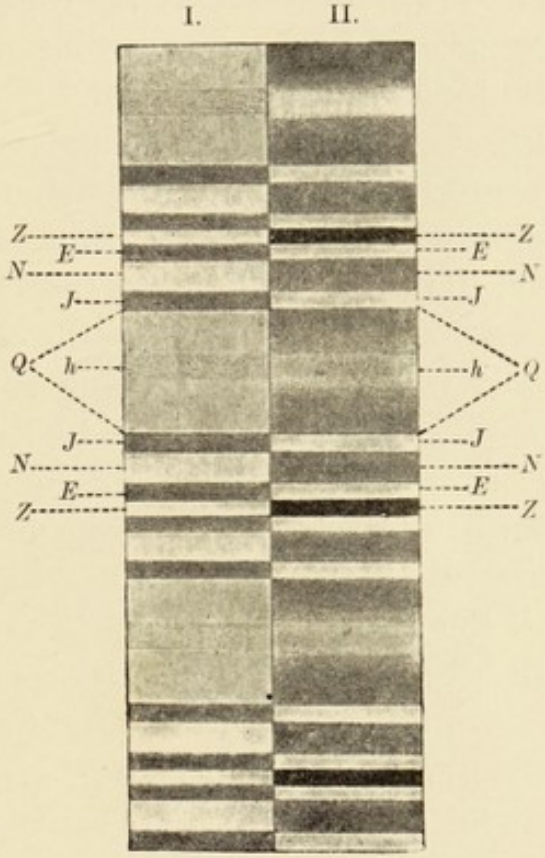


Diagram of cross-striations of a beetle's muscle. (After Rollet.) *I.* with higher; *II.* with lower focussing of the objective; *Q*, Brücke's line; *h*, Hensen's line; *J*, isotropic substance; *N*, accessory line (Nebenscheibe); *E*, isotropic substance (Endscheibe); *Z*, Krause's membrane.

In some arthropods we meet with a still greater differentiation. There is a band present dividing into two equal parts the isotropic substance between Krause's membrane and Brücke's line—*i. e.*, between *Z* and *Q*. This is called the *accessory line* (Nebenscheibe) (*N*). This quite inconstant line usually refracts light more weakly than the Brücke's membrane, but is doubly refractive (Fig. 61).

In a close examination of very thin sections of voluntary muscle, especially of the red variety, the Krause's membranes can often be seen passing from one fibril to another across the sarcoplasm. Although it is much more difficult to make out than in heart muscle, on account of the small amount of sarcoplasm, it is probable that the same relation exists between fibril bundles and sarcoplasm in the two kinds of muscle. If such is the case, the explanation of the nature of Krause's membrane is possible on the hypothesis that the contractile parts of the cell form a continuous network. Concerning the nature of the other striations nothing definite is known.

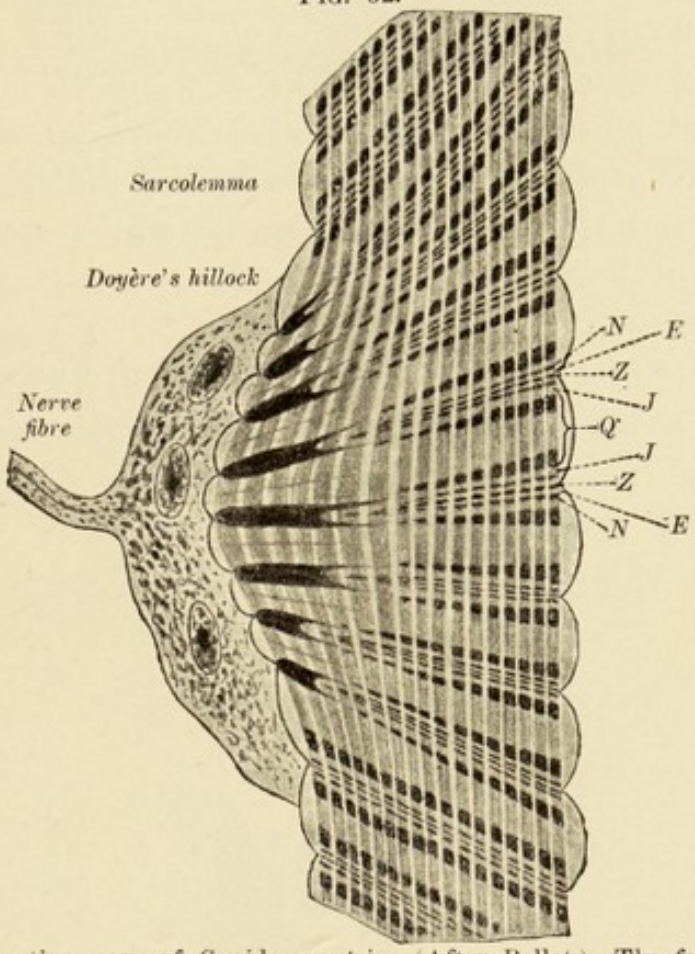
During a contraction of the cell these various striations undergo certain changes. They all become shorter and broader. The isotropic substance becomes very thin, and the Nebenscheiben approach Krause's membranes so closely that new striations are formed, which are known as the *contraction bands*. These bands usually become isotropic, while the Brücke's lines (Q) acquire a doubly refractive index. In Brücke's lines the distinction between the Hensen's line and the rest disappears. These changes can be observed best in cells in which parts of the fibre only are in contraction (so-called *contraction waves*). In such a fibre all the transitions from one state to the other are to be seen. Still plainer pictures can be obtained in fibres which show the so-called *lateral waves* (Fig. 62). This is seen in the neighborhood of a motor end plate.

It appears that the Brücke's lines are active during contraction, and that the isotropic substance has only elastic properties and acts passively. It is certain that the striations are not an essential thing for the cell contraction. Smooth muscle contracts with no striated fibrils, but this contraction is much slower than it is in striated muscle. Supposing that the fibrils are merely a differentiated part of the primitive protoplasmic framework, the contraction may be considered as a contraction of this framework. The further differentiation of the fibrils by the appearance of striations puts them into a physical condition for quicker and more perfect contractions. In the primitive amœboid cells, where the network in the protoplasm

is simple and uniform, the contraction takes place slowly and in no definite direction. When a similar network, however, has been differentiated into longitudinal thickenings (fibrils) and these fibrils further changed physically, the contraction is quick, and takes place in the direction of the stronger strands of protoplasm—*i. e.*, the fibrils.

By the action of weak acids, Brücke's lines swell up and Krause's membranes are unchanged, so that the fibrils have the

FIG. 62.



Lateral contraction wave of *Cassida equestris*. (After Rollet.) The formation of the contraction band is well seen, at the left, as thick black lines.

form of a row of beads. With stronger acids, Brücke's lines split, and disks are formed which contain Krause's membrane in their centre. The so-called Bowman's disks are formed by the action of 93 per cent. alcohol. Here the splitting is at Krause's membrane and Brücke's lines are left intact. The Krause's membranes are the most resistant of all the lines, and seem to be closely related both to the sarcoplasm and the sarcolemma.

The function of these different parts of the cell is not quite clear. The sarcoplasm dissolves in water, dilute acids, and alkalies, and allows the primitive fibrils to be separated. Sarcoplasm plays some rôle in the nourishment, increase, and growth of the muscle fibres. It is present in large quantities around the motor nerve-endings, and serves probably to transmit the nervous impulse equally through the cell.

Cross-striated muscle fibres are found in all the skeletal muscles, the outer muscles of the eye, muscles of the ear, pharynx, larynx, tongue, œsophagus, and those around the anus and sexual organs. All the striated muscles in vertebrates (except heart muscle) are voluntary. There are some exceptions, however, such as the muscles of the upper part of the œsophagus, and the cremaster externus, which are not under the control of the will.

Histogenesis of Voluntary Striated Muscle.

The voluntary muscle of the adult body is derived from the myotomes of the embryo. In pigs' embryos 8 mm. long the myotomes are flattened bodies composed of a dorsolateral epithelium-like layer of cells, and a median mass of spindle-

FIG. 63.

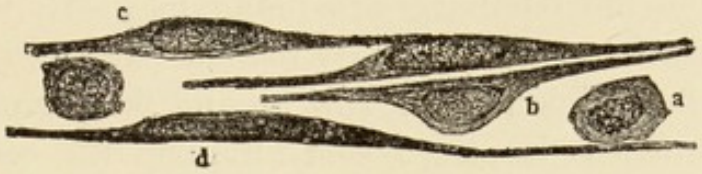


Transverse section through the epithelial lamella of a myotome in the leg region of an embryo pig 8 mm. long. (Bardeen.) *a*, dividing cells; *b*, limiting capsule of external layer; *c*, inner layer; *d*, middle spindle-cell layer; *e*, ectoderm.

shaped and round cells. These have been described in detail by Bardeen. The epithelial lamella (cutis plate) is composed of three layers of columnar cells with fine fibres proceeding

from the external cells. These fibres join to form a limiting capsule. The middle layer is composed of spindle-shaped cells; the main layer, of columnar cells (Fig. 63). The round cells of the median muscle lamella are known as *myoblasts.* From these the spindle-shaped cells are derived by an elongation of the body of the cell (Fig. 64). Karyokinetic figures

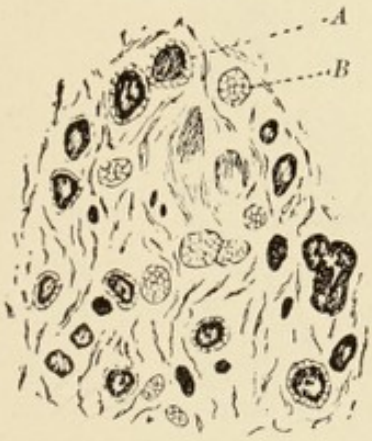
FIG. 64.



Cells from a horizontal section of muscle lamella of a pig's embryo 8 mm. long. (Bardeen.) *a*, myoblast; *b*, young spindle cell; *c*, *d*, older spindle cells.

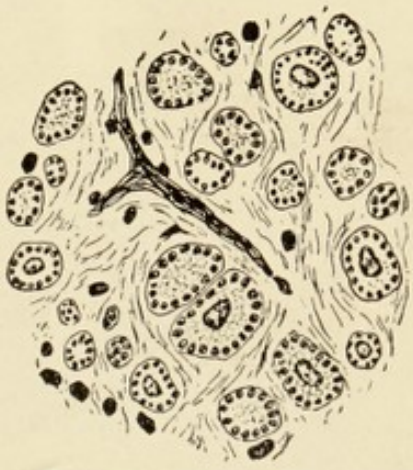
are found abundantly among these cells. In the protoplasm there is to be seen only an irregular network. No fibril bundles are present. The cells of the epithelial lamella become converted constantly into myoblasts. For a detailed description of the development of the myotome and its various cell

FIG. 65.



Cross-section of voluntary muscle from the thigh of an embryo pig 25 mm. long. *A*, cell showing the nucleus; *B*, cell showing sarcoplasmic disks. (MacCallum.)

FIG. 66.

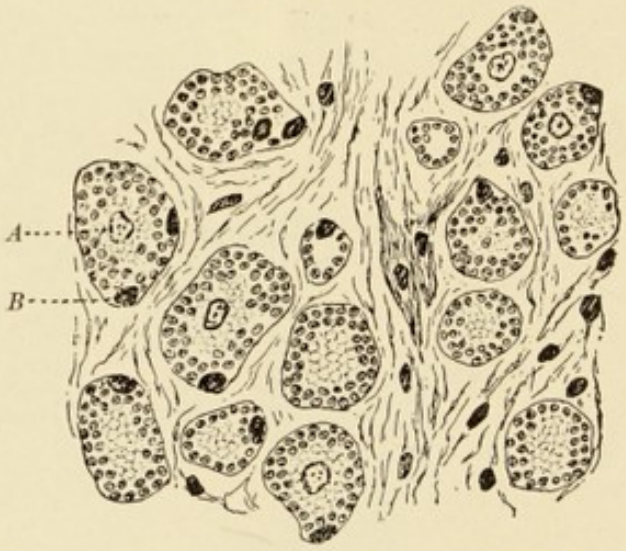


Cross section of voluntary muscle from the thigh of an embryo pig 45 mm. long, showing fibril bundles at the periphery of the cells. (MacCallum.)

layers, the reader is referred to Bardeen's original article. The later stages in the development of the muscle cell are as follows (J. B. MacCallum): In Fig. 65 is represented a cross-section of the muscle fibres of a pig's embryo 25 mm.

long. This shows the cells of the muscle mass which has developed in the leg from the myotomes for that region. In the cells there is a protoplasmic network and no fibril bundles. The nucleus is large and vesicular. At about this stage the fibril bundles begin to be formed. Bardeen has pictured muscle cells from embryos of this age with distinct fibril bundles scattered irregularly around the periphery. In a pig's embryo 35 mm. long the fibril bundles are found in nearly all the cells. They are small and not regularly placed. In embryos 45 mm. in length there is a regular row around the periphery of the cell. The nucleus is placed centrally, and the central protoplasm contains a more or less regular network (Fig. 66). From this on, the fibril bundles increase in number and gradually fill up the entire cell. In embryos about 75 mm. long there are, in addition to the central nucleus, several peripheral nuclei. The latter are not vesicular, like the former, but stain deeply and uniformly, like adult muscle nuclei (Fig. 67). The

FIG. 67.



Cross-section of voluntary muscle from the thigh of an embryo pig 75 mm. in length. *A*, central vesicular nucleus; *B*, peripheral solid nucleus. (MacCallum.)

central nucleus subsequently disappears. The sarcoplasm is more and more encroached upon by the growth of the fibril bundles, and in adult muscle it occupies a very small space. Striations are noticed in the fibril bundles at their first appearance, and frequently the ultimate relation between Krause's

membrane and the sarcoplasm, which has been spoken of above, can be observed.

It seems that the same hypothesis (MacCallum) is applicable here as was suggested for the development of heart muscle. It simplifies the conception of striated muscle very greatly to consider the fibril bundles and the membranes bounding the compartments of sarcoplasm as derived from the primitive network found in the muscle cells of young embryos. The later stages in this development of heart muscle and voluntary muscle differ somewhat on account of the differences in the adult tissues. But since the beginning of the differentiation is the same, the development of the power of contraction must run a somewhat similar course. If this be so, it is conceivable that the contractions in definite directions begin when the irregular network of the primitive cell becomes strengthened in these directions by an accumulation of the substance of the network to form fibril bundles. Why this should take place first around the periphery of the cell is not clear. It is true, however, not only in the development of heart muscle and voluntary muscle cells, but also in the evolution of the heart muscle cell in lower animals.

IV. NERVOUS TISSUE.

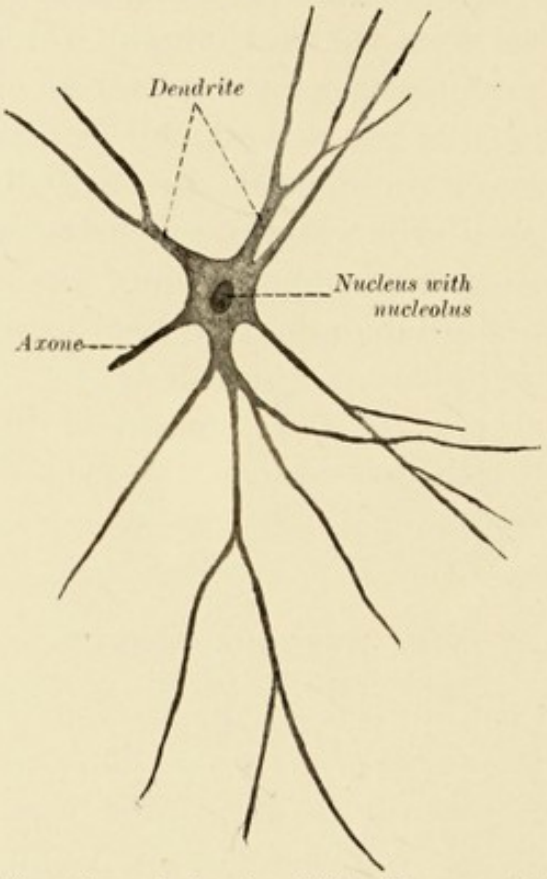
The essential constituents of the nervous system are *nerve cells* and *nerve fibres*. Formerly the latter were considered as separate elements, but now are recognized generally as processes of the nerve cells. It is a characteristic feature of nerve cells that at least one process proceeds from each. Usually there are many of such processes, one of which always becomes a nerve fibre, the so-called *axis-cylinder process*, *Deiter's process*, or *axone*. The rest are known as *protoplasmic processes* or *dendrites*. Independent nerve fibres do not exist in the animal organism. They are in every case in connection with cells. Thus the nerve cell, axone, and dendrites together form a nerve unit which is known as the *neurone* (Waldeyer). The nervous system is made up of such units.

A. Nerve Cells.

The nerve cells (also called ganglion cells) vary in size from 4 to 135 μ in diameter in mammals, and are as large as 200 μ in fishes. Their form is variable—round, spindle-shaped, polygonal, or irregularly stellate. The processes of the cells may be divided into two main groups:

(*a*) The *axis-cylinder process* (axone, neuraxone, Deiter's process) develops more quickly than the other processes, and

FIG. 68.

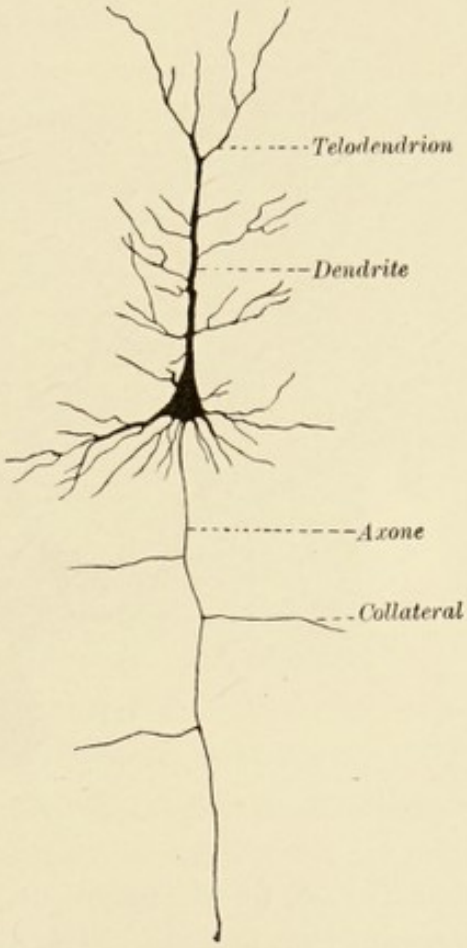


Multipolar nerve cell from the medulla of a rabbit. The axone is broken off. × 150.

has always a smooth, even margin. It leaves the cell at an elevation known as the *axone hillock*, and may proceed out of the central nervous system to form an axis cylinder of one of the fibres of a peripheral nerve. On the other hand, it may end in the central nervous system by branching. It almost always sends off lateral branches, the so-called *collaterals*, which cause a communication to be established between the cells to which the axone belongs and other cells.

(*b*) *Dendrites* (protoplasmic processes) develop later than the axones. In Golgi preparations they appear much branched and with irregular outlines. Their margins are not smooth like those of the axones, but are covered with small elevations (Fig. 70). The terminal branches of the dendrites are called *telodendria* (Fig. 69).

FIG. 69.



Pyramidal cell from the cerebral cortex of the human adult. (After a preparation by A. Bochenek.) × 150.

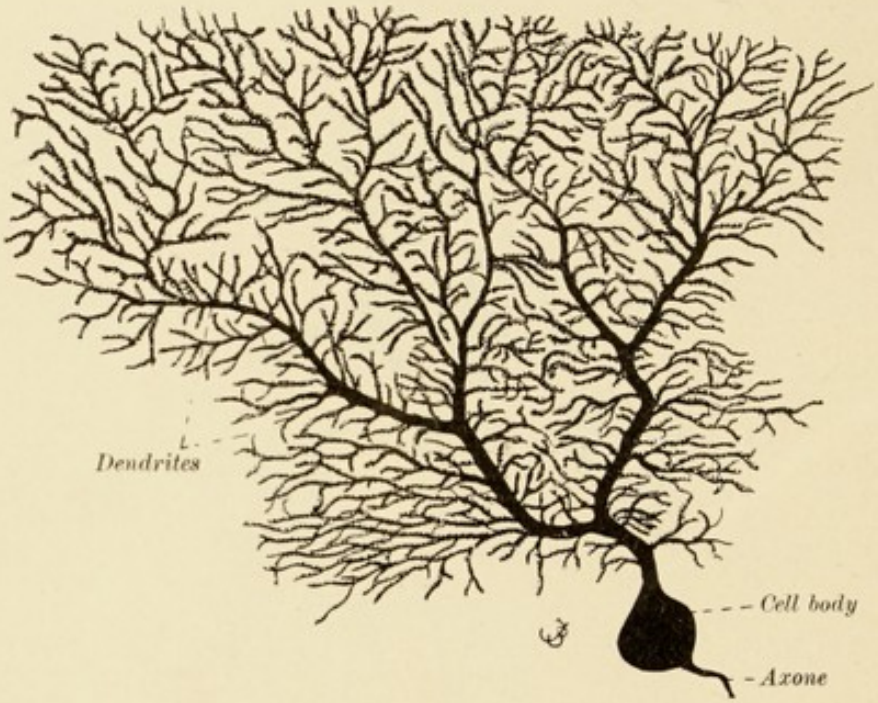
One may divide nerve cells according to their processes into uni, bi-, and multipolar cells. There is always an axone, but the number of dendrites varies.

Unipolar cells are relatively rare. They are found in the nervous system of invertebrates, in the sympathetic ganglia of amphibians, in the olfactory sense cells, and in the spinal ganglia of mammals. In these the axis-cylinder process divides

dichotomously at a little distance from the cell, and gives rise to two nerve fibres, one running peripherally and one toward the central nervous system. The two fibres formed by this division separate at an angle like that of the arms of the letter Y or T (Fig. 71, *d*).

It has been shown that the spinal ganglion cells are unipolar in adults, but bipolar in embryos, the two embryonic processes fusing to form one in the adult (Fig. 71).

FIG. 70.



Purkinje cell from the human cerebellum. × 225.

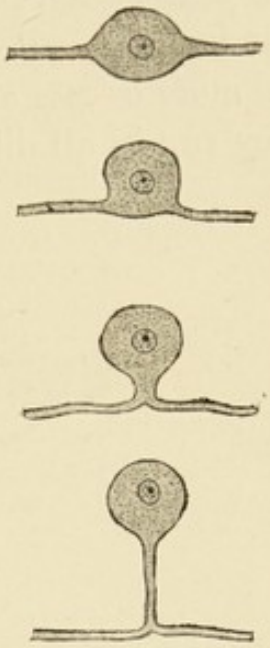
Bipolar cells (Fig. 71, *a*, *b*) are found in the spinal ganglia of fishes and in the ganglion spirale. In such cells there are two processes, one of which becomes the axone and the other a dendrite.

Multipolar cells (Fig. 68) possess one axone and many dendrites. If one process runs a long distance and passes over into a nerve fibre, we have to do with a cell of the so-called *Deiter's type;* while if the process runs only a short course and ends in the gray matter of the nervous system we have a cell of the *Golgi type.*

According to Golgi, Nansen, and others, the axone is the

only conducting portion of the neurone, while the dendrites are nourishing organs. Most authors, however (Ramon y Cajal, van Gehuchten, Retzius, etc.), are of the opinion that both dendrites and axones have the power of conducting impulses. According to Ramon y Cajal, the dendrites can conduct impulses only toward the cell (cellulipetal), while the axone conducts them only away from the cell (cellulifugal). In this way impulses pass from one neurone to another.

Fig. 71.



Semidiagrammatic representation of the transition from bipolar to unipolar nerve cells.

It is therefore to be observed that all peripheral fibres of the sensory nerves bringing impulses from the outer world to the ganglion cells are dendrites, and such fibres as those of the motor nerves carrying impulses out to the muscles are axones.

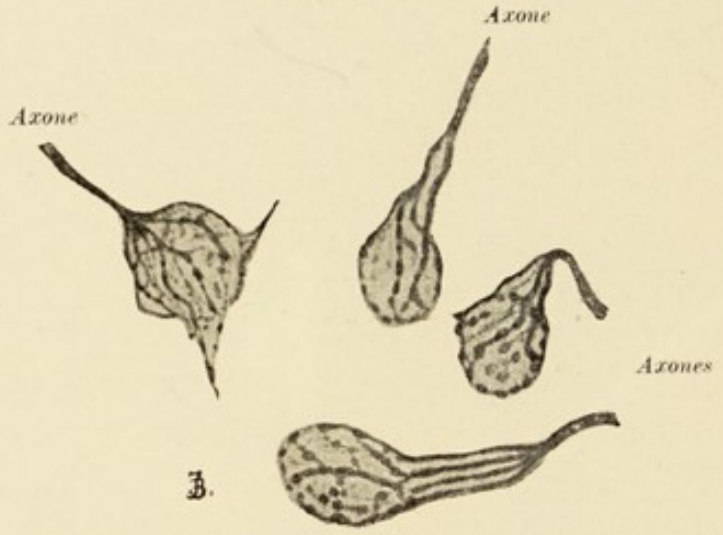
On the basis of investigations by newer methods (especially Golgi's) the idea has gained ground that neurones are connected with one another only by *contact*. But concerning this point there has been much discussion.

For the last few years the neurone doctrine has been generally accepted—*i. e.*, that the nervous system is made up of cells and cell processes forming together units or neurones which combine into systems of fibres and groups of cells. The late work of Apáthy, however, throws doubt on the theory in the eyes of many investigators. Apáthy finds that direct connections exist between ganglion cells, and claims that the nervous system cannot therefore be divided into morphological units (neurones). He makes the last elements of the nervous system not cells, but the so-called *neurofibrils*, which pass, according to him, without interruption from one cell to another. Even though it is possible to find certain cells joined to others, and fibrils continuous from one to the other, there is still nothing in this to disprove the neurone thecry. The neurone doctrine states that the cells and fibres of the nervous system

are not separate, but go to make up morphological units, each fibre being connected with a cell. What Apáthy has shown is, that these morphological units are sometimes connected, and that neurofibrils pass in the protoplasm from one to the other.

The *body of the nerve cell* shows certain finer structures which have been the subject of much investigation in the last few years. All nerve cells possess a fibrillar structure, in the cell body as well as in the processes. The fibrils of the axone are more or less a continuation of those of the cell body. Here they run in all directions, often concentrically, and form a sort

FIG. 72.



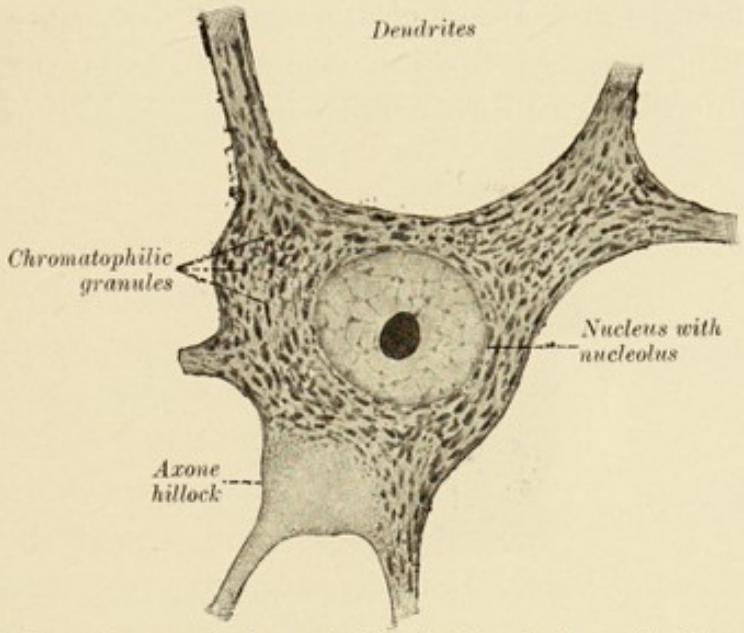
End apparatus of axones from the trapezoid nucleus of a rabbit. (Prepared by S. Meyer's methylene-blue method.) × 700.

of network, especially in the middle of the cell. The protoplasm of the cells contains numerous very fine, deeply staining granules (chromatophile). These granules are usually spindle-shaped, and are called *Nissl bodies* or *tigroid bodies* (Lenhossék). They are found also in the dendrites, but not in the axone hillock (Fig. 73). Their relation to the fibrils of the cell body is not yet explained. Some authors claim that they are connected closely with the fibrils, others that they are independent and lie in the spaces between the fibrils. A few authors regard them as artifacts produced on the death of the cell (Held). Some believe that they have an important trophic

and regulatory influence on the life and function of the nerve cell (Marinesco). It is possible that they are products of metabolism. In favor of this idea is the work of Lugaro, who found that in chronic arsenic poisoning there are definite changes in these tigroid bodies. Changes in these occur also in various diseases.

Around the nucleus a network of fibrils has been recognized by Apáthy, Bethe, and others, which are, according to them, continuous with the fibrils of the axone.

FIG. 73.



Nerve cells from the anterior horn of the spinal cord of a calf. Chromatophile granules are stained in methylene blue by the method of Nissl. × 950.

A centrosome is found in spinal and sympathetic ganglion cells, but is usually not to be made out in other nerve cells. Yellow-brown pigment is found often in the protoplasm.

The nucleus of the nerve cells is characteristic. As a rule, it is single, large, and vesicular. It possesses a distinct cell membrane, usually a large nucleolus, and only a small quantity of chromatin.

A true cell membrane is not present. Cells which are situated peripherally, however, usually possess a secondary capsule of connective-tissue origin.

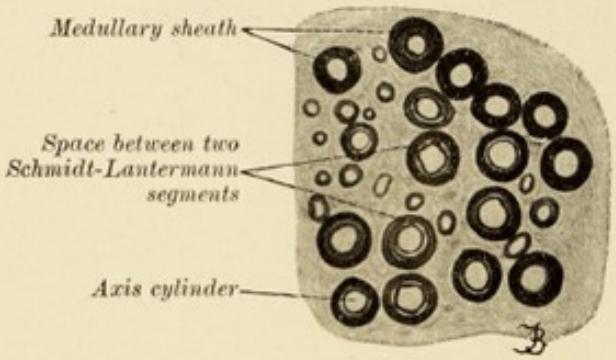
B. Nerve Fibres.

The continuation of the axone of a nerve cell forms the *axis cylinder* of a nerve fibre. This is the only essential part of the nerve fibre. All the other parts may be wanting.

In a cross-section of a nerve fibre possessing all the accessory coverings we see in the centre the axis cylinder. Around this in concentric arrangement we have, from within outward, the *medullary sheath*, *Schwann's sheath*, and *Henle's sheath* (Figs. 74–79).

The axis cylinder runs uninterruptedly from the nerve cell to the nerve-ending. It is characterized by being highly refractive, and possesses a fibrillar structure similar to that of the cell of which it is a process, but contains no tigroid bodies.

FIG. 74.



From a cross-section through a nerve treated with osmic acid. × 350.

Some authors regard it as quite structureless. By special methods it is seen to be made up of a large number of *primitive fibrils* (*neurofibrils*), between which there is a small amount of soft *neuroplasm* (Fig. 80). It is almost generally acknowledged that these neurofibrils are capable of carrying nerve impulses, and that each one is a separate conduction path (Apáthy).

The medullary sheath (Fig. 74) which surrounds the axis cylinder consists of myelin, a fatty, semifluid, homogeneous, highly refractive substance. Medullated fibres have a double contour, formed by the inner and outer margins of the medullary sheath seen in optical section.

Soon after death the so-called *coagulation phenomena* begin.

The contour of the fibre becomes irregular and the myelin sheath shows interruptions in its course. With perosmic acid a characteristic picture is produced. This acid colors only the fat-containing medullary sheath. The interruptions are thus left unstained. These are called *Schmidt-Lantermann lines* or *funnels*, and *Ranvier's nodes* (Fig. 75).

FIG. 75.



Piece of a medullated nerve fibre from the nervus ischiadicus of the frog. A node of Ranvier (*b*) and the lines of Schmidt-Lantermann (*a*) are shown. × 370.

The former appear on optical section as oblique lines running down to the axis cylinder, and are therefore funnel-shaped. They thus divide the myelin sheath into cylindro-conical segments. The apices of these segments may be directed either toward the cell or away from it. Some authors regard these lines as artifacts produced by fixing reagents. Others are of the opinion that they occur normally, and that they are composed of a different substance from the myelin.

FIG. 76.



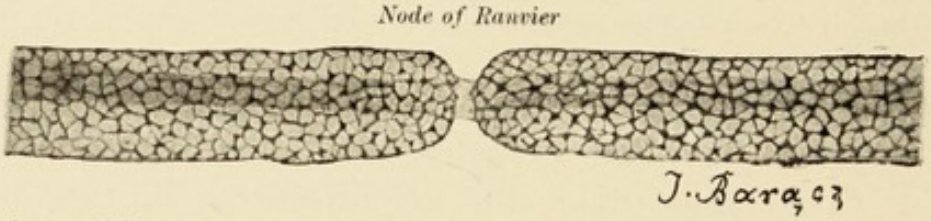
Medullated nerve fibres of a rabbit, treated with silver nitrate. The crosses of Ranvier are shown. × 300.

The Ranvier's nodes (Fig. 75) are large annular interruptions which divide the fibres into what are known as *inter-annular* or *Ranvier's segments*. The absence of the myelin at these nodes is so distinct that the axis cylinder becomes joined with the *neurilemma* by a cement substance. These nodes are probably of use in the nourishment of the axis cylinder, for at these places nutritive fluids could pass more easily into the centre of the fibre. By treating the nerve with silver nitrate and reducing this in the sunlight, we often obtain a brown striation on the axis cylinder (*Fromman's silver line*), which is usually considered as an artifact. This striation is especially marked at the nodes of Ranvier, and becomes less

distinct as we proceed from these on either side. In the node itself there is a characteristic dark-brown coloration, which is due to the staining of the cement substance, which is present in the form of a ring-like sheath between the axis cylinder and Schwann's sheath. There is thus formed with the axis cylinder a brown cross, as shown in Fig. 76. This is known as the *cross of Ranvier.*

If we boil medullated nerve fibres in ether or alcohol, the myelin dissolves, and there remains a fine network surrounding

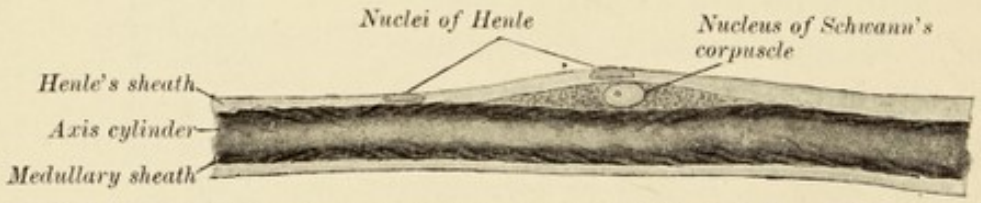
FIG. 77.



Piece of a medullated nerve fibre from a frog, boiled in absolute alcohol. In the centre is the axis cylinder, and around it the neurokeratin network. × 650.

the axis cylinder. The substance of this network has properties similar to those of keratin, not being affected by trypsin digestion. It is for this reason known as the *neurokeratin network* (Ewald and Kuhne) (Fig. 77). It is regarded by some as an artifact (v. Kölliker, Ramòn y Cajal).

FIG. 78.



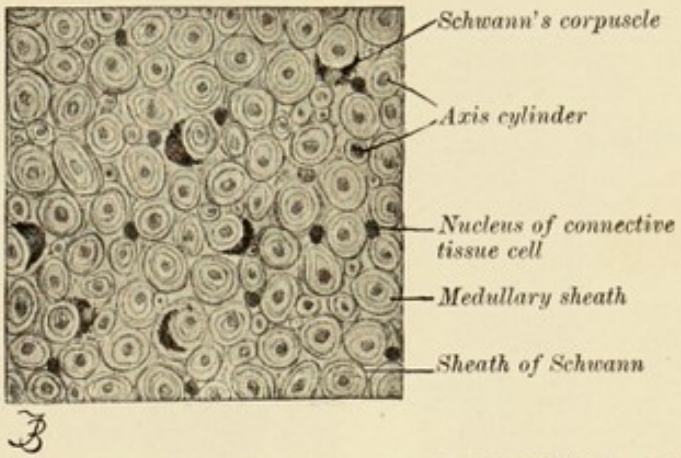
Piece of a medullated nerve fibre from the nervus radialis of man, treated with osmic acid. The nuclei of Schwann and Henle are to be seen. × 400.

The *Schwann's sheath* or *neurilemma* is situated outside the medullary sheath, and is joined with the axis cylinder at the nodes of Ranvier by a cement substance. It is a very fine homogeneous membrane which shows at various places in its course nuclei surrounded by a small quantity of granular protoplasm (Fig. 78). These nuclei, together with the collections of protoplasm, may be termed *Schwann's corpuscles.* These are

seen in cross-section in Fig. 79, where they have a semilunar form; while the Schwann's sheath is continuous around the whole fibre. In higher animals only one nucleus is found in each segment of Ranvier.

Many authors believe that the Schwann's sheath is interrupted at each node of Ranvier, and joins on each side of the node with the axis cylinder, instead of being so connected by cement substance. Others go still farther, and claim that the sheath of Schwann is continuous at the nodes of Ranvier with

FIG. 79.



From a cross-section through the human median nerve, treated with Müller's fluid and safranin. × 380.

the so-called *Mauthner's membrane* or inner neurilemma, which is inside the medullary sheath and next to the axis cylinder (Fig. 80).

The significance of the various coats of the nerve fibre is not clear. It is generally recognized from embryological studies that the axis cylinder is a process from a ganglion cell which has grown very much in length and possesses at its free end a globular thickening—*i. e.*, the growing point. The surrounding coats are of entirely different origin, and arise from the connective tissue .

Concerning the nature of the medullary sheath there are many views. According to some, each segment of Ranvier has the value of a cell, the sheaths of Schwann and Mauthner being regarded as parts of the cell membrane. The whole is considered as a connective-tissue cell, annular in shape, a part

of which has been modified to form the medullary sheath, and the rest left unchanged as Schwann's corpuscles. Others regard the medullary sheath as a product of the axis cylinder.

The function of the medullary sheath is mainly that of an insulator. The irritability of the nerve increases during development with the growth of the medullary sheath.

FIG. 80.

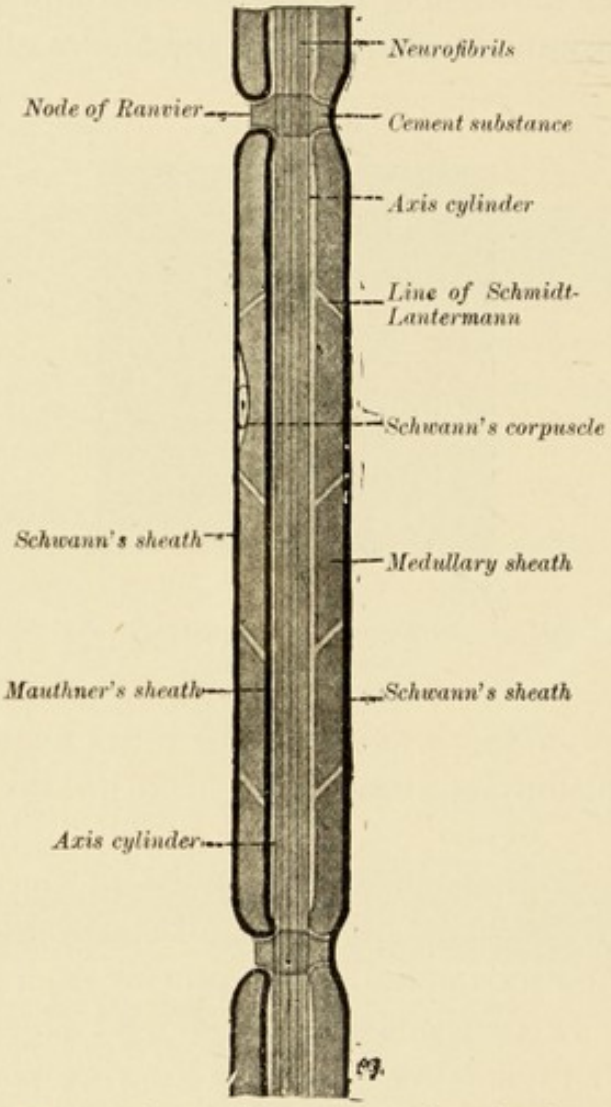


Diagram of the structure of a medullated nerve fibre, showing two different views concerning the relations of the sheaths of Mauthner and of Schwann. Compare the right and left sides.

Medullated nerves usually have a layer outside Schwann's sheath. This is of connective-tissue origin, and often shows a fibrillary structure, but is in many cases homogeneous. It possesses always on its inner surface a number of flat epithelial

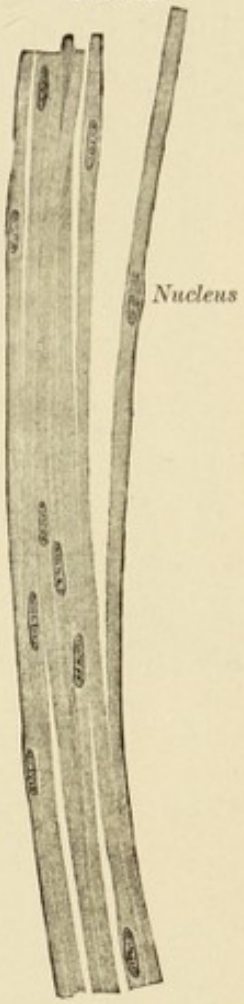
cells, whose outlines can be made out by treatment with silver nitrate. This layer is known as *Henle's sheath* or *the endoneural sheath* (Retzius).

Nerve fibres of such complicated structure as that described are found in the cerebrospinal nerves. They are of variable thickness (1–20 μ in diameter). Usually the longest fibres are also the thickest. The division of a medullated fibre into two, often three or four, branches takes place always at the nodes of Ranvier. As it approaches the nerve-ending it loses its sheaths.

The medullated nerve fibre may lack the sheaths of Schwann and Henle, as is the case in the central nervous system, where the fibre consists of only the medullary sheath and axis cylinder.

Non-medullated or *sympathetic nerve fibres* (Remak's fibres) are characterized by the absence of the medullary sheath (Fig. 81). In adult vertebrates such fibres are found only in the sympathetic nervous system. They are only 1 to 2 μ in thickness, and are direct continuations of axones of sympathetic ganglion cells. Each fibre is surrounded by a covering resembling Schwann's sheath. It possesses at various places nuclei surrounded by granular protoplasm. This sheath seems to be a continuation of the thin capsule that surrounds the sympathetic cells, and is of connective-tissue origin.

FIG. 81.



Non-medullated (Remak's) fibre from the cervical sympathetic of the rabbit. × 300.

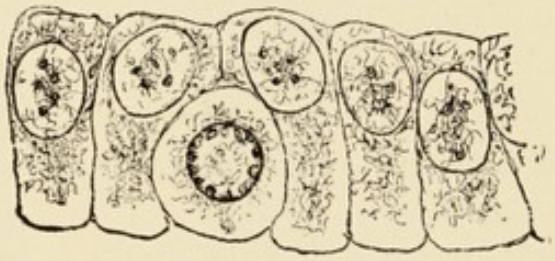
The *olfactory nerve fibres* are of a still simpler type. They are very fine (less than 0.5 μ in diameter) fibres which consist of a naked axis cylinder. More often than other fibres, they are varicose and thickened in places. The bundles of these fibres are surrounded by a homogeneous sheath containing nuclei. This does not resemble Schwann's sheath, because

the latter surrounds only single axis cylinders, and not bundles.

Histogenesis of the Neurone.

The following description is based on the account of the development of the neurone given by Barker, who, in turn, has used as a foundation the writings of His. As is well known, the medullary plate of the nervous system is derived from the ectoblast, by the turning in of a single layer of epithelium (Fig. 82). The neural tube is formed from this, its inner sur-

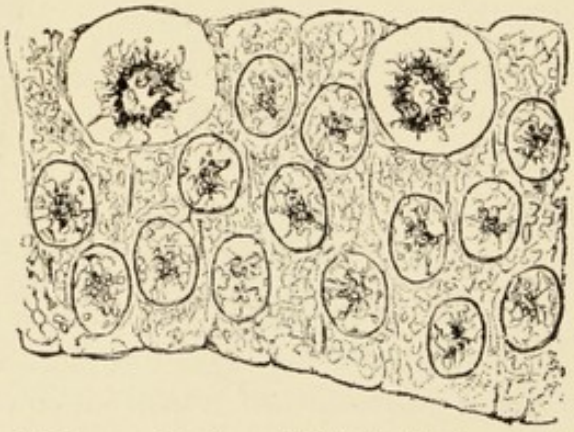
FIG. 82.



Section through the medullary plate of a rabbit. Among the epithelial cells a large round germinal cell with clear protoplasm is visible. (Barker, after His.)

face corresponding with the outer surface of the ectoblast. The cells increase in length and the nuclei come to lie at different levels (Fig. 83). There are formed three zones, however, the

FIG. 83.

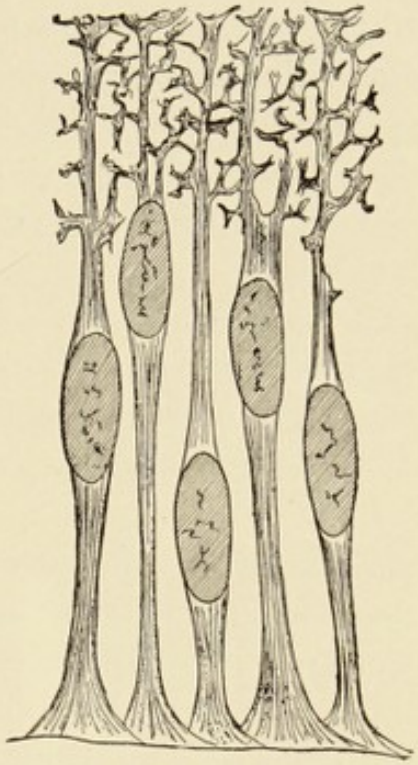


Section through a rabbit's neural tube which is beginning to close. The number of epithelial nuclei is increased. (Barker, after His.)

inner and outer of which are made up of the protoplasmic ends of the cells, while the middle zone contains the nuclei. The distal ends of the cells—*i. e.*, the ends toward the lumen of the

medullary tube—shrink, so that spaces are present between them; the proximal ends break up into irregular branches, which anastomose to form a spongy network, the *neurospongium* of His (Fig. 84). At the outside of the medullary tube this network forms a dense spongy structure known as the *peripheral* or *marginal veil.*

Fig. 84.



Section through the wall of a neural tube of a rabbit older than that in Fig. 83. Differentiation of the two ends of the epithelial cells. (Barker, after His.)

Soon after the formation of the medullary plate large spherical cells appear between the distal ends of the epithelial cells (Figs. 82 and 83). These are the *germinal cells* (Keimzellen of His). The nature of these cells is a matter of dispute. From the proximal end of each of the germinal cells there grows out a process, which, together with the cell, forms a pear-shaped structure known as the *neuroblast.* This becomes converted afterward into a nerve cell, and the process becomes its axone. The dendrites develop later on. The neuroblasts show a tendency to move outward to the marginal veil, where they are stopped. In the spinal cord these arrange themselves parallel to the surface of the marginal veil, and on the ventral part of the cord send out processes through the marginal veil to form the ventral roots of the spinal nerves. The cell bodies become the ventral horn cells. The other neuroblasts do not send processes out of the cord.

The marginal veil itself later becomes a part of the ependyma which is present in the white matter of the whole central nervous system.

The origin of the peripheral sensory neurones is still a subject of much dispute. It is agreed generally that these neurones are derived from the ectoblast at the edge of the

medullary plate. From here the neuroblasts wander out and collect to form cell groups. The later development has been worked out by His. A process grows from each pole, one corresponding with the axone and the other with the dendrites. The axone grows centralward and penetrates the wall of the medullary tube. Here it develops subsequently into a fibre which enters into the formation of the dorsal columns. The dendritic process proceeds in the opposite direction. By a subsequent change in the shape of this bipolar cell the axone and dendrites both come to be processes from one outgrowth of the cell. In other words, the cell becomes unipolar (Fig. 71).

V. BLOOD AND LYMPH.

Blood and lymph are properly to be considered as tissues consisting of formed elements in a fluid intercellular substance.

1. Blood.

The blood of the higher animals is a red fluid, which is made up of blood *plasma* (intercellular substance) and formed elements (blood corpuscles, blood platelets, and various granular elements). We distinguish two kinds of blood-corpuscles: red (colored) and white (colorless).

Red blood-corpuscles (also known as *erythrocytes*) contain the red coloring material, *hæmoglobin*, which gives to them and to thin layers of blood a straw-yellow tint. They are in mammals almost without exception flat, round structures without a nucleus. The flat surfaces are depressed in the centre, giving to the cell the general form of a biconcave lens. The borders are rounded and much thicker than the centre. In optical cross-section the corpuscle is biscuit-shaped.

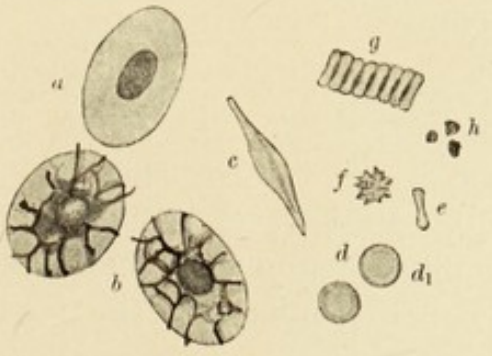
The red corpuscles vary in size in different animals, from 2.5 μ (in *Moschus javanicus*) to 9.4 μ (*Elephas indicus*) in diameter. In man they are from 7.2 to 7.8 μ in diameter, and 1.9 μ thick at the thin middle point. Oval red corpuscles are found among mammals only in the llama and the camel. They are, however, common in lower animals. The red blood-cells of fishes, amphibians, reptiles, and birds, are oval in form and

biconvex. Each cell possesses an oval nucleus, which causes a thickening in the centre. They are much larger than in mammals. In *Rana temporaria* they are 22 μ long, 15 μ broad; in *Salamandra maculosa*, 37 μ long, 23 μ broad; in *Proteus sanguineus*, 58 μ long and 34 μ broad.

The red blood-cell in man consists of two constituents, a protoplasmic part (*stroma*) and the coloring matter distributed on this—*i. e.*, the *hæmoglobin*. Anilin-stains, such as eosin, orange G, etc., are taken up readily by hæmoglobin-containing cells.

Under the influence of reagents, red blood-corpuscles change their form very quickly. In water or dilute acids they swell up and lose their hæmoglobin. They are then colorless and hardly visible, and are known as *blood shadows*. They are decolorized similarly by the action of electricity and continued freezing. Tannic acid causes an extrusion of the hæmoglobin in small globules. Salt solution stronger than "normal" causes a shrinkage of the cells from loss of water. They become irregular in outline, small sharp projections appearing everywhere; and are said to be *crenated* (Fig. 85, *f*).

FIG. 85.



Colored blood-cells (*a–g*) and blood-platelets (*h*). × 800.

a–c, red blood-cells of frog: *a*, seen from above; *b*, changed by addition of water; *c*, seen from the side.

d–g, red blood-cells of man: *d*, on deep focussing; d_1, on high focussing; *e*, seen from the side; *f*, crenated; *g*, rouleau of blood-cells; *h*, blood-platelets.

Red blood-corpuscles have a considerable degree of elasticity, so that they can be much changed by being forced through narrow spaces and still regain their original shape. For

example, a corpuscle may be pressed against the point of division of a capillary, or be crowded with many others in a narrow vessel. This may easily be observed in the mesentery of a recently killed frog.

When blood is spread in a thick layer on a slide and examined while fresh, one almost always sees the so-called *rouleaux* —*i. e.*, cells lying upon one another, as coins do. This condition is probably never present in circulating blood. On being shed, the blood-corpuscles seem to be changed in some way that causes them to adhere to one another. In a properly prepared thin specimen of blood rouleaux never are seen.

The number of blood corpuscles present in 1 cubic millimetre of blood varies in different animals, and ranges from 33,000 in *Proteus* to 19,000,000 in *Capra hircus*.

In man the number of erythrocytes in 1 cubic millimetre is about 5,000,000. This varies under normal conditions. The number is greatest just after birth, and decreases slightly with age. With low atmospheric pressure it increases. Marked changes are noticed in various diseases.

White (*colorless*) *blood-corpuscles* (also called *leucocytes*) are nucleated cells possessing no cell membrane. The protoplasm may be abundant, or very small in quantity. During life these cells have no constant form, being amœboid, but after death they assume a round outline. Their size varies considerably, from about that of a red blood-corpuscle to three times that size. Their number in man is from 7000 to 9000 in 1 cubic millimetre. This number undergoes changes under physiological conditions. It is dependent on the food taken in. After several hours of fasting it is much smaller, while after a full meal there is what is known as a *digestion-leucocytosis*. There is similarly a leucocytosis (an increase in leucocytes) in many febrile diseases. In rabbits the blood from peripheral vessels contains more leucocytes than that from the central ones.

Similar cells are found in the lymph, adenoid tissue, bone-marrow, and distributed throughout connective tissue and epithelial tissue (wandering cells). The white corpuscles are

present in the circulating blood, especially at the periphery of the stream—*i. e.*, near the vessel walls. They can thus easily leave the vessel by pushing in between the endothelial cells and reaching the connective tissue (*diapedesis*).

There are many kinds of leucocytes to be distinguished, and these may be divided according to their general form and the character of their nuclei into the following groups:

1. *Small Mononuclear Leucocytes* (*Lymphocytes*).—These are cells about the same size as a red blood-corpuscle, sometimes a little smaller and sometimes a little larger. Their protoplasm is very small in quantity, slightly granular, and arranged like a ring around the nucleus. It stains not very deeply in acid dyes. The nucleus is large in proportion to the size of the cell and takes a deep stain. The chromatin is in large masses so arranged that the nucleus seems to be mapped out in areas. This has given rise to the term *checker-board nucleus*. These cells are recognized readily in stained preparations by their deeply staining characteristic nucleus, and their almost invisible protoplasm. They form about 20–30 per cent. of all the leucocytes in the blood. They are identical also with the lymphocytes which make up the lymphoid masses in the intestine, lymph glands, tonsils, thymus, and spleen.

2. *Large mononuclear leucocytes* are cells very much larger than lymphocytes. The protoplasm is very abundant, usually clear, and capable of taking only a faint eosin coloring. Occasionally granules of various kinds are present. The nucleus is large, oval, and somewhat vesicular. It is situated usually peripherally, and stains very faintly in basic dyes. These cells form about 4–8 per cent. of all the leucocytes in normal blood.

3. *Transitional leucocytes* are not usually so large as the large mononuclears. They are characterized mainly by the horseshoe-shaped nucleus. This is a nucleus staining fairly deeply, not constricted in any place, but bent either slightly or in the form of the letter U. These cells may contain various kinds of granules in their protoplasm.

4. *Polymorphonuclear leucocytes* are so named from the

form of the nucleus. They are somewhat smaller than the large mononuclear cells, and are irregular in outline. Their protoplasm varies in appearance according to the character of the granules present (see below). The nucleus is absolutely characteristic. With low powers it seems to be made up of three or four small separate nuclei, which usually are arranged in a semicircle at the edge of the cell. On examination with higher powers, however, these nuclei are always seen to be parts of one nucleus, and to be joined together by fine strands. They stain very deeply in nuclear dyes, and can readily be recognized in any tissue. These cells form about 62–70 per cent. of the leucocytes in normal blood, and are found as wandering cells everywhere in the body. They are found more or less abundantly in all inflammatory processes, and are the main cellular constituent of pus. They possess a special power of taking up and either digesting or rendering innocuous bacteria and foreign bodies in the tissues. This was studied specially by Metchnikoff, and was called by him *phagocytosis.*

The cells belonging to these four groups of leucocytes may contain in their protoplasm various granulations, which have been classified by Ehrlich according to their staining properties. Ehrlich divides all anilin-dyes into three groups, namely: acid, basic, and neutral dyes, according as the coloring principle is an acid (as in ammonium picrate), a base (as in rosanilin acetate), or a combination of a basic and an acid dye (as in rosanilin picrate). The most common acid stains are eosin, orange G, acid fuchsin, aurantia, etc., while the basic dyes ordinarily used are methylene-blue, methyl-green, safranin, etc. Speaking generally, acid dyes color the protoplasm, and basic dyes the nuclei of cells.

Ehrlich distinguishes five different kinds of granulations, and names them by the Greek letters α, β, γ, δ, ε.

1. α (*acidophile, eosinophile*) granulations are usually coarse and highly refractive, and are found mainly in polymorphonuclear leucocytes. They stain brightly in eosin, aurantia, indulin, nigrosin, orange G, etc. In normal human blood they are found in very small numbers (0.25–4 per cent.), but in-

crease enormously in some anæmias, and especially in trichinosis.

2. β (*amphophile*) granulations are colored both by acid and basic dyes. They appear as very fine granules. They occur in the bone-marrow, but not in the normal blood of man. They are found, however, in the blood of guinea-pigs, rabbits, chickens, etc.

3. γ granulations are quite coarse and stain in basic dyes. Cells containing these are called *Mastzellen*, and occur very seldom in normal human blood, but are abundant in leukæmia. They are found usually in the blood of lower animals, and are abundant in connective tissue. They can be stained best by the violet basic dyes: dahlia, gentian-violet, methyl-violet, etc.

4. δ (*basophile*) granulations are fine granules, occurring mainly in large mononuclear leucocytes in human blood. They stain in basic dyes, and especially well in methylene-blue.

5. ε (*neutrophile*) granulations are small, and are colored only in neutral dyes and with mixtures of acid and basic dyes (*e. g.*, acid fuchsin with methyl-green, or acid fuchsin with methylene-blue). They are found in the great majority of polymorphonuclear leucocytes.

As to the nature of these different kinds of leucocytes, various views are held. According to some, all are derived from one common form, and are not to be considered as different cells. Others claim that they are entirely distinct cell types, and that each has a special organ to which it belongs (*e. g.*, lymphocytes in the lymph glands, myelocytes in the bone-marrow, splenocytes in the spleen).

Blood-platelets are small, colorless, round or ellipsoid bodies of unequal size, usually about one-third the diameter of a red blood-cell, first described by Hayem, Bizzozero, and Osler. They possess no nucleus, and their place as independent morphological constituents of the blood has been denied by many authors. Some regard them as portions of other blood cells. According to most writers, they play an important rôle in the coagulation of blood. As soon as blood is shed, they disappear,

and cannot be found in an ordinary fresh blood specimen. Clumps of débris, which probably represent their remains, are seen usually. By pricking the finger through a drop of osmic acid or methyl-violet, these bodies can be preserved. The number in 1 cubic millimetre is given by some authors as 200,000, by others as much as 635,000.

Everywhere in normal human blood there are small fat globules and other fine colorless granules, known as *blood dust* or *hæmokonien* (H. F. Müller). Their size is usually less than 1 μ, and their function and significance are unknown. The fat globules probably come from the chyle.

Histogenesis of Blood.

Concerning the development of blood-cells there is a great diversity of opinion. Some authors claim that they are of mesodermal origin, while others trace their origin to the entoderm. There is also discussion as to whether or not red and white blood-cells have the same origin.

We shall, first of all, speak of the development of the red corpuscles of mammals. The cells from which these arise, the so-called *erythroblasts*, are round nucleated cells somewhat larger than the erythrocyte, possessing a homogeneous protoplasm which contains hæmoglobin. The origin of the erythroblasts and the way in which they acquire their hæmoglobin are not known definitely. They, however, increase by indirect division and pass over into the form of erythrocytes. In mammals this involves the loss of the nucleus, for in the newborn all the red blood-cells are non-nucleated, while in embryos the majority of the blood-corpuscles possess nuclei. Some authors believe that the nucleus is simply extruded from the cell, and have not only followed all stages in the extrusion, but also have observed free nuclei in the blood. Other investigators, on the contrary, claim that the nucleus disintegrates in the cell and disappears.

The development of red blood-corpuscles in embryonal life takes place in the liver, the walls of the umbilical vesicle, the lymph glands (exceptionally), the spleen pulp, and the bone-

marrow. The formation of erythrocytes in the spleen and liver takes place in embryonic life. In the adult individual it is exclusively in the bone-marrow.

The colorless blood-corpuscles (leucocytes) are derived, according to some authors, from a different kind of cells which, in contradistinction to erythroblasts, are called *leucoblasts.* Originally the embryonic blood contains no leucocytes. These come later, after the development of the lymph glands. In post-embryonic life leucocytes increase in connective tissue and in the so-called *germinal centres* (see below), which are present in adenoid tissue.

It is believed almost generally now that the polymorphonuclear leucocytes are derived from the myelocytes of the bone-marrow; and that lymphocytes arise in the germinal centres of the lymph glands. Uskow and others regard the polymorphonuclear leucocytes as the terminal stage in the development of leucocytes, and that the other forms constitute a series which leads up to this stage.

The blood as a whole has two main functions, namely, to carry oxygen to the various parts of the body from the lungs, and to carry waste products to the different excretory organs. As mentioned above, the white corpuscles have a protective action in the so-called phagocytosis. According to some authors, they not only are capable of surrounding and digesting bacteria, etc.; but they also secrete a substance (alexine) which is a powerful poison for bacteria.

The coagulation of blood, which takes place as soon as it leaves the vessels, or in the vessels after death, is dependent on the formation of *fibrin.* Details concerning this process should be sought for in works on physiology. Fibrin appears in thin layers, in the form of fine fibrils which form a network. This forms the clot which is characteristic of coagulated blood, and contains within the meshes of the fibrin network all the formed elements of the blood.

Hæmoglobin, the coloring matter of the red corpuscles, separates in most animals under certain conditions in the form of rhombic crystals. Such crystals are found in old alcoholic

preparations in the blood-vessels, in the red blood-cells of the bony fishes, and sometimes in the liver cells.

Hæmoglobin is easily broken up into *hæmatin*, *hæmatoidin*, and *hæmin*. The first is amorphous, but the other two may be crystallized. Hæmatoidin appears in the form of rhombic prisms of an orange-red color. These are found in all extravasations of blood (*e. g.*, in the corpus hæmorrhagicum of the ovary, and in clots on the brain). Hæmin occurs in the form of rhombic plates lying singly or crossed to form stars. These are called *Teichmann's crystals*. They are colored mahogany-brown, and can be obtained even in blood which has been dried for a long time. They are thus of forensic significance. Their demonstration shows the undoubted presence of blood, but it does not determine that the blood is necessarily human. In making this hæmin test for blood, a small crystal of common salt and two drops of glacial acetic acid are placed on a slide with the suspected material. This mixture is heated to boiling-point until the acid is almost evaporated, and is then examined with high magnification.

2. Lymph.

The lymph is a colorless fluid whose only cellular elements are the colorless cells called *lymphocytes*. There are also found in it particles of fat which after fat digestion give to it a white, milky appearance. The fluid part of lymph is called lymph plasma.

PART II.

MICROSCOPIC ANATOMY OF THE ORGANS.

In this section we have to deal with the structure of organs which are built up of the tissues which have been studied. Some of these organs, it will be seen, are made up of all the different tissues, while others are much more simple. A feature to which special attention will be directed is the unitary structure of many of the organs. In other words, the tissues are grouped together into units, which are repeated many times to form the whole organ. These may be secretory, excretory, or circulatory units.

The organs will be treated in the following order:

I. Circulatory system.
II. Alimentary system.
III. Respiratory system.
IV. Urinary system.
V. Reproductive system (sexual organs).
VI. Motor system:
    1. Skeletal system.
    2. Muscular system.
VII. Nervous system and sense organs.

I. CIRCULATORY SYSTEM.

Under this heading it is necessary to take up the heart, blood-vessels, lymph-vessels, and blood-forming organs—*i. e.*, the lymph glands, spleen, thymus, bone-marrow, and those ductless glands whose internal secrêtion is poured into the circulatory system and exercises on it a profound influence—*i. e.*, the thyroid, adrenal, pituitary body, and carotid gland.

1. BLOOD VASCULAR SYSTEM.

This whole system is lined with endothelium, which forms a complicated epithelial or endothelial tube. The heart is much thickened outside this tube by muscular development, while the capillaries consist of the endothelial tube alone. The thicker vessels have the so-called *accessory* coats, which are divided into *intima*, *media*, and *adventitia*.

(*a*) Capillaries.

These are very small vessels with a diameter of between 7 and 15 μ, situated between the venous and arterial systems. The wall consists of a single layer of flat endothelium, the cells of which are joined together by a small quantity of cement substance, which is easily demonstrated by means of silver nitrate. The outlines of these cells are shown in Fig. 93, and are seen to be irregular and jagged. They are arranged usually with their long axes parallel to that of the vessel. The nuclei are arranged similarly and show a small collection of protoplasm in their immediate neighborhood. Stigmata and stomata (small openings between the cells) are seen frequently. The thinness of the walls allows diffusion and osmosis to go on freely, which is of great importance in the body metabolism.

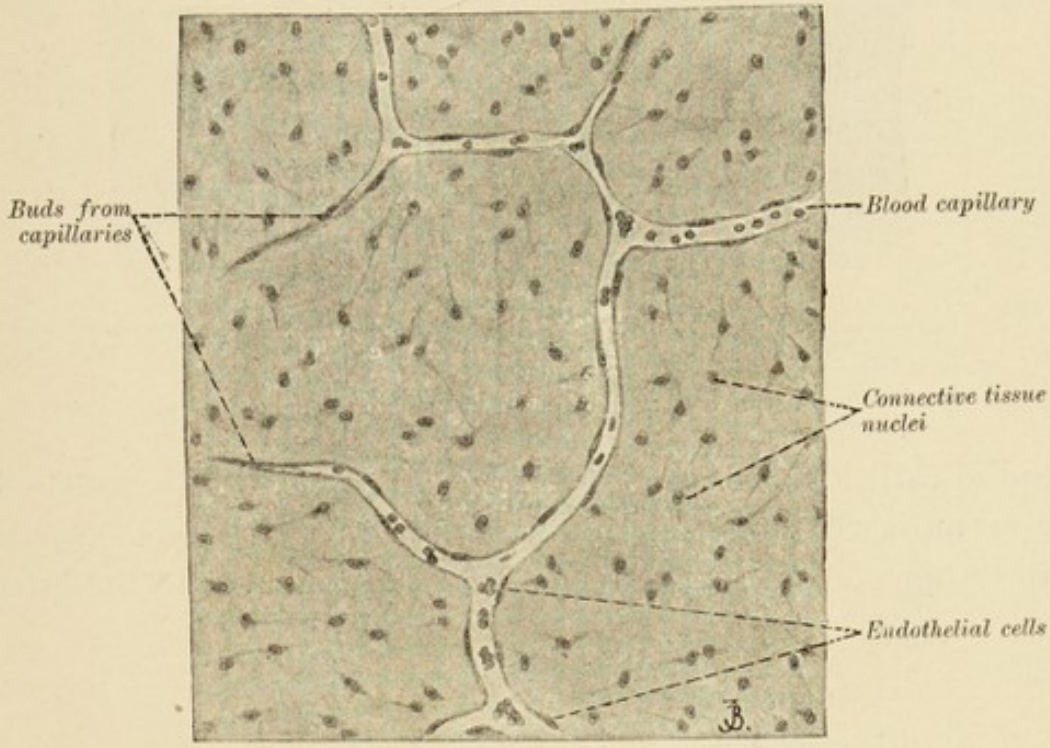
The capillaries anastomose freely with one another, forming a network which is easily seen in the mesentery In muscle the meshes of this network are long and narrow. In the liver they are much smaller.

The vessels which pass over from the capillaries to the arteries, on the one hand, and to the veins on the other hand, are known as *precapillary* arteries and veins.

The new formation of capillaries is seen best in the greater omentum of young animals (Fig. 86). From already developed capillaries protoplasmic sprouts branch off and extend into the surrounding tissue. These sprouts are the result of karyokinetic division of the endothelial cells. They begin to become hollow and to form a blind canal, which meets another similar sprout and joins with it, the lumen becoming continuous in the two. Other authors describe special *vasoforma-*

tive cells, which form capillaries independently of already existing vessels (Ranvier). These cells are associated with the so-called *intracellular development* of red blood-corpuscles. In their protoplasm are to be found well-formed red cells, as well

FIG. 86.



Piece of the omentum majus of an eight day dog's embryo, seen from the surface. × 180.

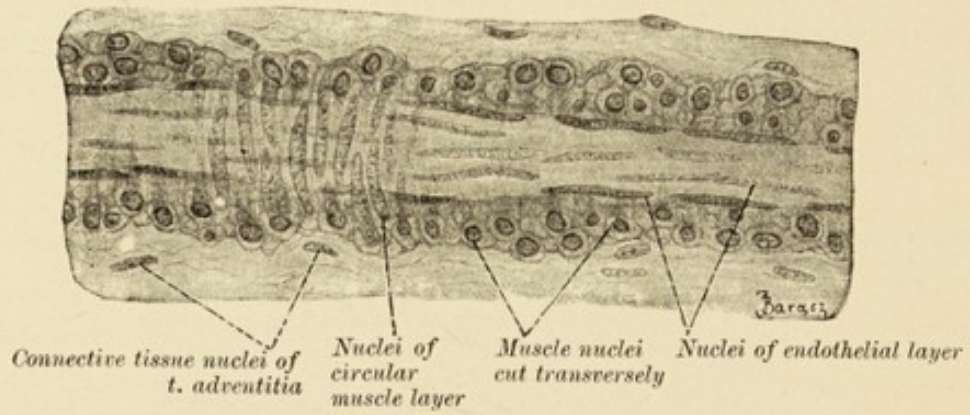
as granules containing hæmoglobin. Sig. Mayer considers these cells, on the contrary, to be the result of degenerative changes in capillaries, and claims that the hæmoglobin-containing granules are broken-down erythrocytes.

(*b*) Arteries.

The precapillary arteries show only a thin sheath of connective tissue or a structureless elastic membrane outside the endothelial tube. The accessory coats become thicker as they approach the heart. Those of the smaller arteries begin as a thin discontinuous layer of smooth muscle cells circularly arranged around the sheath of connective tissue which covers the endothelial tube. In somewhat thicker small arteries the muscle cells form a definite circular coat (Figs. 87 and 88). In the longitudinal section of such an artery the muscle-cell

nuclei can be seen to run at right angles to the nuclei of the endothelial cells (Fig. 87). The inner connective-tissue coat contains many elastic fibres which are fused together to form

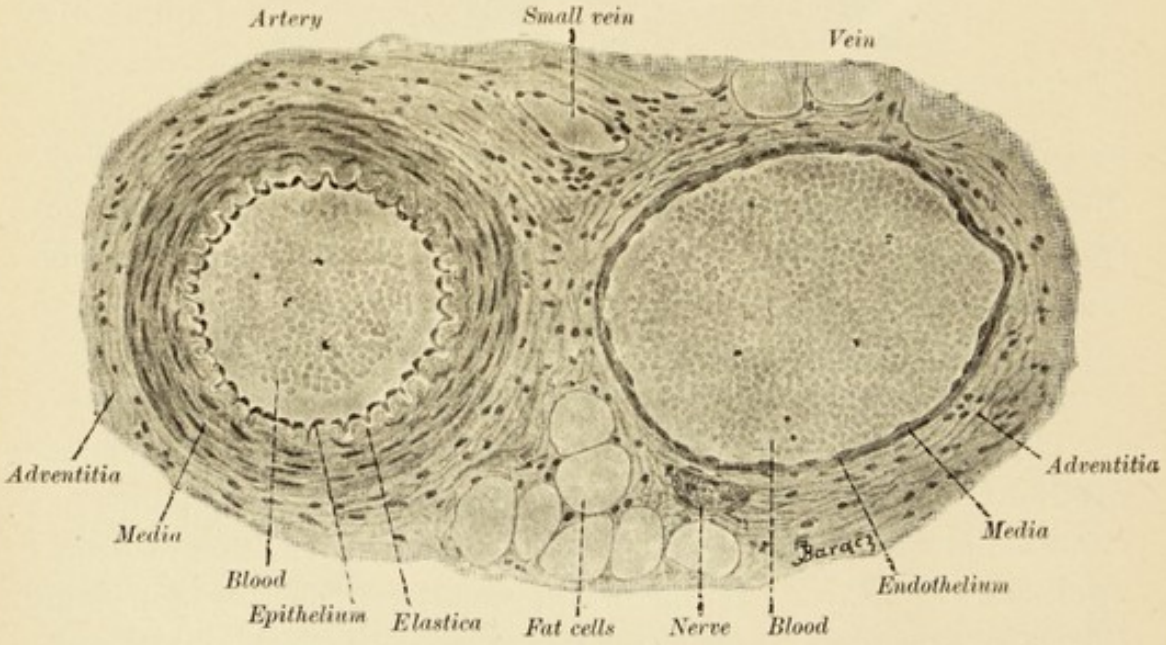
FIG. 87.



Longitudinal section of a small artery from the lymph gland of a cat. × 600.

the so-called *fenestrated membrane of Henle.* This forms the innermost coat of the intima, and in cross-section has the appearance of a wavy refractive line running around the lumen

FIG. 88.

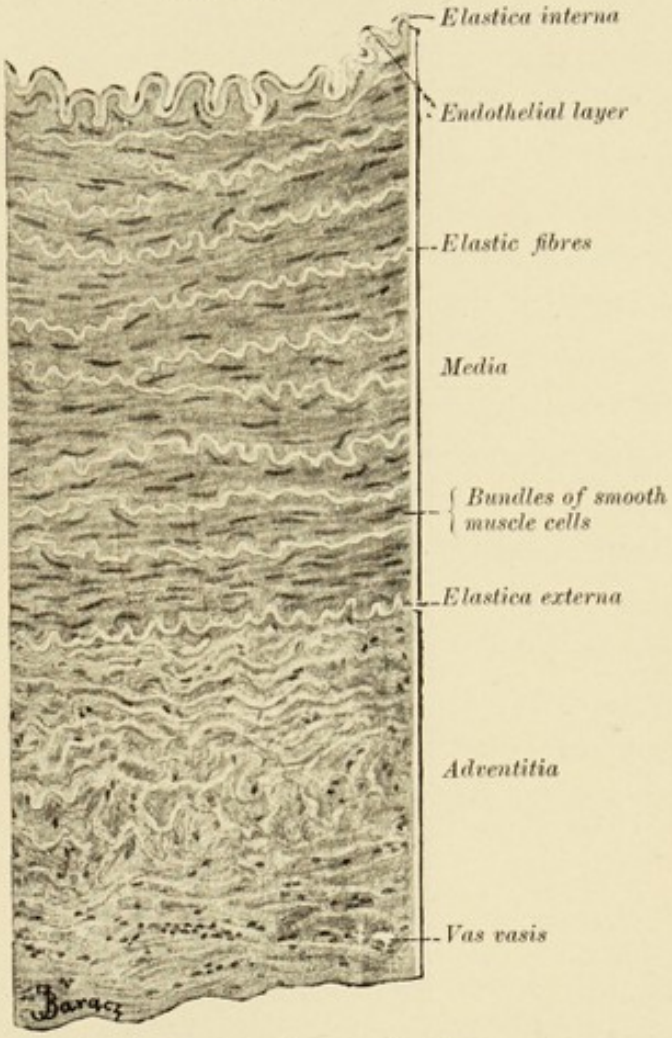


Cross-section through a small artery and a corresponding view of a dog. × 220.

of the vessel. It is colored bright yellow in any stain containing picric acid (*e. g.*, van Gieson's fluid). From fresh arteries it can be dissected out, and pieces of the membrane of a con-

siderable size can be obtained. These have a peculiar fenestrated appearance, clear unstainable areas being present throughout. They are due to the fact that the membrane is made up of three layers, of which the middle can be stained with magenta, and the other two not. At the fenestra the middle layer is absent. As described above, the individual

FIG. 89.



Part of a cross-section of the femoral artery of a dog. × 150.

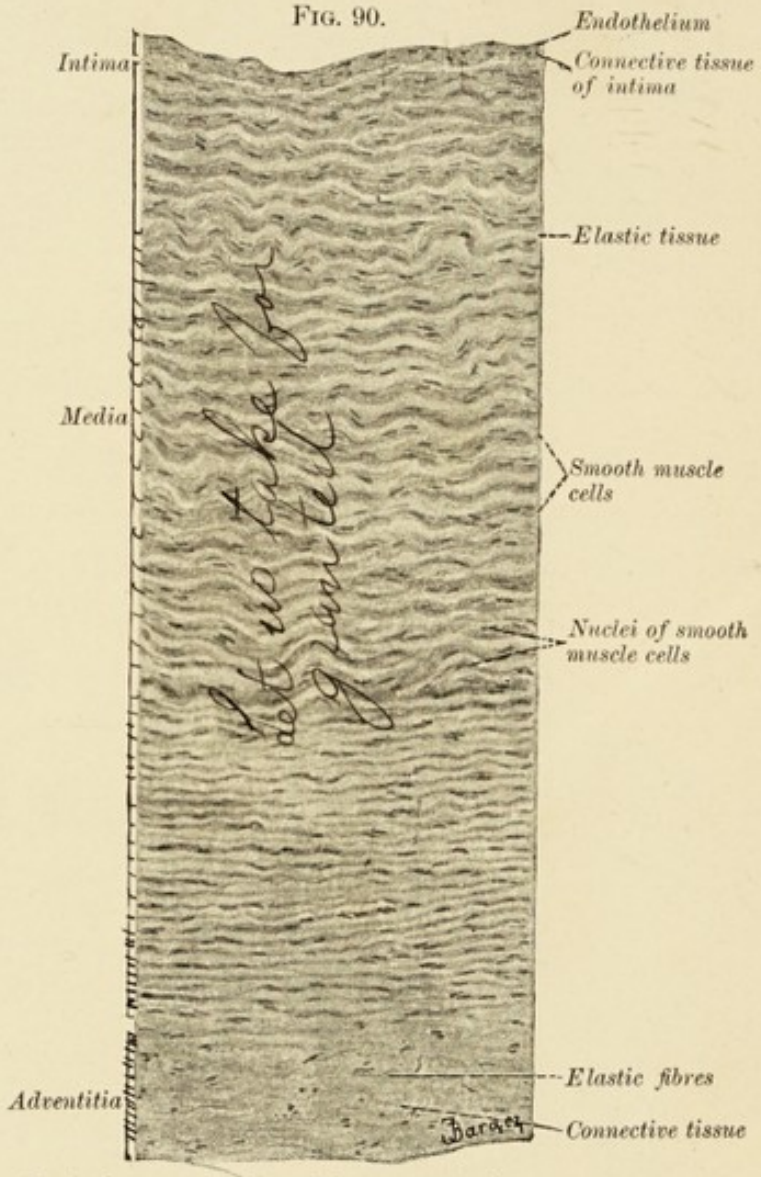
elastic fibres consist of a central stainable part and a capsule which does not take up the dye. By the fusion of many of these fibres the membrane with three coats is formed, the two outer coats corresponding with the capsules of the fibres (Mall).

The media consists of circular layers of smooth muscle fibres, and the adventitia is made up of connective tissue.

A medium-sized artery (Fig. 89) is composed of three dis-

tinct coats: the intima, media, and adventitia. The *intima* consists of a thin connective-tissue layer immediately surrounding the endothelial tube, and Henle's fenestrated membrane or the *elastica interna*. Around this is a thick layer, the *media*, consisting largely of smooth muscle, but containing as well

FIG. 90.



Part of a cross-section of the aorta of a dog. × 140.

many white fibrous and elastic connective-tissue strands. The muscle runs circularly, and is arranged in layers separated by connective tissue in the form of concentric bands of elastic tissue (Fig. 89). There are often seen longitudinal strands of muscle between the circular layers. The outermost sheath, the *adventitia*, is composed largely of connective tissue and muscle.

It is usually separated from the media by a more or less distinct elastic membrane, the *elastica externa*. The fibres of the adventitia are divided roughly into two layers. The elastic fibres of the inner layer, next the media, run circularly, while those in the outer layer are longitudinal. Between the connective-tissue coats of the inner layer are longitudinal bands of smooth muscle. Vasa vasorum are present in the media and adventitia.

Arteries of large calibre (*e. g.*, carotid, aorta, etc.) cannot be so distinctly divided into layers (Fig. 90). The endothelial tube is made up of short polygonal cells. The intima consists of a subendothelial connective-tissue sheath, and the elastica interna. The subendothelial sheath is made up of white connective-tissue fibrils and elastic fibres. The elastica interna is not a firm homogeneous membrane, but is split up into several lamellæ, and in some places is only a simple layer of elastic fibres.

The media contains a great many membrane-like masses of elastic tissue, and thick elastic fibres. Between these are bundles of smooth muscle fibres. The adventitia is similar to that of medium-sized arteries. The elastica externa is wanting in the aorta.

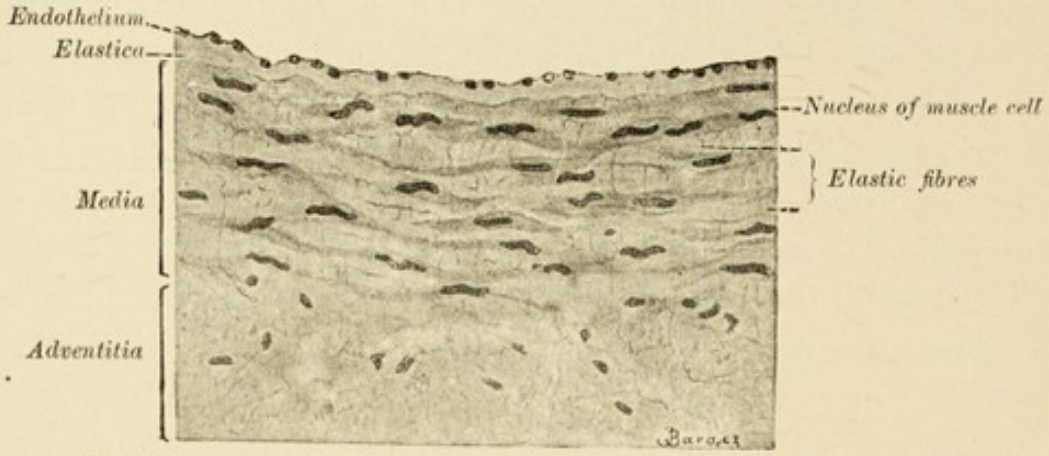
The arteries in the skull cavity have no elastic elements in the media. This perhaps explains why they are more likely to yield to pressure than other arteries. The elastica externa is not present in them, but there are circular elastic fibres in the inner coat of the adventitia.

(*c*) Veins.

The important features which distinguish veins from arteries are the weak development of the media in the former, the small amount of elastic tissue, and the strong development of the adventitia. There is also a marked lack of uniformity in veins of the same size. The same three coats may be spoken of as in arteries, namely, intima, media, and adventitia. The *intima* is a connective-tissue layer containing only a few elastic fibres. In the larger vessels there are often bands of muscle running in various directions, and a layer of elastic tissue which may take on the form of a membrane. The latter is

never as sharply marked as the fenestrated membrane of arteries. The *media* of veins is developed weakly in comparison with that of arteries (Fig. 92). It consists of a few circular muscle bands separated by thin elastic fibres. The veins of the lower extremities possess the most strongly developed media. It may

FIG. 91.



Part of a cross-section through a medium-sized vein of a dog. × 280.

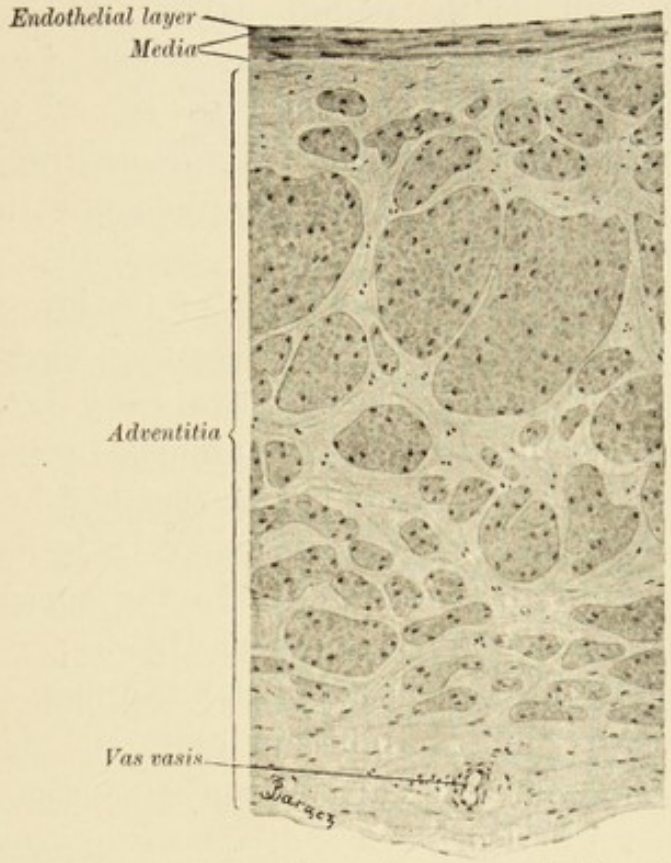
be quite wanting in others (*e. g.*, vena cava superior, subclavian, veins of pia and dura mater, veins of bones, retinal veins, etc.). The *adventitia*, on the contrary, is usually strongly developed. It consists of white connective-tissue and elastic fibres, with often well-developed longitudinal smooth muscle bundles (Fig. 92).

The *valves* of the veins are derived from the intima, and, like it, consist of connective tissue and elastic fibres. Their surface is covered by cells of the endothelial tube, which on the inner side toward the blood stream are long, and on the other side polygonal. On the inner surface of the valves there is under the endothelial cells a network of fine elastic fibres.

The main points of distinction between arteries and veins are the following: The walls of arteries in relation to the size of their lumina are much thicker than in veins. The elastic tissue and muscle elements in the media are more strongly developed in arteries. After death the muscle of the media contracts, and in arteries throws the intima and elastica interna into folds, giving it a wavy appearance in cross-section. Veins usually contain a small quantity of blood after death; arteries are often empty. These differences are illustrated by Fig. 88.

All the medium-sized and large blood-vessels are supplied with small vessels (vasa vasorum) which supply their walls with blood. They run in the adventitia, and only to a small

FIG. 92.



Part of a cross-section of the vena cava inferior of a dog. × 150.

extent in the media. They never reach to the intima. Small blood-vessels are often surrounded by lymph capillaries, and sometimes by endothelium-lined spaces which are in communication with the lymphatic system. These are called *perivascular lymph spaces*, and are found in the central nervous system, bones, etc.

The vessel walls are also supplied with nerves. Medullated and non-medullated fibres form a network in the media, and may end in any of the accessory coats. Capillaries are surrounded usually by a fine network of nerve filaments.

(*d*) The Heart.

The heart is a much complicated part of the circulatory system, with walls that are made up of three main layers:

1. *Endocardium;* 2. *Myocardium;* and 3. *Epicardium* (visceral layer of the pericardium).

(1) The *endocardium* is a connective-tissue membrane which contains smooth muscle and elastic tissue fibres. It is situated immediately outside the endothelial sac which lines the cavity of the heart. The endocardium is spoken of usually as including both the endothelial layer and the smooth muscle and elastic fibres outside it. The cells making up the endothelial layer are polygonal, and are continuous with the endothelial lining of the vessels.

(2) The *myocardium* forms the main part of the heart wall. The layer is much thicker in the left ventricle than elsewhere. The finer structure of the muscle cells has already been described. By joining together laterally the branched cells form a network, the strands of which are bound together by connective tissue. The course of these strands of cells is not the same in different parts of the heart wall. In the auricles we find a superficial layer common to both, and a deeper layer belonging to each chamber. In the ventricles the most superficial layers are seen to run at right angles to the deepest. Between these there are fibres in all stages of transition. At the apex they form a whorl or vortex, disappearing from the surface in the depths. This very complicated structure is much simplified by a study of embryonic hearts by macerating methods. If hearts be taken from pigs' embryos, about 150 mm. in length, and macerated in nitric acid (commercial), 1 part; glycerin, 2 parts; water, 2 parts, the connective tissue binding the muscle strands together is dissolved or destroyed. The course of the fibres may then be traced by dissection, and has been described in some detail (J. B. MacCallum). The superficial fibres are found to have their origin in either auriculoventricular ring, to wind about the heart spirally, and to end in tendons of the papillary muscles of the opposite ventricle. The deep layers also begin in the tendon of one auriculoventricular ring, pass around to the interventricular septum, cross over forward or backward in this septum, and end in the papillary muscles of the other

ventricle. Practically none of the strands of fibres begin and end in the same ventricle. It will thus be seen that the heart is made up of various layers of muscle, all of which have their origin in the tendon of the auriculoventricular ring of one side, and end in the tendon of a papillary muscle of the other side. Their fibres in passing over in the septum thus take a scroll-shaped course. In the light of this, the heart consists of several bands of muscle with tendons at each end, rolled up like a scroll or like the letter S. At the same time it is to be observed that the growing points in a very young heart are just under the endocardium. Karyokinetic figures are found there, and the cells in that region are younger than at the periphery of the heart. If the heart be then unrolled, these growing points would appear at each end of the bands of muscle that make up the heart. For a more detailed description of this dissection of the heart, the reader is referred to the original article.

In the muscle of the heart wall there is a rich network of blood capillaries, which run parallel to the fibres and send branches which surround them.

Elastic tissue is found abundantly in both the auricles and ventricles.

The *annuli fibrosi*, which consist of firm connective tissue containing elastic fibres, separate the muscle of the auricles from that of the ventricles, and form a place of attachment for those muscles.

(3) *Epicardium* is a connective-tissue membrane rich in elastic fibres. Under it there is usually a quantity of fat, which is gathered in masses in certain places. The upper surface of the epicardium is covered by flat endothelial cells.

The *heart valves* are connective-tissue structures formed by a reduplicature of the endocardium, and contain connective tissue and smooth muscle. Their surface is covered by endothelial cells. No blood-vessels are present in the heart valves.

The *pericardium* is a connective-tissue membrane containing many elastic fibres, and on its free inner surface is covered by a layer of endothelial cells.

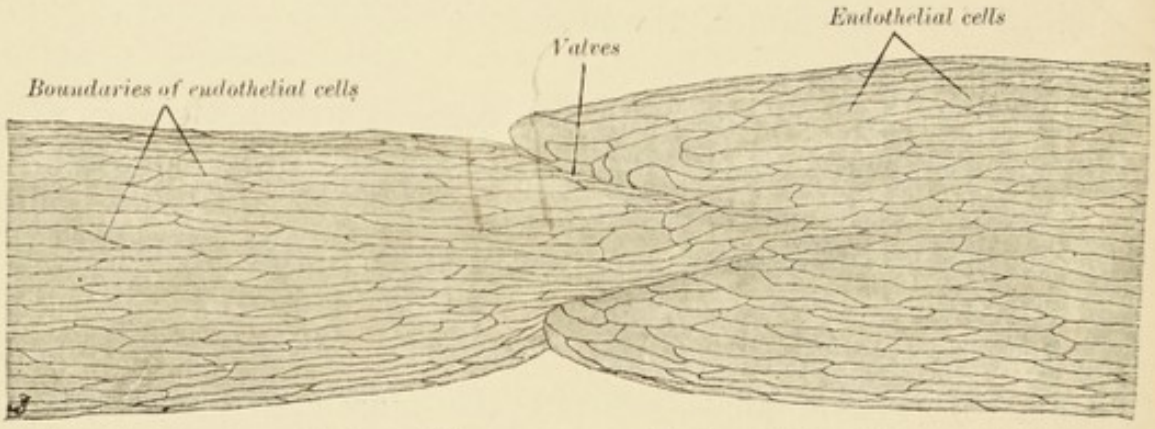
The *nerves* are derived from the cardiac plexus, the vagus, and the sympathetic system. They are both medullated and non-medullated, partly motor and partly sensory nerves. Small ganglia are present at various places. Concerning the mode of ending of nerves in the heart, see under Nerve-endings.

2. LYMPHATIC SYSTEM.

(*a*) Lymph-vessels.

The lymph capillaries are not, like the blood capillaries, intermediate structures situated between two other systems. They form the beginning of a great lymphatic system which empties finally into the blood vascular system. The walls of the lymph capillaries consist of a flat endothelial tube, the

FIG. 93.



Piece of a lymph-vessel of a rabbit's mesentery. The boundaries of the endothelial cells are made visible by silver nitrate. × 235.

boundaries of whose cells are irregular. The capillaries form networks that have a characteristic appearance on account of the unevenness in calibre of the vessels. There are many dilatations and constrictions, and in many places valves are present (Fig. 93).

The walls of thicker lymph-vessels resemble in structure those of veins. There is an endothelial lining, an intima containing elastic fibres, a media consisting largely of smooth muscle, and an adventitia. The latter is made up of longitudinal connective-tissue bundles which contain elastic fibres and longitudinally disposed smooth muscle bundles.

Development of Lymphatics.

The problem as to the origin of the lymph-vessels is one which is not yet satisfactorily solved. While some authors believe that the lymph capillaries form a completely closed system bounded by endothelial cells, others believe that they are in open communication with tissue spaces which have no endothelial lining. According to the first view, fluids must pass by endosmosis through the walls of the lymph capillaries. The second view implies that fluids pass from the tissue spaces into the lymph capillaries through the open beginnings of the lymphatics. It has been shown by Mall that no closed system of lymphatics exists in the liver (see below). It has recently been shown by Miss Florence R. Sabin that the lymphatic system in the embryo pig develops as two blind diverticula from the veins of the cervical and inguinal regions. These grow toward the skin and widen out into four lymph sacs, from which the final lymphatics proceed. By a special growth of the lymphatics along the dorsal line, the thoracic duct is formed.

(*b*) Lymph Glands.

Lymph glands are situated in the course of the lymph-vessels, and are grouped together in various places (*e. g.*, axilla, neck, groin, etc.). They vary considerably in size, and are usually bean-shaped.

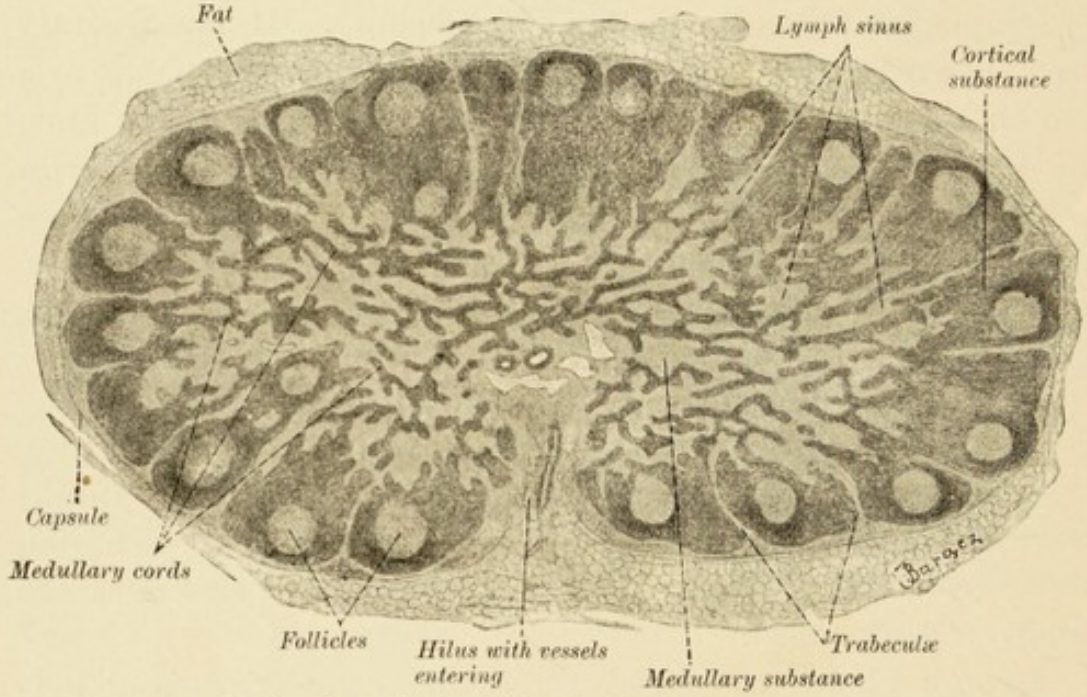
Lymph glands consist of a reticular connective-tissue network which contains lymphocytes (*adenoid tissue*). The framework of the organ consists of connective tissue with a few smooth muscle cells. The connective tissue is mostly of the kind known as reticulum. It forms at the surface of the gland a continuous covering, the so-called *capsule*. From this, leaf-like projections pass down into the substance of the gland, as shown in Fig. 94. These are called *trabeculæ*. They run in such a manner that the outer part of the gland is divided into round masses of adenoid tissue. Toward the middle of the gland they branch to form a network of connective-tissue strands, in the meshes of which are narrower masses of aden-

oid tissue continuous with the round masses outside. The gland is thus divided into two zones, a *cortex* and a *medulla*.

The cortex is divided by the trabeculæ into *follicles*, while the medulla consists of much smaller masses of adenoid tissue, known as *medullary cords* (Fig. 94). These are directly continuous with one another.

The reticular connective tissue which fills the spaces between the trabeculæ contains very few lymphocytes in the immediate neighborhood of the trabeculæ and the capsule. Farther away from these, however, the lymphocytes are very numerous and

FIG. 94.

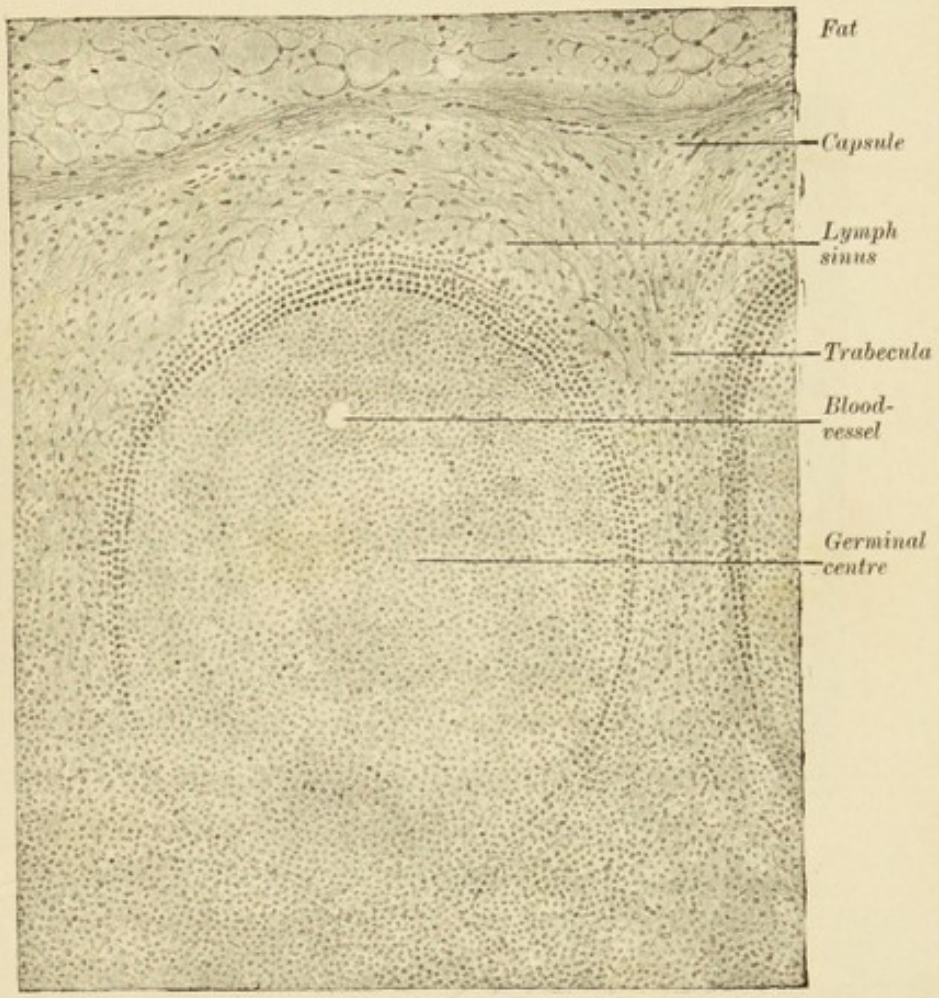


Section through a small lymph gland of a dog. × 20.

make up the follicles and lymph cords. These latter masses are therefore surrounded by almost empty spaces which separate them from the trabeculæ and capsule. These spaces are called *lymph sinuses* (Fig. 96). They contain a fine reticulum, which passes over the trabeculæ on one side and the follicle on the other. The lymph sinus is a continuation of the lymph-vessels, and, like these, is lined with flat endothelial cells whose presence can be demonstrated by silver nitrate. This endothelium probably does not form a continuous membrane. The cells are often found separated and lying freely in the lymph sinus.

The follicles of the lymph gland consist of a dense, more or less spherical mass of lymphocytes. At its periphery next to the lymph sinus these cells are much crowded together, while in the centre there is always a more or less clear space where the lymphocytes are much less abundant. Here there are usually found an artery and one or more veins. By close observation karyokinetic figures may nearly always be found in this region.

FIG. 95.



From the cortex of a dog's lymph gland. × 150.

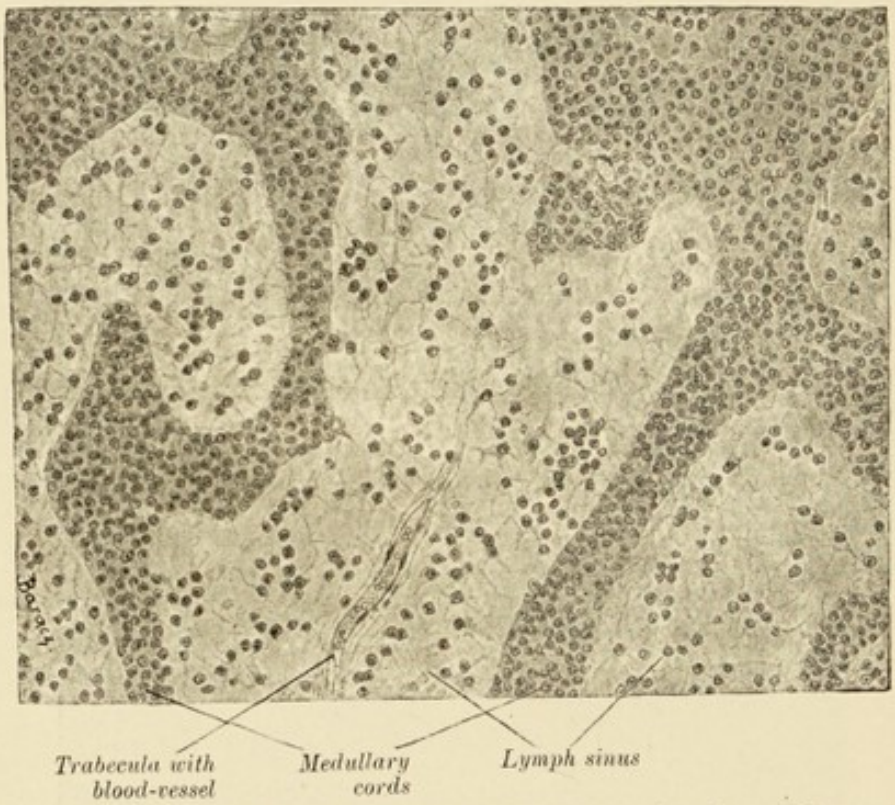
According to Flemming, the reproduction of lymphocytes takes place in the centre of the follicle, and this area is known as the *germinal centre* (Keimcentrum) (Fig. 95).

The *afferent lymph-vessel* enters the gland usually at one pole, and after dividing passes through the capsule. Its walls become always thinner until, on forming the lymph sinus, they

consist only of an endothelial layer. The lymph sinuses pass from the cortex to the medulla, join together, and leave the gland at the *hilus* by the *efferent vessel.* At this place the capsule is thick and compact, and is known as the *hilus stroma.* The *sinus terminalis* is formed at the hilus by the junction of the other lymph sinuses.

The *blood-vessels of the lymph gland* were described in detail by Calvert, and worked out in relation to the follicle of the gland. The following account is based on his description: The

FIG. 96.



From the medullary substance of a cat's lymph gland. × 250.

gland is supplied with arteries mainly from the hilus, but also to some extent from the capsule. The arteries at the hilus leave the stroma-substance and enter the trabeculæ, in which they run for a short distance. After leaving the trabeculæ they enter the medullary substance and break up into smaller arteries, sometimes sending a small branch to anastomose with the arteries of the capsule (Fig. 97, E). Other arteries at the hilus run directly into the gland substance and enter the medul-

lary cords, giving off fine branches to form capillary plexuses around their peripheries (Fig. 97, F). These capillaries unite to form small veins (G), which empty into larger veins. The arteries supplying the follicles of the cortex (H) break up into many branches, which run from the centres of the

FIG. 97.



Composite section of three follicles and the medullary cords of the mesenteric lymphatic gland of a dog. × 50. (Calvert.) A, artery; B, medullary artery; C, follicular vein; E, artery going to the capsule; F, capillaries on the periphery of a cord; G, medullary vein; H, follicular artery; I, arterial capillaries in a follicle; J, vein from capsule; K, cord; L, trabecula; V, vein.

follicles to the periphery, where they form capillary networks. These capillaries unite to form the venæ folliculi (C), which give origin to the larger veins of the gland returning to the hilus.

It is seen that in this system there is a blood vascular unit

which is repeated many times to make up the organ. It corresponds also in this case with the cellular unit which is represented by the follicle.

(*c*) Peripheral Lymph Nodules.

Collections of lymphoid tissue are present in many organs in the form of single follicles, or many of these together. They are not so definitely connected with the lymph-vessels as the true lymph glands are. They may occur merely as a diffuse infiltration of the tissue by lymphocytes. The so-called *solitary follicles* of the alimentary canal are definite well-circumscribed masses of lymphocytes, possessing germinal centres, and all the characters of lymph follicles. Collections of these follicles are seen in the Peyer's patches of the small intestine.

3. SPLEEN.

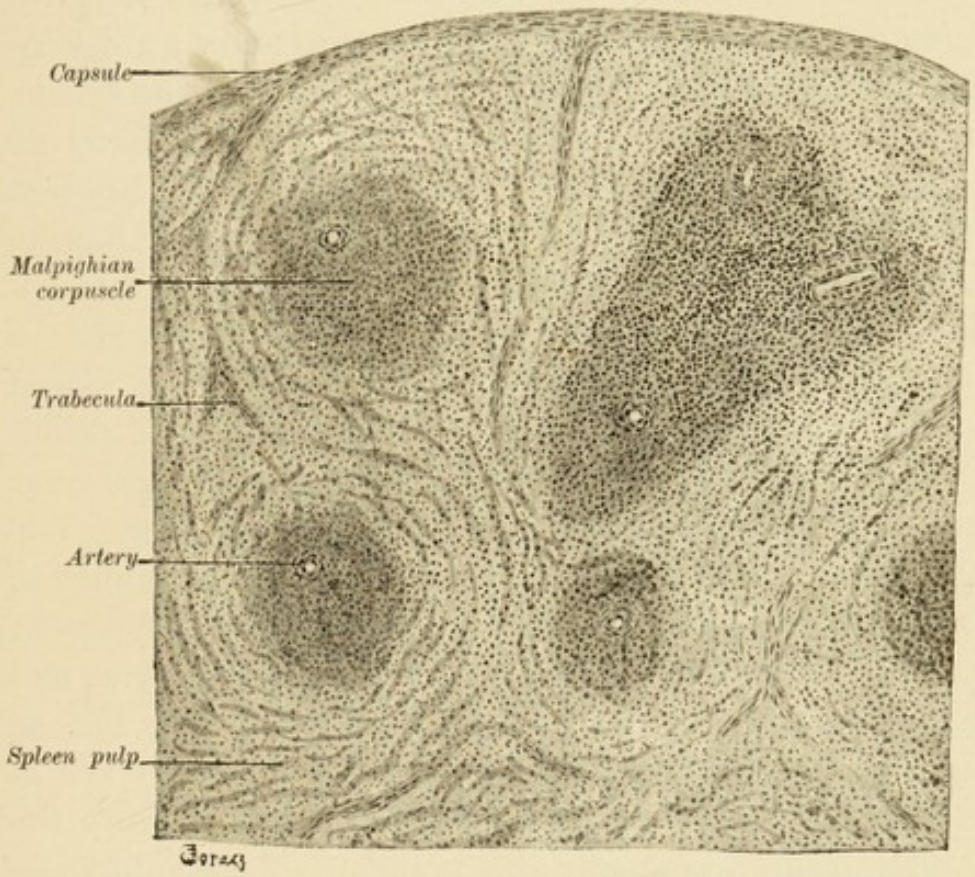
In the spleen, as in the lymph gland, we can distinguish a connective-tissue *capsule*, sending processes down into the organ to form its framework; and adenoid tissue contained in the framework, the so-called *spleen pulp*.

The capsule and the trabeculæ proceeding from it are made up of connective tissue with a considerable number of smooth muscle cells and elastic fibres. They can be easily distinguished from the corresponding structures in the lymph gland by their strong, coarse appearance. They are nearly always thicker, and the muscle cells give to them a less finely fibrous character. At the hilus the trabeculæ and capsule form a sheath for the blood-vessels which enter there. This sheath retains its firm fibrous character throughout the course of the veins, but with the arteries it gives place to a fine reticular tissue when these vessels by branching have become as small as 0.25 mm. in diameter. This reticular tissue contains in its meshes large quantities of lymphocytes.

The arterial sheath, consisting of adenoid tissue, forms, in some animals, a continuous layer around the vessel wall. In other animals, however, it is gathered into spherical or ovoid masses which resemble the follicles of the lymph gland. These

are the *Malpighian corpuscles* (Fig. 98). If the lymphoid tissue is equally distributed around the artery, this vessel is found in the centre of the Malpighian corpuscle. It may be placed excentrically, on account of the unequal development of this tissue. In sections of the spleen the Malpighian corpuscles are round structures with a diameter of 0.2–0.7 mm. They are situated often at the place where an artery branches, and each shows a germinal centre (Keimcentrum), in which there is multiplication of the lymphocytes.

FIG. 98.



Part of a section through the spleen of an ape. × 60.

The spleen pulp has the characteristic features of adenoid tissue. It consists largely of lymphocytes, but contains also large cells, with many nuclei containing red blood-corpuscles and pigment. Nucleated and non-nucleated red corpuscles are also found.

The pigment granules which occur free or in leucocytes are formed from broken-down red blood-corpuscles. The

adenoid tissue of the pulp is distinguished from that of the Malpighian bodies by the fact that the latter consists entirely of lymphoid cells.

Some authors claim that the spleen is a blood-forming organ because erythroblasts are found there. Others regard it as an organ in which destruction of blood takes place, for the reason that fragments of blood corpuscles and blood pigment are frequently found.

The character of the blood-vessels in the spleen shows some peculiarities. The arteries do not anastomose with one another; their adventitia often shows a lymphoid character—*i. e.*, in Malpighian corpuscles. The terminal arteries show a thickening of this lymphoid sheath to form the *ellipsoids* of the spleen. In their final divisions the arteries branch like the hairs of a brush (*penicilli*). The blood-vessels of the spleen are best considered together with the so-called *lobule.* According to Mall, the framework of the spleen, which can be demonstrated by washing out the cellular elements of a spleen macerated in water, is divided into sacs, each of which contains a spleen lobule. These lobules have a distinct relation to the blood-vessels. By injecting the vessels with celloidin or agar-agar and macerating the tissue, this relation is demonstrated. The arteries enter at the hilus, and divide into many branches, one of which enters each lobule and passes along its centre. The veins are always intimately related to the trabeculæ, and are always found at the periphery of the lobules. This is shown in Fig. 99. The Malpighian corpuscle usually lies at the hilus end of the lobule—*i. e.*, at the side away from the capsule. The veins accompany the branches of the interlobular trabeculæ into the lobule, which is divided by these branches into several compartments. The veins as well as the trabeculæ may be spoken of as interlobular and intralobular. The central artery of the lobule branches to supply the various compartments formed by the intralobular trabeculæ, and the blood is collected finally by the intralobular veins. A venous injection of the lobule fills a plexus of veins (Fig. 99, P), in whose meshes there are small areas of spleen pulp, the so-

PLATE VI.

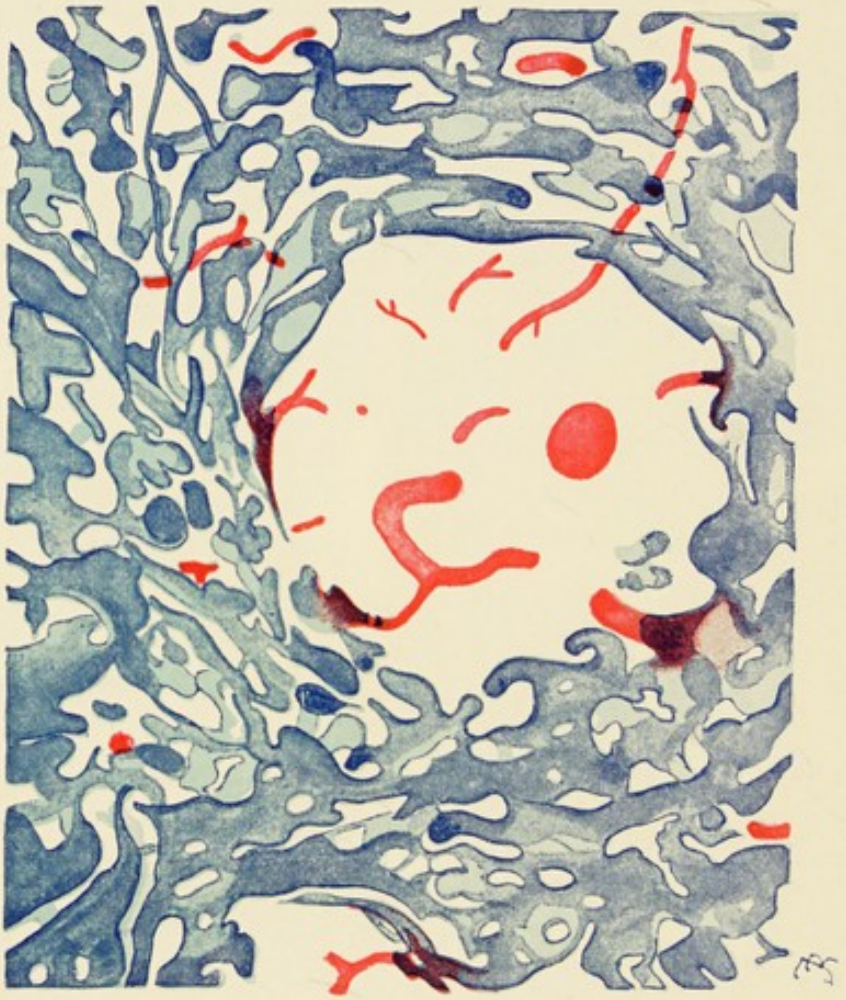


FIG. 100.—From the spleen of a rabbit. The blood-vessels are doubly injected, the veins blue, the arteries red. In the centre a Malpighian corpuscle is shown. × 100.

called *histological units* (Mall). These units are, however, in communication with one another. The terminal arteries run into these units and end in the *ampullæ of Thoma*, a small

FIG. 99.

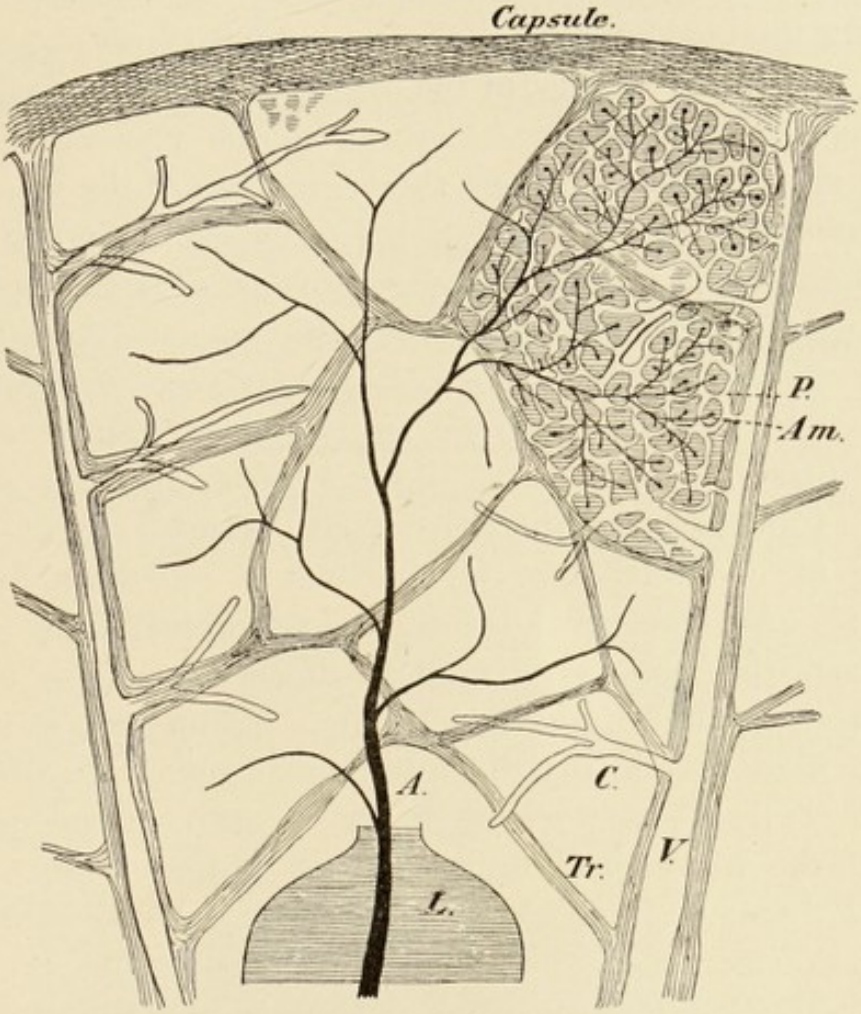


Diagram of the lobule of the spleen. (Mall.) *A*, artery in the centre of the lobule; *V*, interlobular vein within the interlobular trabeculæ; *Tr.*, intralobular trabeclæ; *L*, Malpighian follicle; *C*, intralobular collecting vein; *P*, intralobular vein plexus which surrounds the pulp cords or histological units; *Am*, ampulla of Thoma.

dilatation. There is evidence to show that these ampullæ communicate both with one another and with the terminal veins.

According to some authors, the capillaries open directly into the veins, while others have described a system of lacunæ between them. This is known as the intermediary path for the blood. The capillaries show a funnel-like widening as they pass over into the veins (Plate VI., Fig. 100). This interme-

diate space is, according to some authors, lined with epithelium, so that there is here a closed system. Most authorities, however, claim that these lacunæ have no wall or possess only an incomplete wall, so that the blood does not flow in a closed channel. These authors base their belief on the fact that in injecting the blood-vessels the injection mass flows also into the spleen pulp; and because of the constant presence of red blood-corpuscles in the pulp. According to the view held by the second group of investigators, the beginnings of the veins stand in communication with spleen pulp. These endothelial cells are flattened and spindle-shaped, and show a striated structure. The nuclei project markedly into the lumen. According to Weidenreich, there is a system of spaces (*spleen sinuses*) in the spleen pulp which anastomose freely and open into the pulp veins (intralobular).

The framework of the spleen pulp is made up of anastomosing fibrils which have the character of reticulum, as shown by Mall. As mentioned before, the reticulum of the capsule and trabeculæ is more resistant to the action of the ordinary reagents than that of the spleen pulp. "The main strands of the reticulum accompany the interlobular venous plexus, while a more delicate network with more open meshes extends through the histological unit. In the centre of the unit the network becomes dense again, which marks the position of the terminal artery with its accompanying ellipsoid lymphatic tissue" (Mall). The reticulum surrounds the veins, and also forms a layer around the arteries, holding in its meshes the cells of the lymphoid sheath. Kyes has shown that the network surrounding the smaller veins is not elastic tissue, but is made up entirely of true reticulum. The reticulum of the follicles is directly continuous with that of the pulp cords.

Lymphatic vessels in relation to the Malpighian follicles do not exist in the spleen. In the capsule and trabeculæ of the spleens of certain animals there are large lymphatic channels. These are seen also at the hilus of the organ, but, according to Mall, the lymphatics are not to be observed in the spleen pulp.

Much of the above description is based on the work of Mall. For further details the reader is referred to his articles on the subject.

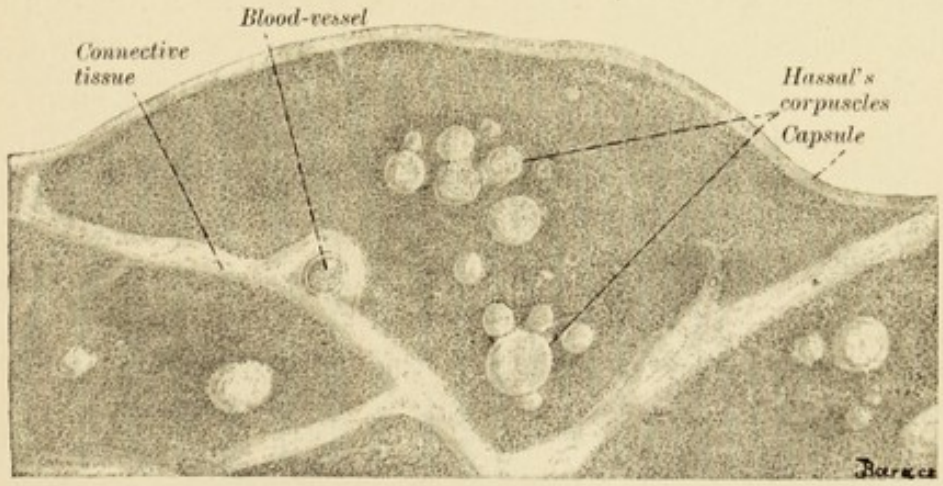
4. THYMUS.

The thymus is a gland-like organ found only in embryos and young animals. It undergoes with age a retrogression, and at the twentieth year in man we find only a connective-tissue vestige of it.

In the first years of life the thymus consists of various lobes, which are made up of lobules 0.5 to 1 cm. in diameter, joined together by connective tissue. These lobules consist of smaller lobules about 1 mm. in diameter, which are separated by connective-tissue septa. The smaller lobules are made up of adenoid tissue, which is richer in blood-vessels and lymphocytes at the periphery than at the centre. We may thus distinguish a dark cortical substance and a light medulla.

The thymus is of epithelial origin, and develops later its adenoid structure. It is an outgrowth from the foregut of the embryo, and, according to the majority of authorities, the

FIG. 101.



Section through a secondary lobule of the thymus of a child six months old. × 50.

Hassal's concentric corpuscles which are found in the medullary substance are the remains of this epithelial tissue (Stieda, His, Maurer, etc.). These corpuscles (Figs. 101 and 102) consist at

the periphery of concentrically arranged semilunar cells, while the centre usually contains nuclear and cell detritus.

According to Afanassiew, the Hassal's corpuscles arise from vascular epithelium, which in the involution of the organ proliferates until it fills the lumen.

It seems that the thymus at first takes part in the formation of red and white blood-corpuscles. Nucleated red corpuscles and evidences of mitotic division are met with frequently.

FIG. 102.



Two Hassal's corpuscles from a section through the thymus of a child six months old. × 470.

The arteries which extend into the interior of the lobule from the connective-tissue septa break up at the inner boundary of the cortical substance to form a fine capillary network. Some of the branches of this supply the cortex and empty into the veins at the periphery; while other branches run to the medullary substance, from which veins collect to carry the blood back to the connective-tissue septa.

Fine nerve plexuses have been observed in the septa and in the medullary substance.

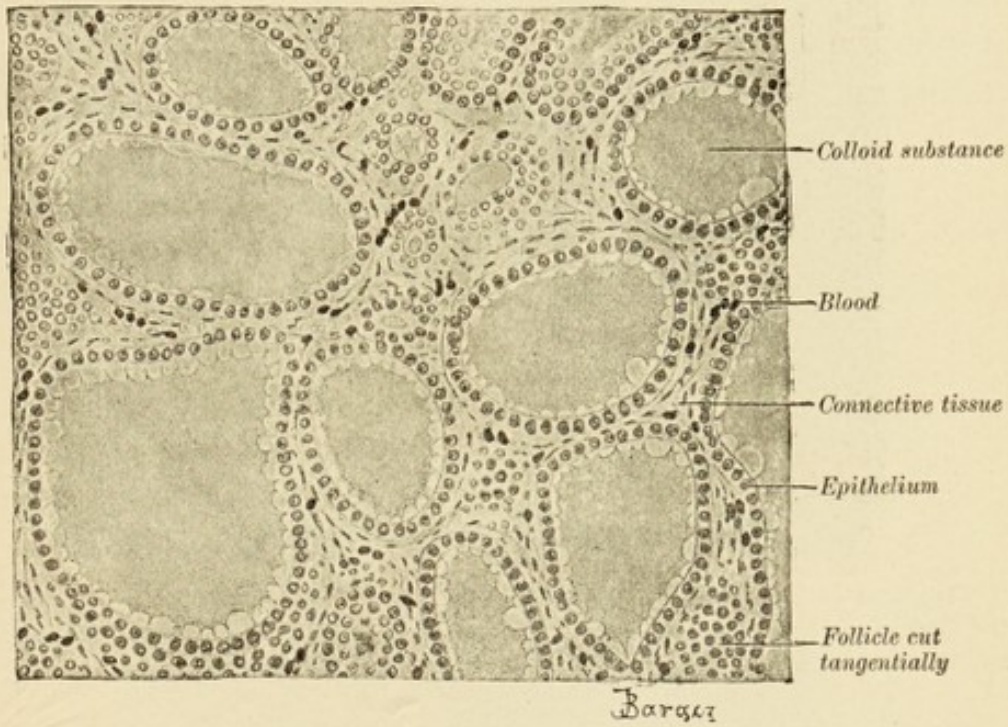
5. THYROID GLAND.

The thyroid is an alveolar gland possessing no duct. It consists of a connective-tissue framework in the form of an outer capsule, with strands of connective tissue dividing the gland into lobules, and finer septa separating the individual alveoli which make up the secretory portion.

The alveoli are round, oval, or polygonal on section (Fig. 103), and, taken as a whole, are somewhat bent or coiled closed tubes. They are lined with one layer of cubical or low cylindrical epithelial cells. These have a nucleus near the centre of the cell, and often refractive granules in the protoplasm. According to some authors, there is a membrana propria outside the epithelium. The cells formerly known as chief cells and colloid cells represent different stages in secretion seen in the same cell.

The alveoli contain a colloid substance secreted by the epithelial cells. This does not usually fill the whole lumen, but is

FIG. 103.



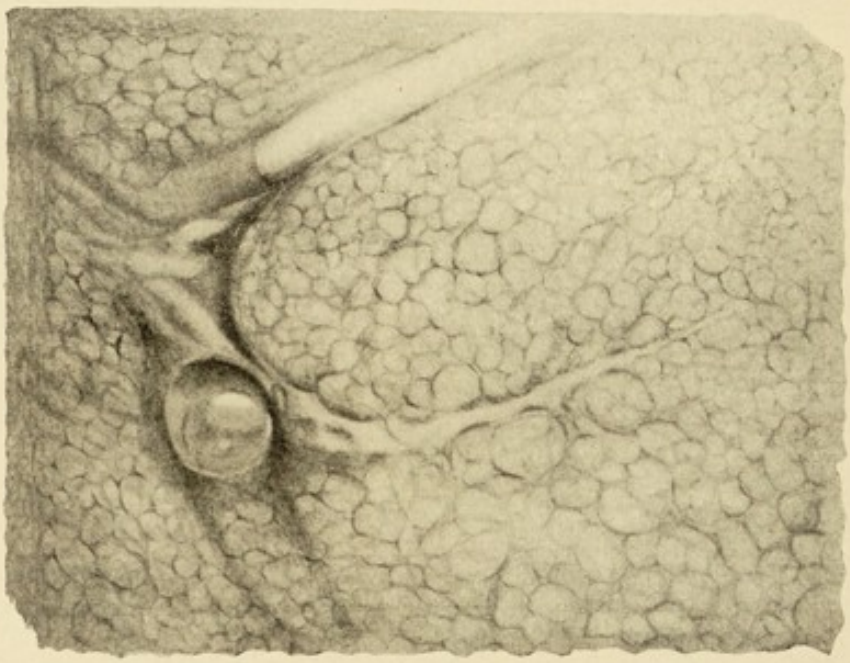
Part of a section through a human thyroid. × 180.

separated from the walls, especially in hardened specimens, by clear spaces, as though the colloid had clung to the walls at various places, but was pulled away in the intervals (Fig. 103). The colloid takes a characteristic eosin stain and appears to be quite homogeneous. Whether this colloid has any part in the formation of the internal secretion which is characteristic of the thyroid is not known. It is possible that the colloid corresponds with the external secretion of glands that have ducts,

and that the internal secretion is taken up directly by the blood capillaries, which form a thick network around the alveoli. Changes take place both in the epithelium and the colloid in hypertrophy of the gland, and in such cases symptoms show that the internal secretion also is altered, either in quantity or quality, or in both.

The interalveolar connective tissue brings many blood-vessels, lymphatics, and nerves to the organ. The blood-vessels form a rich capillary network around the alveoli.

FIG. 104.



Digested section of a human thyroid (Flint), showing the framework of the gland and the form of the alveoli. (Fixed in Van Gehuchten's fluid, hardened, extracted with ether, and digested with pancreatin, and cleared in glycerin.)

The framework of the thyroid has been studied by Flint. The gland was hardened and then digested in pancreatin until all cellular elements had disappeared. The main bundles of connective tissue follow the large vessels. More delicate strands form the supporting membranes of the alveoli. The basement membranes stand out clearly, and the form of the alveoli can be made out (Fig. 104). The alveoli are spherical structures, which lie close to one another, and are separated by a very little connective tissue. The basement membranes

are made up of fine interlacing or parallel fibrils of reticulum which are somewhat coarser than in other organs.

Parathyroid Gland.

The parathyroid is a paired gland closely associated with the lateral lobes of the thyroid. It is composed of solid columns of epithelium-like cells. These columns are separated by a very vascular connective tissue, and anastomose with one another so as to form a network similar to that found in the suprarenal gland. Masses of lymphoid tissue are frequently found in connection with the parathyroids.

According to some authors, these bodies represent embryonic thyroid tissue. Others believe them to be separate organs having a function of their own. If the thyroid be removed and the parathyroids left, the effects of a complete thyroidectomy are not obtained.

6. ADRENAL (SUPRARENAL GLAND).

This is a small gland situated just anterior to the kidney,

FIG. 105.



Part of a cross-section through the adrenal of a dog. *Z. gl.* represents the zona glomerulosa. × 22.

often resting upon it. On sectioning, it can be seen with the naked eye to be made up of a *cortex* and a *medulla*. The cortex

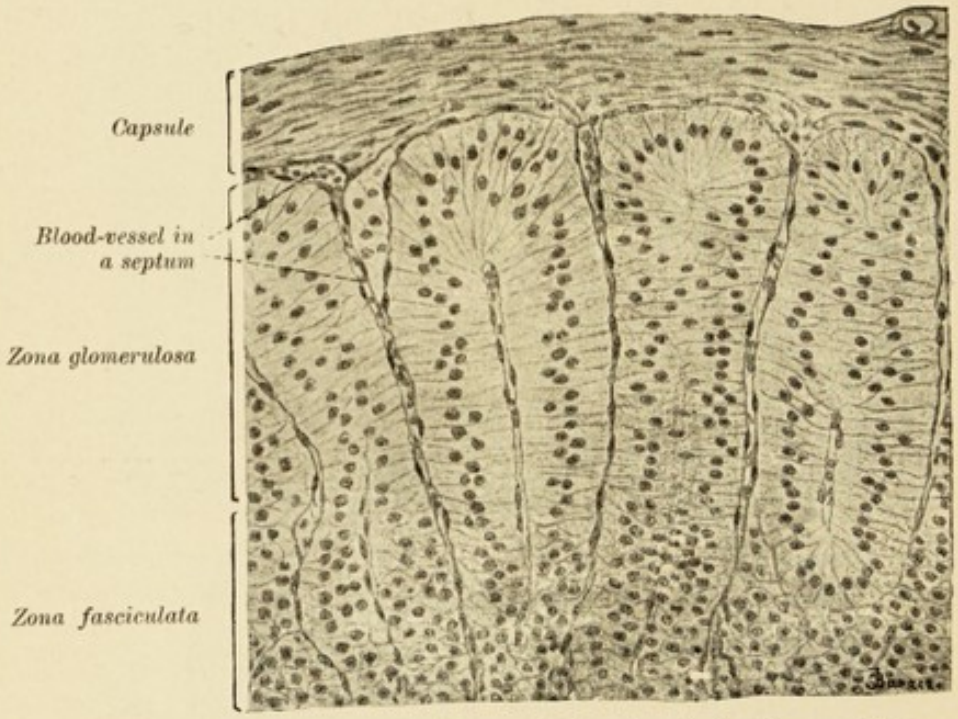
shows a radial structure, which is caused by the radial arrangement of the connective-tissue framework (Fig. 105). In the medulla the cells are arranged less regularly. The following description is based largely on an account of the structure of the gland given by Flint.

The whole gland is surrounded by a *capsule* (Fig. 106), which is composed largely of reticulum. Elastic fibres and smooth muscle cells are also present.

The *cortex* may be divided into three layers: 1, the zona glomerulosa; 2, the zona fasciculata; and 3, the zona reticularis (Figs. 105–107).

1. The *zona glomerulosa* is made up of cylindrical epithelial

FIG. 106.



From the cortical substance of the adrenal of a dog. × 245.

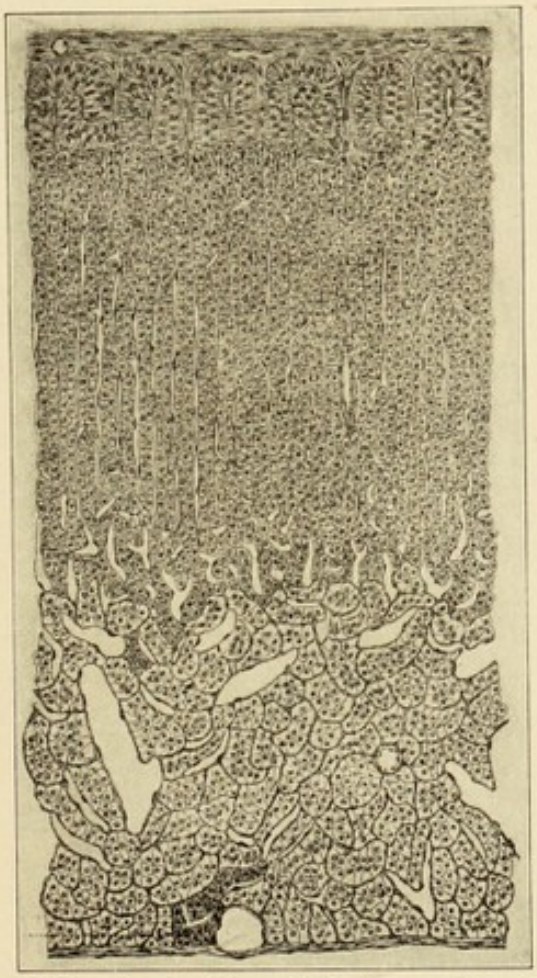
cells arranged in more or less coiled columns separated by strands of connective tissue derived from the capsule (Figs. 106, 107). The nuclei are situated in the middle part of the cell bodies. They are oval or round, and stain deeply.

2. The *zona fasciculata* consists of smaller polygonal cells arranged in anastomosing columns whose long axes are at right angles to the surface of the capsule. The columns are sepa-

rated by blood capillaries. The cells possess a granular protoplasm which often contains fat droplets. The nuclei are placed centrally, and are vesicular in character.

3. The *zona reticularis* is composed of cells somewhat similar to those of the zona fasciculata. They are arranged in columns which form a distinct network, as shown in Figs. 105 and 107. They occupy the meshes of a fine capillary plexus.

FIG. 107.



Longitudinal section of the adrenal of an adult dog. × 150. Hardened in corrosive acetic mixture and stained with iron hæmatoxylin and erythrosin. (Flint.)

The *medulla* consists of polygonal cells with lightly staining protoplasm and deeply-staining nuclei. They are grouped together into round or oval masses, which are surrounded by numerous blood-vessels and separated by septa of reticulum. The cells often surround a blood-vessel like the epithelial cells of a gland duct.

According to Flint, lymphoid nodules with germinal centres are found sometimes in the medulla of the adrenal, and scattered groups of lymphoid cells also in the cortex.

Blood-vessels of the Adrenal.—These, as they occur in the dog, have been described in detail by Flint. In the capsule the suprarenal arteries form a poorly defined plexus from which the whole gland is supplied. Three systems of arteries are derived from this plexus, supplying the capsule, cortex, and medulla, respectively. The *arteriæ capsulæ* form a network of capillaries in the capsule, which empty into the capsular venous plexus, which lies just beneath the arterial plexus. The *arteriæ corticis* break up into a capillary plexus surrounding the cell columns of the zona glomerulosa, from which the blood flows into the parallel capillaries of the zona fasciculata, and thence into the network of the zona reticularis. These capillaries empty into five veins which join to form the larger trunks of the medulla. "The *arteriæ medullæ* which run from the capsule entirely through the cortex without anastomosing break up into a capillary plexus in the medulla." The blood flows from this plexus into the fine veins of the medulla, and finally into the vena centralis. Usually two large venous trunks are present in the medulla, one draining the anterior and one the posterior lobe. These receive branches on all sides from the peripheral parts of the medulla. The relations of these vessels can be made out in Fig. 108. Lymph-vessels form capillary networks around the cell columns.

The *framework* of the adrenal has been described by Flint. According to him, it consists of reticulum. That of the zona glomerulosa consists of septa derived from the capsule. These separate the coiled columns of cells making up this zone. The framework of the zona fasciculata is made up of parallel strands of reticulum running at right angles to the capsule. These pass over into the framework of the zona reticularis, which has the form of a spongy network of fibrils. The medulla is supported by strands of reticulum which surround the cell groups.

Development of the Adrenal.—It has been stated that the

PLATE VII.

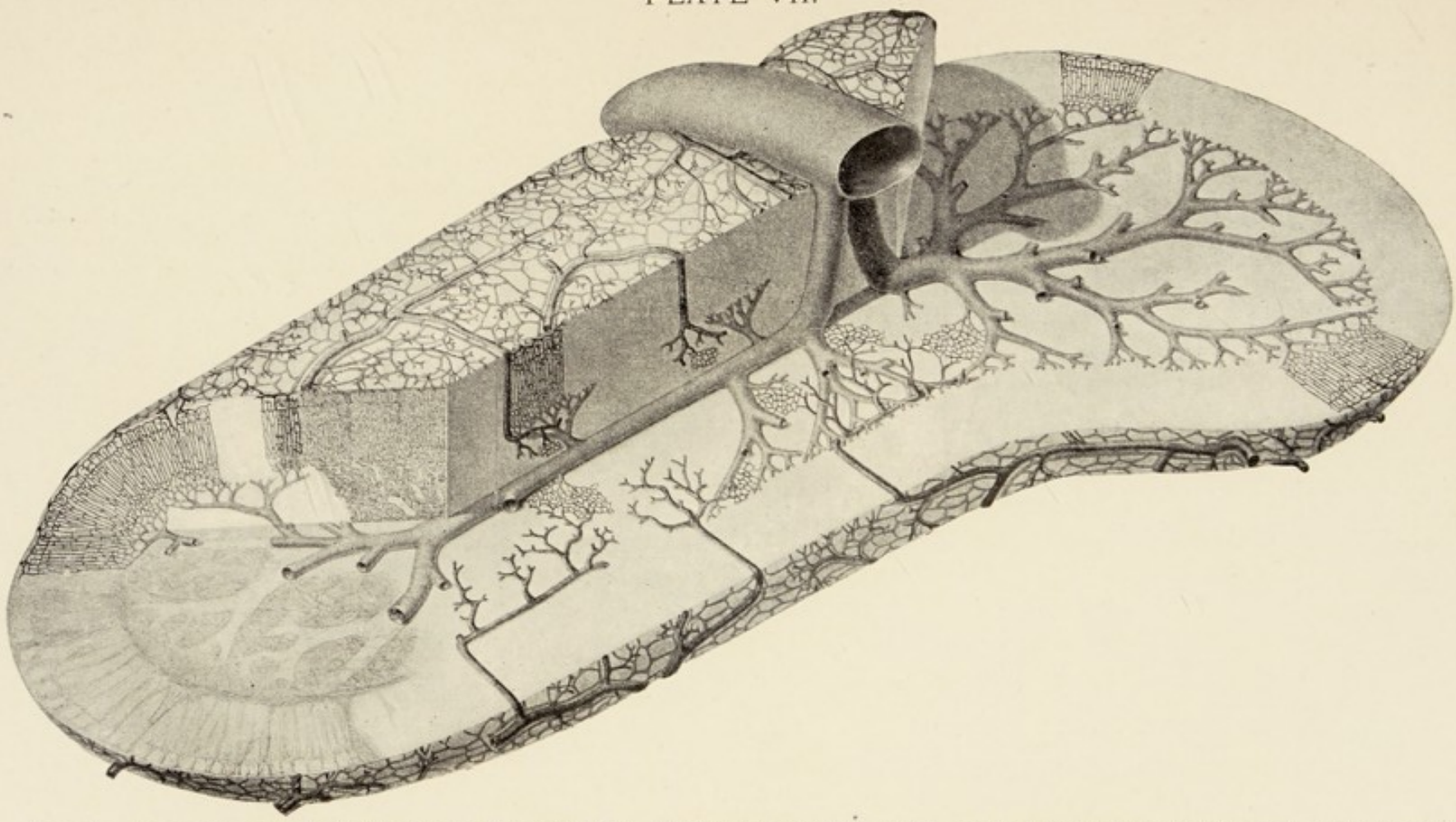


FIG. 108.—Reconstruction of the left adrenal of an adult dog. Slightly schematized. × 25. Viewed from the ventral surface. The reconstruction was made from a model of the gland, and it represents the combination of a series of drawings of actual injected specimens. The histological structure and reticulum, as well as the blood-vessels, are shown. (Flint.)

cortex and the medulla of the adrenal have different origins. According to Mitsukuri, the cortex is derived from the mesoblast, while the medulla arises from the peripheral part of the sympathetic nervous system. Gottschau believes that the medulla is derived from the cortex, and that the nervous system takes no part in its formation. This latter view is supported by Janošik, Minot, and Inaba. Flint is of the opinion that the medulla is formed separately and grows into the cortex subsequently. From his description it appears that the adrenal in a pig's embryo 3½ cm. long consists entirely of cortex surrounded by a delicate capsule. In its centre is a vein toward which capillaries converge. By its medial surface the capsule is attached to the sympathetic plexus. Beneath the capsule there appear small groups of cells, which are quite distinct from the cortical cells, and form the beginning of the medulla. These receive their blood supply from the capsular vessels, and grow into the interior of the gland until they reach the central vein. At this stage no differentiation into layers is visible in the cortex. In embryo pigs 10 cm. long the zona glomerulosa is first seen. The arrangement of the cells into definite columns does not take place until after birth. On account of peculiarities of this development certain variations from the normal are observed in the adrenal. Islands of cortical substance may be found in the medulla, and similarly small groups of medullary cells sometimes are seen in the cortex. The medulla in certain places may extend out to the capsule; and in other places the cortex is found adjacent to the central vein.

It is still uncertain what the exact origin of the medullary cells is. They develop after the cortical cells are laid down and grow in from the periphery of the cortex. They do not seem to be derived from the sympathetic nervous system, although the relation of the gland to this system is intimate, and there are often found large numbers of ganglion cells included in the cortex and medulla.

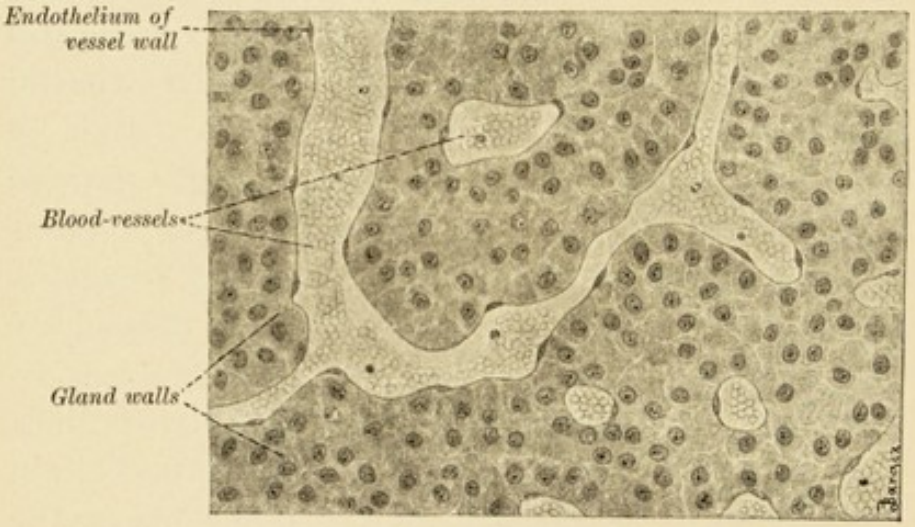
Non-medullated nerve fibres penetrate the capsule and extend in large numbers through the cortex and medulla. In the cortex they give off fine branches which end on the sur-

faces of the cells. In the medulla the network of nerves is much richer. A part of the branches from this end in the vessel walls, while the greater number surround the gland cells and form fine plexuses around them.

7. HYPOPHYSIS CEREBRI (PITUITARY BODY).

The pituitary body in adult animals consists of two lobes, a posterior and an anterior. The posterior lobe is made up mainly of neuroglia elements. There are, however, in this region other cells which are considered by some to be nerve cells. Their nature is uncertain. The anterior lobe consists, on the contrary, of solid glandular masses separated by connective-tissue septa and capillary networks (Fig. 109). This glandular tissue

FIG. 109.



From a section of the hypophysis cerebri of a dog. × 300.

consists of epithelial cells, concerning whose glandular nature there can be no doubt. They are round or polyhedral, and, according to some authors, are of two types. One kind of cell is of dark appearance, large and granular, and has a marked affinity for staining fluids. These are called *chromophile cells.* The other kind is small and clear. The two types are about equally distributed. Other authors regard the differences in appearance between the two kinds of cells to be due to post-mortem or functional changes.

In the posterior part of the anterior lobe there are found

alveoli which, like those of the thyroid, are filled with a colloid substance. Sometimes these alveoli are lined with ciliated epithelium.

There is a close relation between the glandular elements and the blood capillaries. A dense network of vessels surrounds all the gland alveoli. The glandular nature of the organ has been further proved by physiological experiments. The internal secretion seems to have an important influence on the organism as a whole.

8. CAROTID GLAND (GLOMUS CAROTICUM).

The carotid gland is a structure the size of a grain of corn, situated, in man, at the bifurcation of the common carotid artery. It is associated closely with the vessel wall, and is surrounded by a connective-tissue capsule which sends strands of tissue into the organ. The organ thus is divided by three connective-tissue *septa* into *follicles*, which are usually small round masses of cells, the so-called *cell balls* (Zellballen) of Schaper. These follicles, or cell balls, are made up of cells containing much protoplasm and resembling epithelial cells. They are polyhedral or round, and seem to be associated closely with the blood capillaries. They are apparently of connective-tissue origin, and are arranged in small groups in the meshes of a connective-tissue network. The true nature of this connective tissue has never been determined. In all probability it is largely true reticulum. In advanced age the cell groups break up, and there is a marked increase in the connective tissue and blood-vessels (Schaper).

The carotid gland is supplied very richly with blood-vessels. A branch from the carotid artery enters the gland and breaks up into many small branches, each of which supplies one follicle. The capillaries formed by division in the follicle anastomose and make up a dense plexus, which is connected at the periphery of the follicle with small veins. These join with veins from other follicles, and form on the surface of the gland a venous plexus.

Numerous medullated and non-medullated nerve-fibres are

present in the gland, and run as fine branches into the follicles. Ganglion cells are rarely found.

9. COCCYGEAL GLAND (GLOMUS COCCYGEUM).

This organ is situated on the arteria sacralis media. Its general structure resembles that of the carotid gland. The same polygonal epithelioid cells are found, and these stand in the same close relation to the blood-vessels. Small branches of the median sacral artery enter the gland and break up into a capillary network. In the capillaries that make this up there are peculiar dilatations mainly situated on the venous side of the network.

All the glands that have been described in this section must be considered as made up primarily of two parts, namely, a connective-tissue framework, and a cellular part contained in the meshes of this framework. The cellular part is divided in each case into masses of cells (follicles or lobules), which have a similar and complete structure of their own. By the repetition of these follicles the organ is built up. The connective-tissue framework of the gland is in every case closely connected with the blood supply. The vessels follow, to a certain extent, the course of the trabeculæ and connective-tissue strands, which divide the organ into units. The cellular units (follicles or lobules) correspond often to blood vascular units, in which the artery usually enters the centre of the follicle and breaks up into capillaries which join with the veins at the periphery of the follicle. The arteries and veins are always as far apart in the follicle as possible. All these glands, then, are composite structures, so that in their study we should consider not only the units themselves, but also the relation of these units to one another and to the framework.

II. DIGESTIVE SYSTEM (ALIMENTARY TRACT).

The whole alimentary tract is lined with mucous membrane. This is a soft membrane consisting of epithelium, glands, and connective tissue. The epithelium consists of one or more

PLATE VIII.

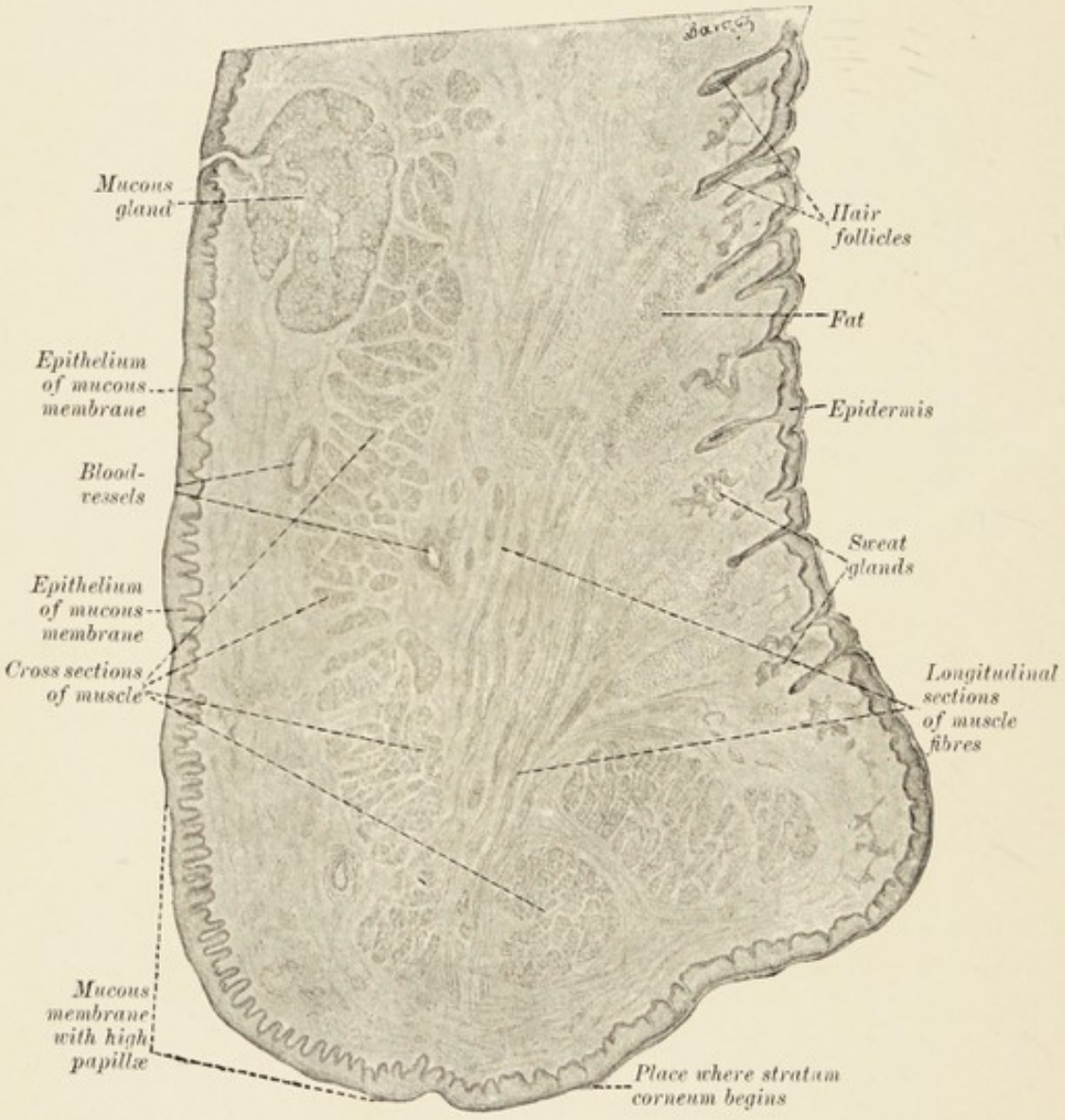


FIG. 110.—Section through the upper lip of a two and a half year old child. × 14.

layers. When there are many layers the superficial cells are flattened, as in stratified epithelium. Under the epithelium there is a connective-tissue layer, the *tunica propria* or *stratum proprium*. Under this is a firm connective-tissue coat, the *tela submucosa* or *stratum submucosum*. This combines the mucosa with the underlying parts.

A. MOUTH CAVITY.

1. Mucous Membrane of the Mouth Cavity.

The *epithelium* of the mouth cavity is a stratified pavement-epithelium. It is not, as a rule, corneous, and the stratum granulosum and stratum lucidum are usually absent.

The *tunica propria* consists of interlacing bundles of connective-tissue fibres, among which are many elastic fibres. On the surface the tunica propria forms so-called *papillæ*, of which the highest are found in the red border of the lips and in the gums (Plate VIII.). At the border of the lips we find sebaceous glands, but these are absent elsewhere in the mucous membrane.

Everywhere in the tunica propria we find the ducts of mucous glands (glandulæ buccales, palatinæ, et labiales), whose bodies lie in the submucosa. These are branched tubular glands whose ducts are lined usually with stratified epithelium. The details of their structure will be discussed with the larger glands of the mouth cavity.

The *tela submucosa* is a firm connective-tissue layer possessing only very few elastic fibres. On the gums the mucosa is attached firmly to the underlying structures. Elsewhere it is more loosely connected with the submucosa. The *blood-vessels* form two plexuses more or less parallel to the surface. The deeper, which consists of larger vessels and wider meshes, lies in the submucosa; the upper is made up of a fine meshwork of small vessels which are derived from the deeper layer and is situated in the tunica propria. From these networks fine branches proceed to the papillæ, where a capillary plexus is formed. The *lymph-vessels* follow a course very

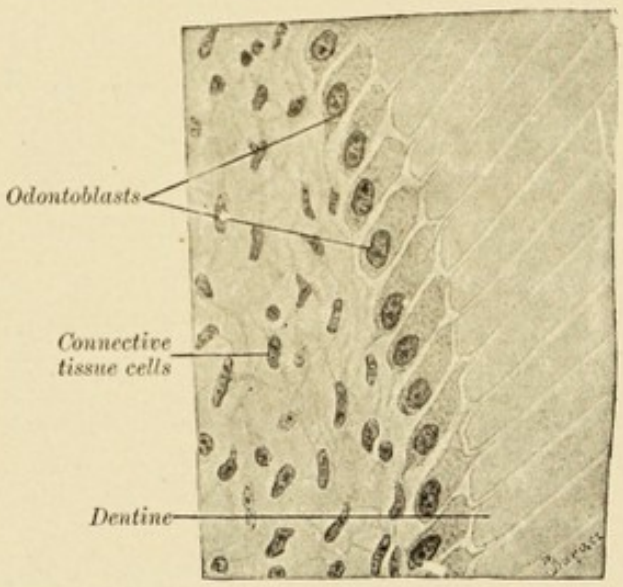
similar to that of the blood-vessels. The *sensory nerves* end in the mucous membrane in two ways: on the papillæ as *Krause's end bulbs*, and in the epithelium as fine intra-epithelial nerve-endings (see under Nerve-endings).

2. The Teeth.

The teeth in man and the higher animals are hard structures, of which one part is sunk in the alveolus of the jaw (*root*) and the other part projects to the outside, and is called the *crown* of the tooth. The place of junction of the two parts is called the *neck* of the tooth, and this part is covered by the gum.

The teeth consist of three hard substances: 1, *enamel;* 2, *dentine;* 3, *cement.* These substances surround a cavity in

Fig. 111.



From a longitudinal section of the crown of a milk tooth of a newborn baby. The boundary between pulp and dentine is shown. × 500.

the centre of the tooth known as the *pulp-* or *tooth-cavity.* This cavity extends into the root of the tooth as the *root-canal*, through which vessels and nerves enter the pulp from below.

The *tooth pulp* consists of a finely fibrous cellular connective tissue, and is characterized by its richness in nerves and blood-vessels. On the surface of the pulp there are large cells

PLATE IX.



B

FIG. 113.—From a longitudinal section of the lateral part of the crown of a human canine tooth. The canaliculi, filled with pigment, in some places extend outward between the enamel prisms. × 330.

PLATE X.

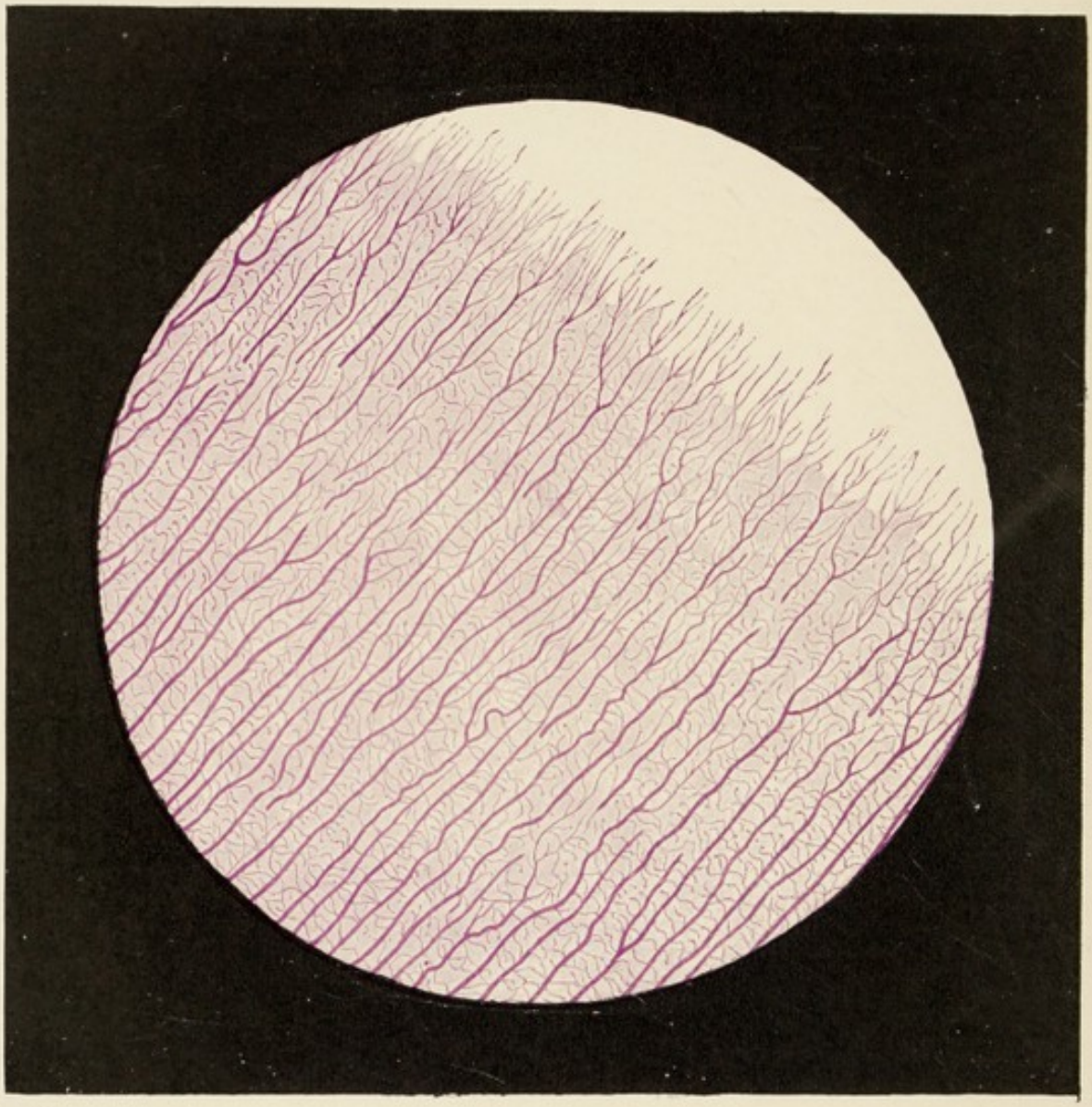


FIG. 114.—From a cross-section of the neck of a human molar tooth. The dental canaliculi show divisions and numerous anastomoses. × 330.

PLATE XI.

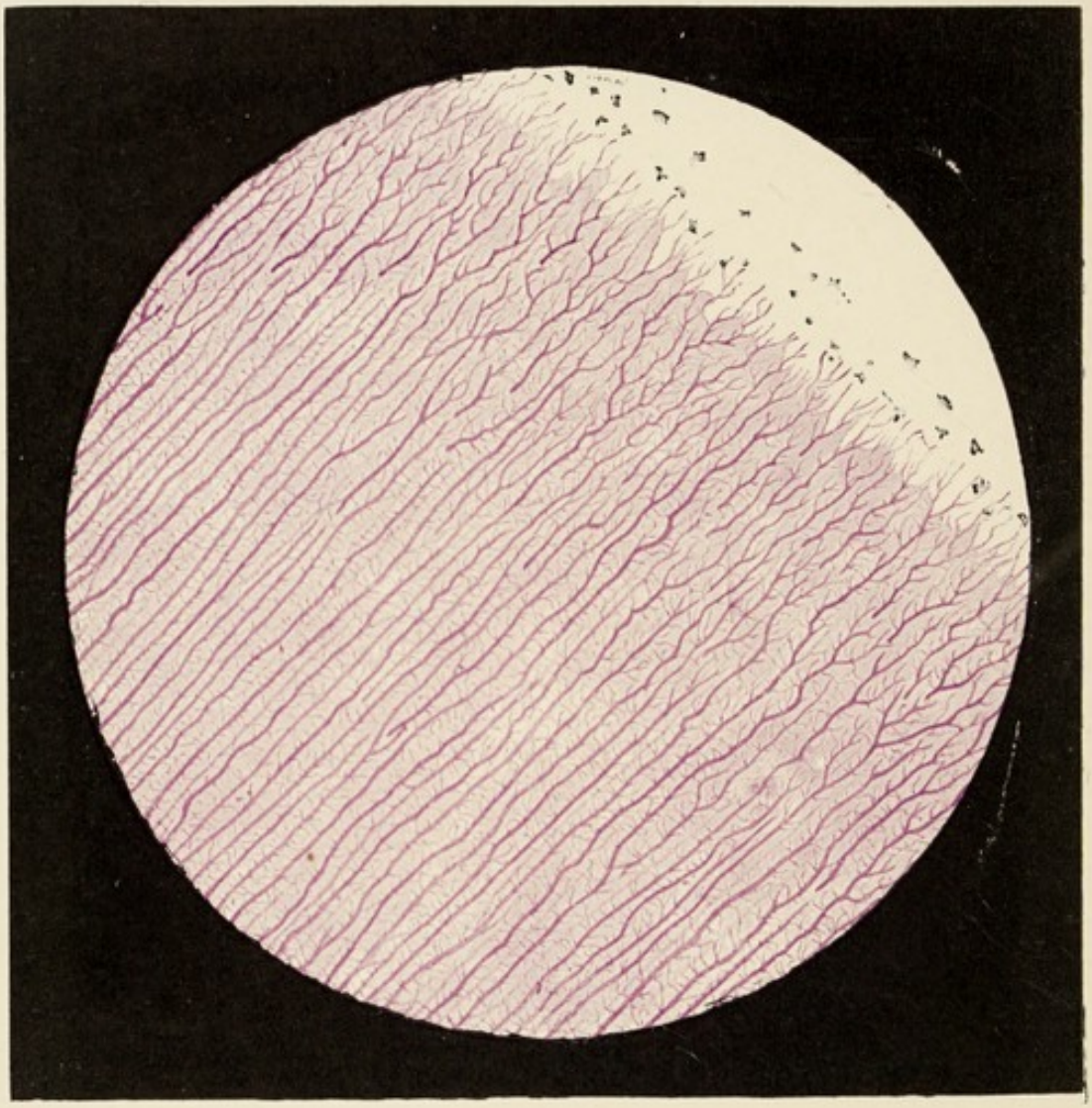


FIG. 115.—From a cross-section of the root of a human molar tooth. The canaliculi, filled with violet pigment, show numerous divisions. Small interglobular spaces are to be seen in the granular sheath. × 330.

—the *odontoblasts*—forming a continuous layer (Fig. 111). These are long cylindrical cells with the nucleus in the inner half of the cell. They each send one process, seldom more, into the dentine toward the outside. These processes form the fibres in the dentine. There are other processes sent out by the odontoblasts in the direction of the pulp. These branch and surround the pulp elements. The whole pulp is surrounded by dentine, which forms the main mass of the tooth. The dentine itself is covered entirely by two other coats, on the crown of the tooth by the enamel, and on the root by the cement. These two coats meet at the neck.

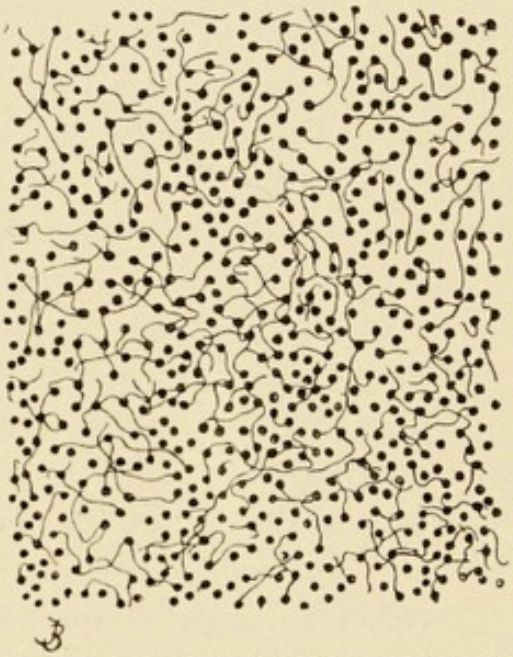
The *dentine* (substantia eburnea) is a kind of bone which is distinguished from ordinary bone by the fact that its cells are not situated in cavities of the ground substance. The cell bodies lie on the surface of the pulp close to the dentine, so that the dentine itself contains only their processes, the so-called *dental fibres*, which lie in the *dental canals*. These canals begin at the pulp surface of the dentine, and run radially toward its outer surface in a slightly curved direction, like the letter S. At their beginning the canals are 2.5–5 μ in diameter, but become narrower as they proceed outward, on account of division. At the outer surface of the dentine they measure only 0.6 μ. They give off throughout their course fine side-branches in every direction, thus joining with neighboring canals. These side-branches are usually 0.3–0.6 μ in diameter. A section cut at right angles to the course of the canals shows their relation to the side-branches. Fig. 112 shows that they join not only canals near one another, but also those at some distance from one another.

The relation of the main dental canals, as well as of the side-branches, is characteristic for different parts of the tooth (Plates IX., X., XI.). In the part near the pulp the lateral branches leave the canals at almost a right angle. In the more peripheral parts of the dentine, on the contrary, the angle is acute. In the former position the side-canals are less numerous than in the peripheral parts.

In the crown of the tooth the main canals take a fairly

straight course and do not often branch to form canals of the same calibre. In the neck they are slightly wavy. In the root they are more uneven, and branch frequently to form equal-sized canals (Szymonowicz). The peripheral ends of the main canals are different according to their surroundings. In the crown just under the enamel they break up into finger-like branches (Plate IX.), some of which run past the boundary line between the enamel and dentine for 10–40 μ

Fig. 112.



From a ground-section through the parts of the dentine, near the pulp, of a human canine tooth which has been impregnated with pigment. The dental canaliculi are cut across and are joined together by side branches. × 400.

into the cement substance joining the enamel prisms (Fig. 117). Dilatations are observed often at the ends of these branches. Most of the main canals, however, end blindly at the border of the enamel.

In the lower part of the tooth the main canals do not leave the dentine, but end blindly at the border of the cement—*i. e.*, at Tomes' granular sheath. They often reach as far as the spaces of the sheath, which are filled with uncalcified ground substance (Fig. 116). Rarely they arch over and form with neighboring canals a kind of loop.

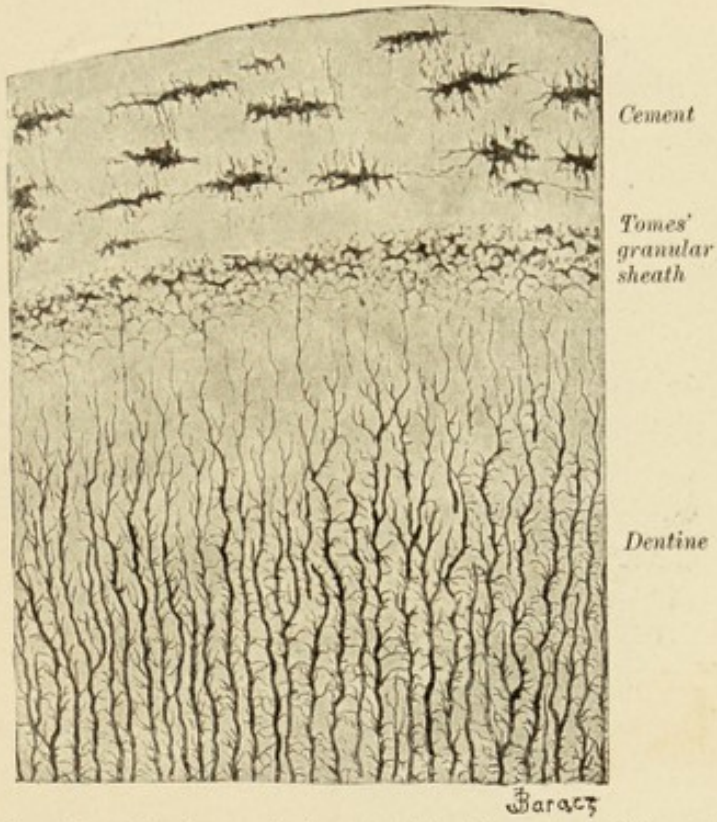
The part of the ground substance immediately surrounding

the canals is harder and more resistant than the rest, and is known as *Neumann's dental sheath.*

The *ground substance* itself has a structure finely fibrous, like that of ordinary bone. The fibrils are joined to form bundles, which run mainly in the long axis of the tooth.

In the dentine of the crown there is, near the outer enamel surface, a layer of so-called *interglobular spaces.* These are large or small spaces of irregular shape, situated in the calcified

FIG. 116.



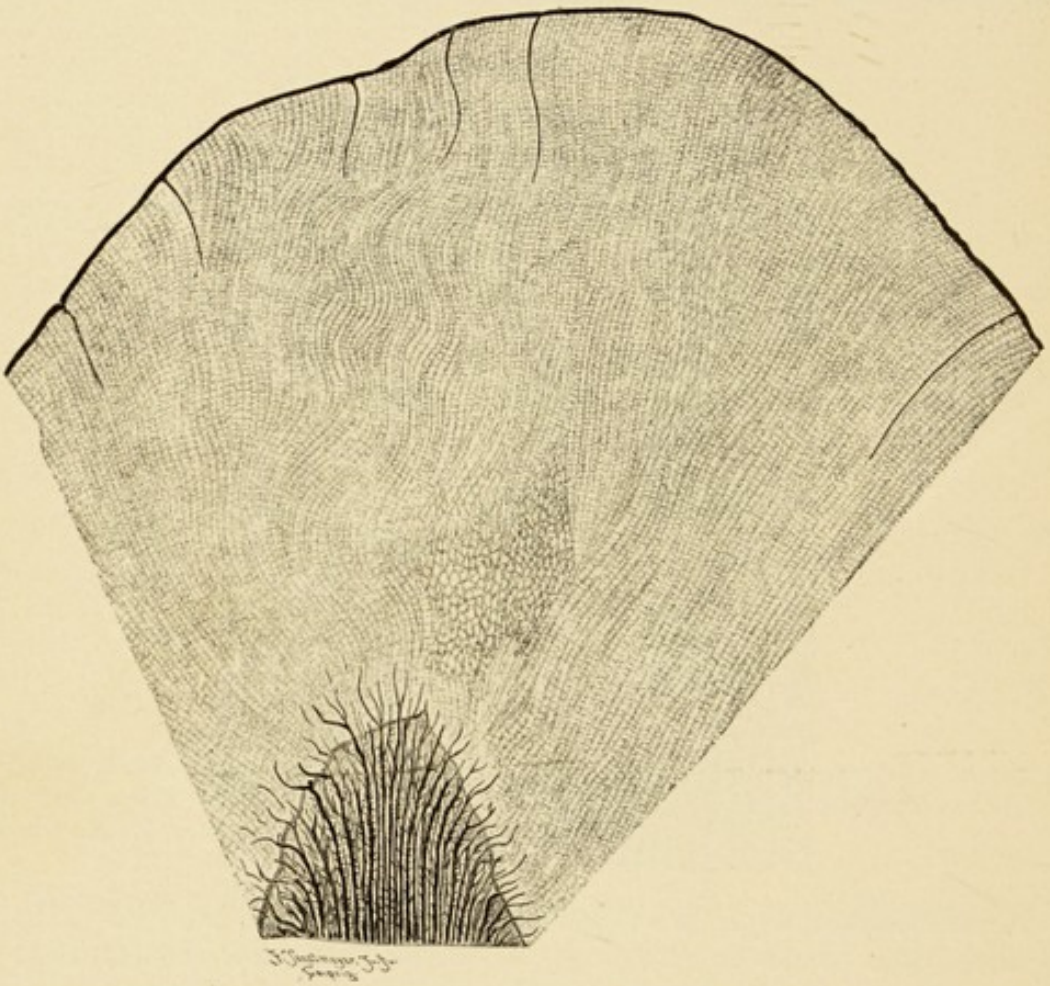
Part of a cross-section through a human incisor tooth in the region of the root. × 360.

ground substance and filled with a soft substance which corresponds with the uncalcified substance of the dentine (Plate IX.). The dental canals pass through these spaces without interruption. These spaces are an indication of the unequal and incomplete calcification of the dentine.

In the lower parts of the tooth we find in the outer part of the dentine the so-called *Tomes' granular sheath*, which is nothing more than a layer of small interglobular spaces (Fig. 116).

The *enamel* (*substantia adamantina*), which is the hardest of all animal tissues, contains only 3–5 per cent. of organic substance. It is soluble in dilute acids without residue. It consists of the so-called *enamel fibres*, which appear in the form of hexagonal prisms, and are on this account known as *enamel prisms*. These extend from the surface of the dentine to the

Fig. 117.



Longitudinal ground-section through the apex of a canine tooth from a three and a half year old boy. The entrance of the dental canaliculi between the enamel prisms and the course taken by the latter are shown. × 135.

free surface of the enamel, and are thicker at the outer end than near the dentine. They usually appear to be structureless, but under the influence of certain reagents they acquire a striated appearance. They usually run radially and their course is slightly wavy. They lie pressed together, and joined with one another by a small amount of cement substance. The

enamel prisms are in general arranged in parallel rows, but there may also be bundles of prisms running diagonally and at angles to one another (Fig. 117).

The surface of the enamel is covered by a very thin (about 1 μ thick) structureless membrane, the *cuticula dentis.*

The *cement* (*substantia ossea*) (Fig. 116) is a true bony tissue, which in young teeth as a rule possesses Haversian systems and bone lacunæ. These lacunæ are wanting in the neck of the tooth. The lamellated structure is seldom observed. Large numbers of Sharpey's fibres are present.

Blood-vessels and nerves reach the tooth through the pulp cavity. Small arteries enter the pulp and break up into numerous branches. These form a network with oblong meshes which extend up to the odontoblast layer as a capillary plexus (Lepkowski).

Lymph-vessels are not known in the pulp of the tooth.

The *nerves* enter the pulp in several bundles, which run mainly in the centre, giving out numerous branches. These fibres form a network which runs toward the periphery. The fibres lose their medullary sheath and extend as fine non-medullated fibres between the odontoblasts, to end freely in small swellings (Retzius).

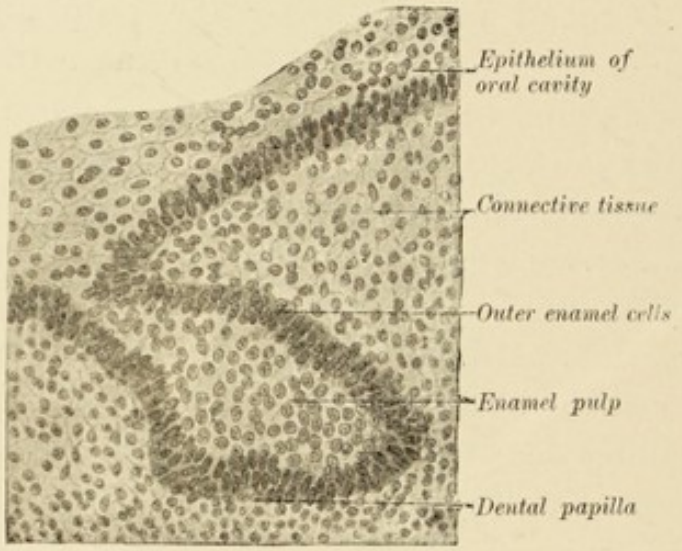
Development of Teeth.

In the beginning of the seventh week of fœtal life the epithelium covering the edge of the jaw grows into the deeper-lying connective tissue in the form of a ridge—the so-called *dental ridge.* In the third month round thickenings occur on the labial side of this ridge, which form the beginnings of the milk teeth (Fig. 118). At the same time certain changes take place in the connective tissue. It projects into the lower side of the thickenings in the dental ridge, and forms in each thickening a dental *papilla* or *tooth germ.* In consequence of this invagination the epithelium forms a sort of mantle for the dental papilla. The epithelial covering forms the starting-point for the enamel, and is known as the *enamel organ.* It later separates off from the dental ridge by a gradual narrowing of

its connection with it. The place of junction which remains is called the *neck of the enamel organ* (Fig. 119). In the region of the neck the dental ridge grows downward into the connective tissue on the lingual side of the milk tooth, and forms another ridge, in which thickenings occur. Into these the papillæ of the permanent teeth grow, so that in the fifth month of fœtal life there are present the beginnings of both milk and permanent teeth (Fig. 119).

Certain changes take place in the enamel organ. The cells bordering on the tooth papilla, the so-called *inner enamel cells*,

FIG. 118.

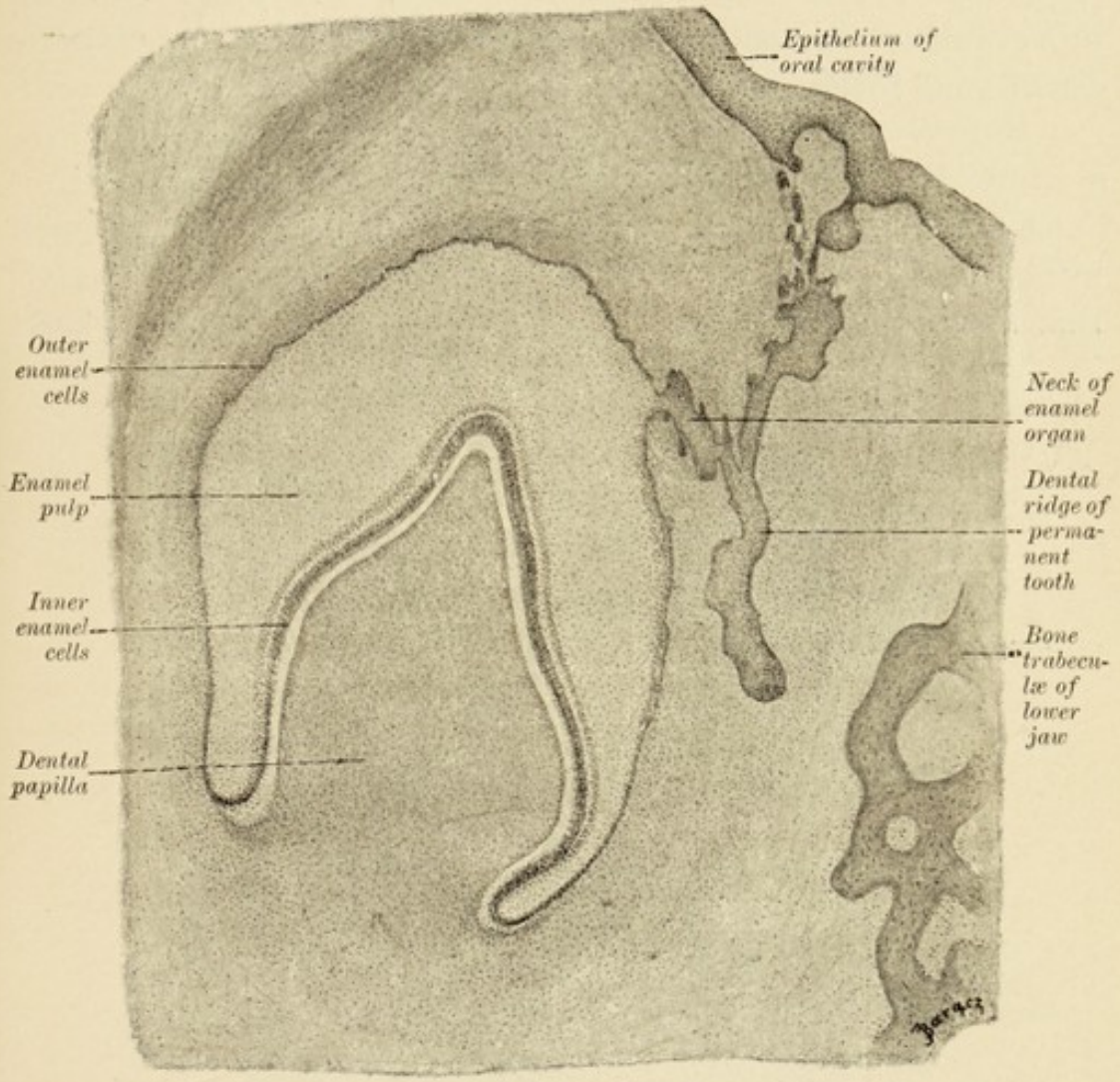


An early stage in the development of a tooth in a pig's embryo. × 240.

become higher, while the outermost layer of cells, the *outer enamel cells*, become more flat. The cells between these two layers form the *enamel pulp* (Fig. 119). In the latter region the intercellular substance increases in amount; the cells become stellate and anastomose with one another. As growth goes on, the enamel pulp becomes gradually less in quantity, and finally vanishes almost entirely. Meanwhile the connective tissue around the tooth forms a capsule, the so-called *tooth sac*. The development of the hard tissues of the tooth begins with the dentine. This is a product of the connective-tissue cells which lie on the surface of the dental papilla, and are known as *odontoblasts*. These are columnar cells arranged in a layer. The dentine begins as a thin homogeneous membrane, the *membrana*

præformativa, which lies between the odontoblasts and the inner enamel cells. This membrane is converted into dentine and in the beginning is a non-fibrillar structure. The development of dentine starts at the apex of the tooth papilla. The odontoblasts send processes out into the fine canals which are formed in the dentine, and these processes become the dental fibres.

Fig. 119.



An advanced stage in the development of a tooth in a three and a half months human embryo. × 65.

Calcium salts are laid down in the fibrillar ground substance in layers. Numerous small areas where calcification is incomplete or absent form the interglobular spaces.

Soon after the beginning of the dentine formation the *development of the enamel* starts. In the region of the future crown

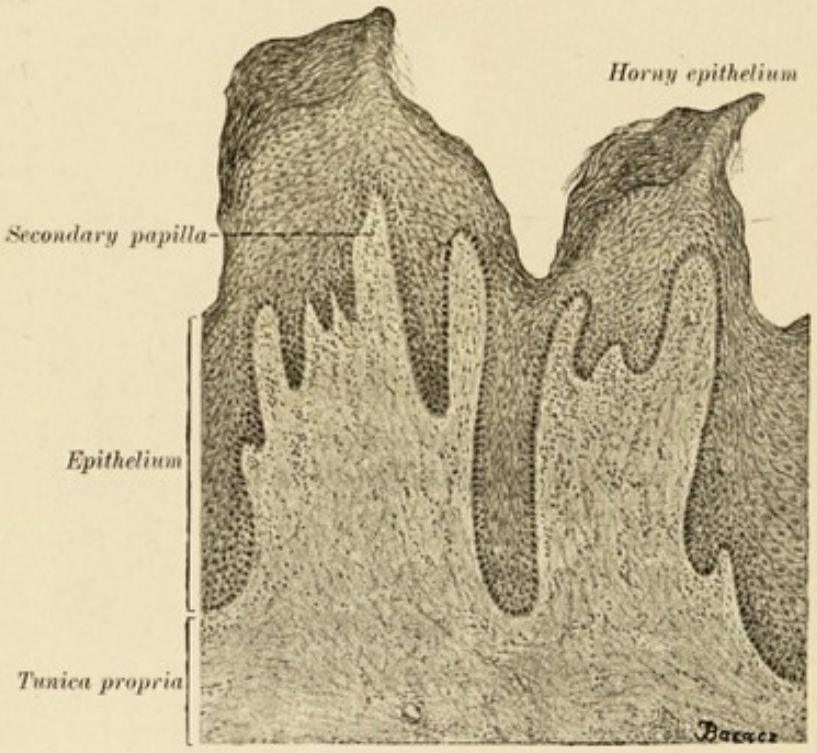
of the tooth the inner enamel cells develop a cuticle-like border. Toward the dentine the so-called *Tomes' processes* are sent out, which give rise to the *enamel prisms*. Finally, calcification takes place from the centre to the periphery, both in the prisms and in the cement substance joining them. The enamel cells disappear, the cuticle is pushed to the surface and forms the dental cuticle.

The *development of the cement*, which is a product of the inner wall of the tooth sac, takes place later as a sort of periosteal bone formation.

3. The Tongue.

The tongue is an organ consisting largely of striated muscle. Its mucous membrane, which is a continuation of that lining the mouth cavity, is differentiated in certain places

FIG. 120.



Two filiform papillæ from the anterior part of the human tongue. × 80.

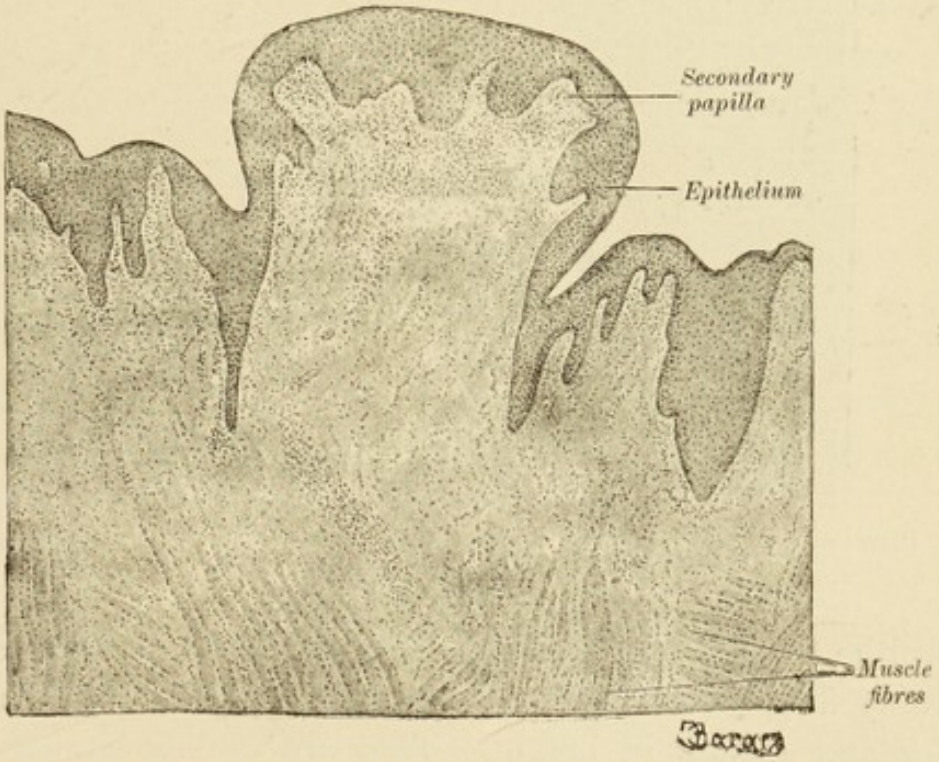
in a characteristic fashion. In most animals certain parts of it possess a distinct corneous layer, but the most essential structures are the so-called *papillæ*. In man there are three kinds of these:

Papillæ filiformes;
Papillæ fungiformes;
Papillæ circumvallatæ.

The *papillæ filiformes* (Fig. 120) are 0.7–3 mm. in length, round or pointed, and covered by a layer of cornified flat stratified epithelium. This in some animals (*e. g.*, cats) forms a sharp, pointed projection of hard epithelial cells. The tunica propria under the epithelium shows several (five to twenty) small papillæ, the *secondary papillæ*, which correspond with the vascular papillæ of the skin. The filiform papillæ are distributed over the entire upper surface of the tongue.

The *papillæ fungiformes* (Fig. 121) are 0.7–1.8 mm. in length, and have a round form which suggests that of a small

FIG. 121.

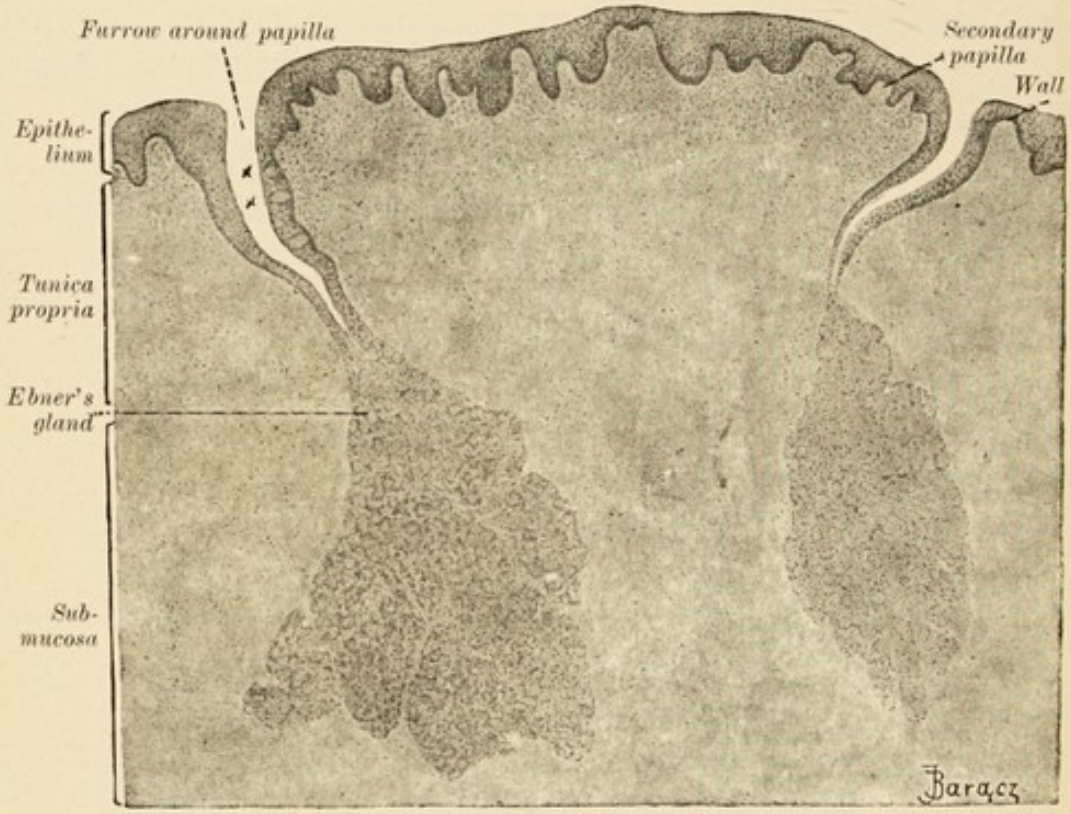


Perpendicular section through a papilla fungiformis of the human tongue. × 45.

mushroom. They are present mainly on the anterior part of the tongue, and are distinguished easily from the other papilla by their red color, which is due to their thin epithelial covering and rich blood supply. They are covered with epithelium similar to that of the mouth cavity, and show many secondary papillæ.

The *papillæ vallatæ* or *circumvallatæ* (Fig. 122) are so named on account of being surrounded by a sort of trench. They are about nine or ten in number in man, and are arranged in two lines which diverge forward from the foramen cæcum at the back of the tongue. They thus form a V-shaped line, with the apex behind and the arms forward. They resemble the

FIG. 122.



Perpendicular section through a papilla vallata of the human tongue. *x x*, taste buds. × 37.

papillæ fungiformes somewhat in general form, but are considerably larger than these, usually measuring 1–2 mm. in diameter and 1 mm. in height. They are usually sunken in the mucous membrane and surrounded by a groove and a wall. The latter is somewhat lower than the papilla. Only the upper surface possesses secondary papillæ; the side walls remain free from them. The latter, however, show the end apparatus of the nerves of taste, the so-called *taste bulbs*. These are sometimes found also in the wall on the opposite side of the trench. Their intimate structure is described in the section on Sense

Organs. Into the trench numerous serous glands (v. Ebner's) open (Fig. 122).

At the side of the tongue of some animals (mainly the rabbit) there is found another kind of papilla, the *papilla foliata.* There is in the rabbit a white area about 1 cm. long, situated on each side of the posterior part of the tongue. It is made up of many papillæ foliatæ somewhat resembling the circumvallate papillæ, separated from one another by trenches or furrows. They are covered with stratified epithelium, and on their adjacent sides are many taste bulbs (see under Organs of Taste).

The *submucosa* of the tongue is firm at the tip and along its dorsal surface, but looser elsewhere.

The *muscles* of the tongue are cross-striated. Their arrangement will be found in works on gross anatomy. In the frog the muscle fibres are frequently seen to branch. Between the muscle bundles there are glands, fat, and intramuscular connective tissue. The lymphoid tissue of the tongue is spoken of under "Lingual tonsils."

The blood-vessels are spread out in a capillary network under the epithelium, which is especially well developed in the papillæ. The lymphatics have a similar course. The nerves end in part freely between the epithelial cells, and partly in various terminal end organs (Krause's end bulbs, Meissner's taste corpuscles and taste buds).

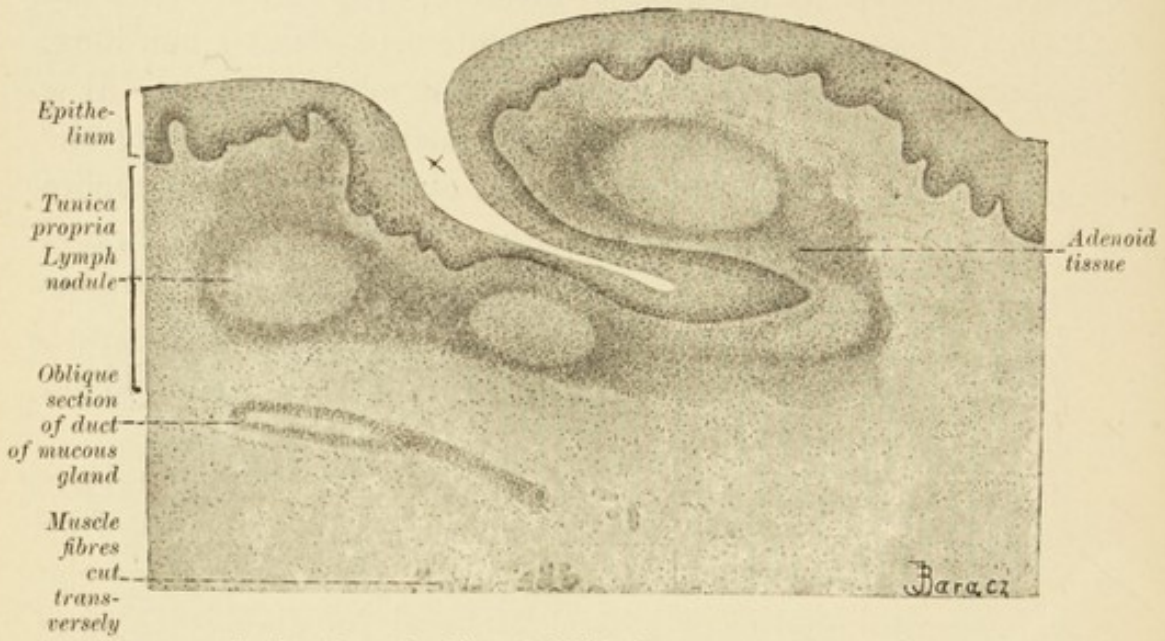
4. The Tonsils.

The adenoid tissue is well developed around the borders of the mouth cavity, forming an organ which Waldeyer has called the *lymphatic pharyngeal ring.* This tissue may be divided into three main masses, that which is in the tongue (*lingual tonsils*), that associated with the palate (*palatine tonsils*), and that situated in the pharynx (*pharyngeal tonsils*).

The *lingual tonsils* (*folliculi linguales*) are situated in that part of the tongue between the circumvallate papillæ and the epiglottis. They are round masses of adenoid tissue lying in the upper part of the tunica propria, easily visible to the naked

eye, and slightly projecting above the surface of the mucosa. In the centre of these masses is a deep depression, known as

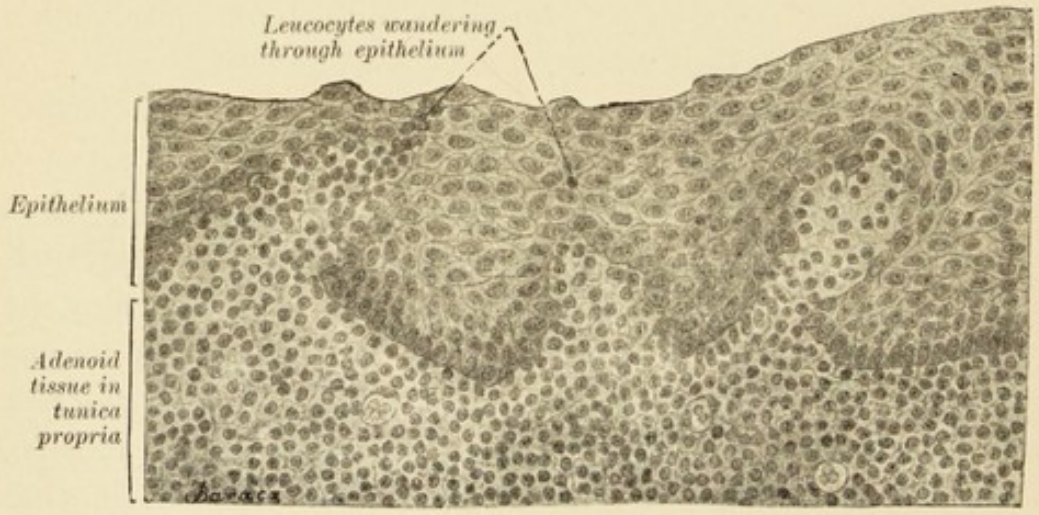
Fig. 123.



Section through a lingual follicle in man. *x*, crypt. × 50.

the *crypt*. This is a blind canal lined, like the surface of the tongue, with stratified epithelium (Fig. 123). It is distinguished from the epithelium of the tongue, however, by

Fig. 124.



From a thin section through a lingual follicle of man. × 260.

the presence of places where the lymphocytes have pushed their way between the epithelial cells to reach the surface

PLATE XII.

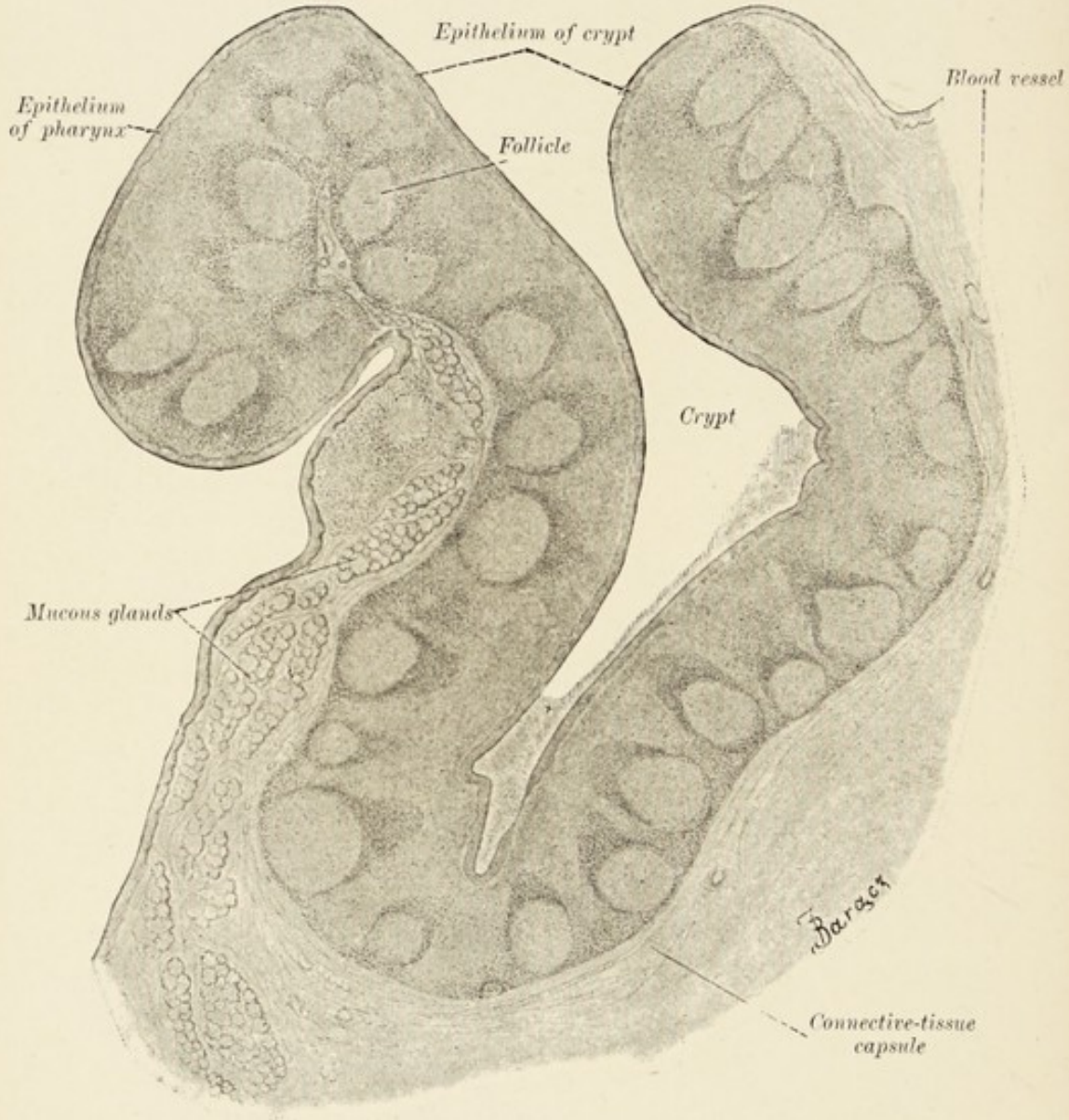


FIG. 125.—Section through a dog's tonsil. At $x\ x$ there are seen leucocytes which have wandered out from the follicles. × 15.

(Fig. 124). The lymphocytes which escape at these places form the *salivary corpuscles* of the saliva. The adenoid tissue under the epithelium is divided into *follicles* which resemble those of the lymph glands, possessing a germinal centre and a dense periphery.

The ducts of the mucous glands of the root of the tongue often open into the crypts.

The *palatine tonsils* have a structure similar to that of the lingual tonsils, with the exception of being much larger and possessing ten to twenty follicles and a number of crypts (Plate XII., Fig. 125). The follicles are situated at about the same level as the tunica propria and possess usually very distinct germinal centres. The epithelium covering them is in many places pierced partly or completely by an encroachment of the adenoid tissue. The crypts always contain a number of lymphocytes and may be branched.

The tonsils can easily be seen at the pillars of the fauces, and when inflamed may become so large that they almost or quite meet in the median line.

The *pharyngeal tonsils* lie at the upper part of the pharynx, mainly in the naso-pharynx. Their structure is essentially the same as that of the palatine tonsils. The crypts are clothed often with ciliated epithelium, and are five or six in number. Into these open the mixed glands, which form a distinct layer under the follicles. There is here also a migration of lymphocytes through the epithelial covering of the organ. It is these tonsils which on hypertrophy form the so-called adenoids which often are found in children.

Development of Tonsils.

The *development of lingual tonsils* begins, according to Stöhr, in the eighth month of fœtal life. Leucocytes wander out from the veins of the tunica propria and infiltrate the loose connective tissue around the ducts of the mucous glands. The further growth of the adenoid tissue thus formed takes place by the continued migration of leucocytes and by mitotic division of these. The wandering of leucocytes from the lingual

tonsils into the mouth cavity through the epithelium begins early. It may be noticed in the eighth month of fœtal life, and increases after this.

The *palatine tonsils* arise, according to His, in a depression which represents the space between the second and third branchial arches. This is clothed by the mucous membrane of the mouth cavity. The crypts are formed by the downward growth of solid masses of cells from the epithelium (Stöhr), a process which occurs at the end of the fourth month in the life of the human fœtus, and continues throughout the entire fœtal life and for the first year or two after birth. The solid masses of cells later on become hollow and give rise to the blind canals or crypts of the adult organ. In the connective tissue of the mucous membrane leucocytes begin to gather from the blood-vessels during the third month. This continues up to the time of birth, and it is only during the first year after birth that definite follicles with germinal centres are to be found.

5. Glands of the Mouth Cavity.

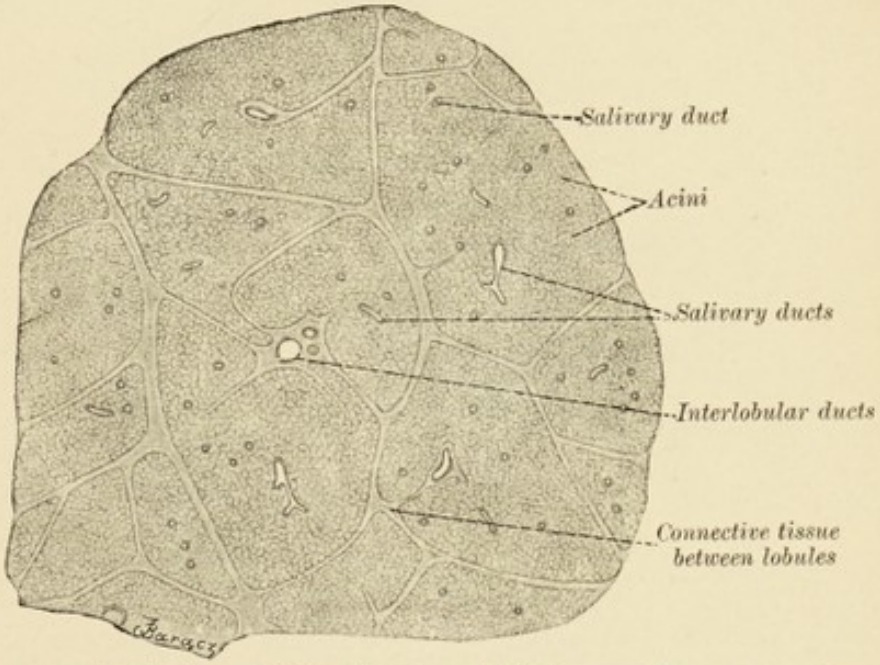
Under this heading are to be discussed the large salivary glands whose ducts open into the mouth cavity—*i. e.*, the parotid, submaxillary, and sublingual glands, as well as the smaller glands which are named according to their situation. All the glands of the mouth may be divided, according to their products, into: 1, *Serous glands*, which secrete an albuminous serous fluid; 2, *Mucous glands*, which produce a mucin-containing secretion; and 3, *Mixed glands*, which simultaneously secrete both kinds of fluid.

All these glands are *tubular*. The smaller are simple branched tubular, while the larger are compound tubular glands. The latter are capable of division into larger and smaller lobules, which are separated by connective tissue (Fig. 126). Each lobule contains ducts which divide in its interior. The small lobules correspond with simple branched tubular glands.

The ducts in the lobules are more or less curved, so that

in a section they are cut at various angles. The *main ducts*, which open into the mouth cavity, are covered by one or two layers of cylindrical epithelium. In the connective tissue which makes up their outer sheath, we often (submaxillary duct) find smooth muscle fibres running longitudinally. The main duct divides into many smaller branches (*interlobular ducts*), which are lined with a single layer of cubical or cylindrical epithelium. Each of these smaller ducts passes over into a *salivary duct* (*intralobular duct*), which is made up of cylindrical epithelium, whose cells are characterized by the fact that

FIG. 126.



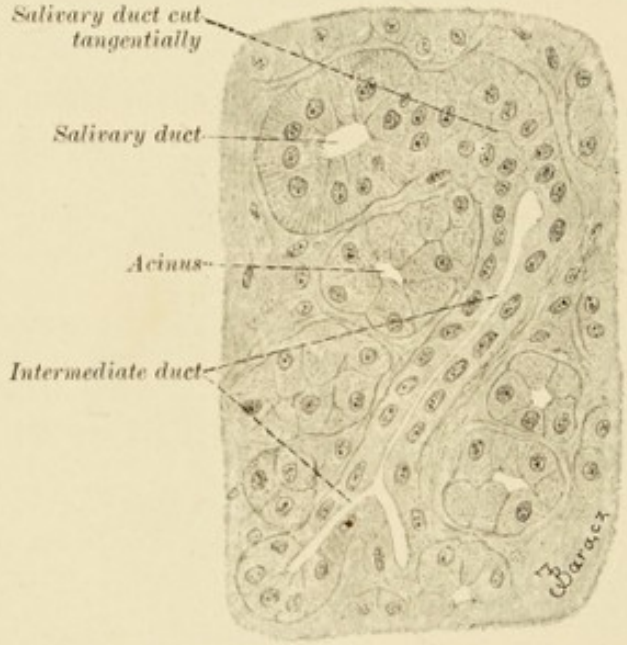
From a section through a dog's parotid gland. Several lobules are to be seen. × 22.

their basal ends are plainly striated. This striation is due to small granules in the protoplasm, which are arranged in rows (Figs. 127 and 130). While the interlobular ducts are always present in the connective tissue between the lobules, the salivary ducts or intralobular ducts are in the lobule itself. The intralobular divides in the lobule, and each division passes over into a so-called intercalary part, or intermediate duct, which is a tube lined with low cubical epithelium (Figs. 129 and 130; Fig. 127). Many authors have ascribed to the intralobular ducts secretory functions, while the interlobular ducts conduct the

secretion. The same secretory function has been supposed to be possessed by the intercalary part. The intercalary part finally passes over into the *main glandular tubes.* The latter are blind tubes, consisting of a glandular epithelium limited on the outside by a fibrillar *membrana propria*, on whose inner surface there are branched cells surrounding the epithelia cells. These are of doubtful origin, and are known as *basket cells.*

The gland cells of a *serous* tubule at rest possess a protoplasm filled with highly refractive granules. The nucleus is small, shrunken, and irregular in outline. During secretion

FIG. 127.



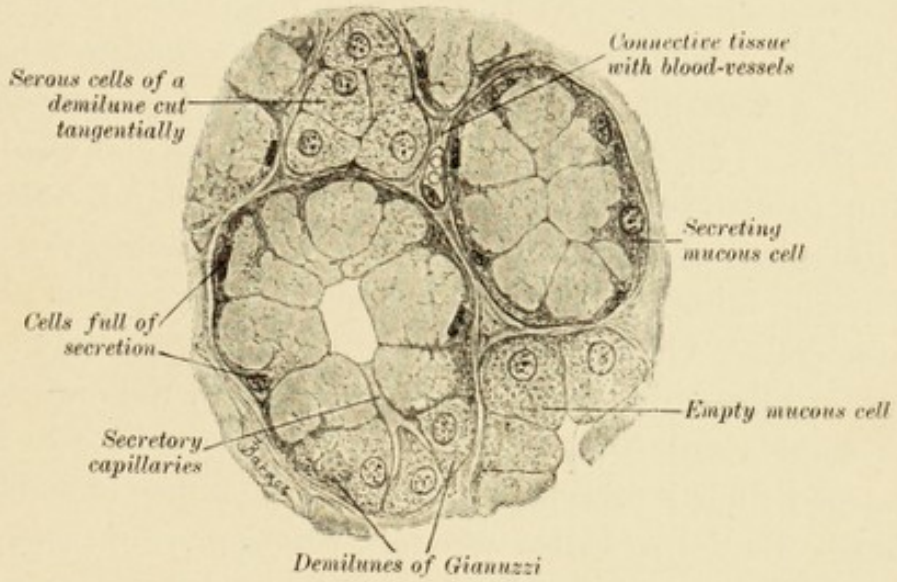
From a section through a human parotid gland. × 450.

the cells decrease in size, and the protoplasm, especially in the part near the membrana propria, becomes free from granules. At the inner side the cells still contain a few granules, while the outer part has a plainly reticular structure. The nucleus becomes round and shows a distinct chromatin network (Fig. 130).

The *mucous cells* have an appearance varying with the condition of their functional activity. The *empty cells—i. e.*, those which have been active and have begun to rest—are small and contain a granular protoplasmic network. The round or oval nucleus lies near the membrana propria and possesses a well-

marked chromatin network. During the *formation of mucus* the granules increase in size, and finally are converted into fluid material. The meshes of the protoplasmic network become wider as the mucus fills them. The cell grows in size and has a clear, transparent appearance. The nucleus becomes irregular and is pressed into a corner of the cell or against the membrana propria. In the immediate neighborhood of the nucleus there is a small quantity of unchanged protoplasm. During *active secretion* the mucus escapes from the cell, and the granular protoplasm near the nucleus increases in amount. The

FIG. 128.



From a section through a human sublingual gland. (Preparation by R. Krause.) × 560.

nucleus becomes oval and the chromatin framework more distinct, and we have again the appearance of an empty cell (Fig. 128).

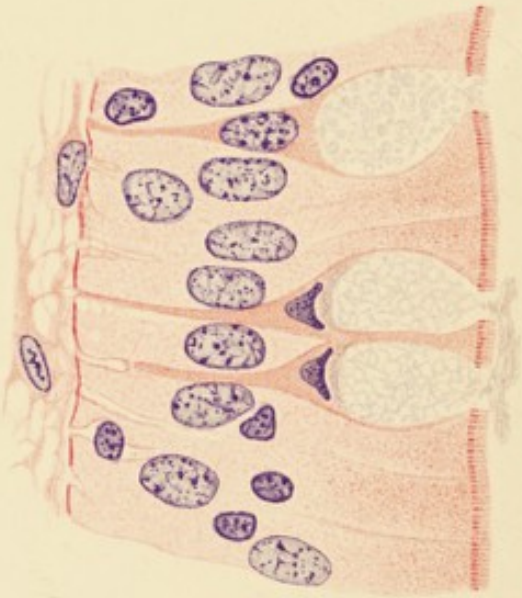
A mucous cell which has just emptied out its secretion, and a serous cell are very similar in appearance. Usually cells in the same tubule are found in different stages of secretion, so that their appearance is very different. Sometimes a whole tubule is made up of one kind of cell, but in a great many glands both serous and mucous cells are present in the same tubule, and we have then to deal with mixed glands. The parotid in all animals is a purely serous gland; also the submaxillary of rabbits, and the small glands in the region of the

circumvallate papillæ of the tongue are serous glands. The pure mucous glands are usually small and scattered throughout the mouth cavity. The submaxillary and sublingual belong to the mixed glands.

In order to study the cell arrangement in both serous and mucous glands, we shall consider that of a typical mixed gland, human submaxillary, in which both are present. A diagram of such a gland is given in Fig. 129. Here one can see an intermediate part of the tube entering in one place serous tubules; in another place it enters a mucous tubule, which becomes composed at the end of serous cells. To the right of the diagram is an intermediate duct entering a mucous tubule which ends blindly. At the end of this there is a cap-like mass of cells resembling serous cells. In section they have the form of a half-moon, and are known as the *demilunes of Gianuzzi.* The significance of these cells is doubtful. According to R. Heidenhain, they are young gland cells which take the place of mucous cells which have disintegrated. No evidence of mitotic or amitotic division has ever been observed in these cells. Other authors regard them as entirely separate secreting cells, which have nothing to do with the mucous cells; while some think they are merely mucous cells which have discharged their secretion. There are sometimes to be observed in these cells the so-called *secretory canals* or *capillaries*, which are a continuation of the lumen of the tubule between neighboring cells. They are found often in serous tubules, and are sometimes much branched. They possess no wall of their own, and are demonstrated most easily by Golgi's method, in which the whole lumen is filled with the black precipitate. It is highly probable that the demilunes of Gianuzzi have the power of secreting an albuminous fluid; and if this is the case, it is necessary to consider all those mucous glands which contain these cells as mixed glands (R. Krause).

The salivary glands are richly supplied with blood-vessels. The larger vessels run in the connective tissue between the lobules. Here they break up into fine branches, enter the lobules, and surround the tubules with a thick capiliary net-







J. Barącz ad nat. del.

Szymonowicz, Histology

Lith. Anst. v. Werner & Winter, Frankfurt a/M.

FIG. 129.

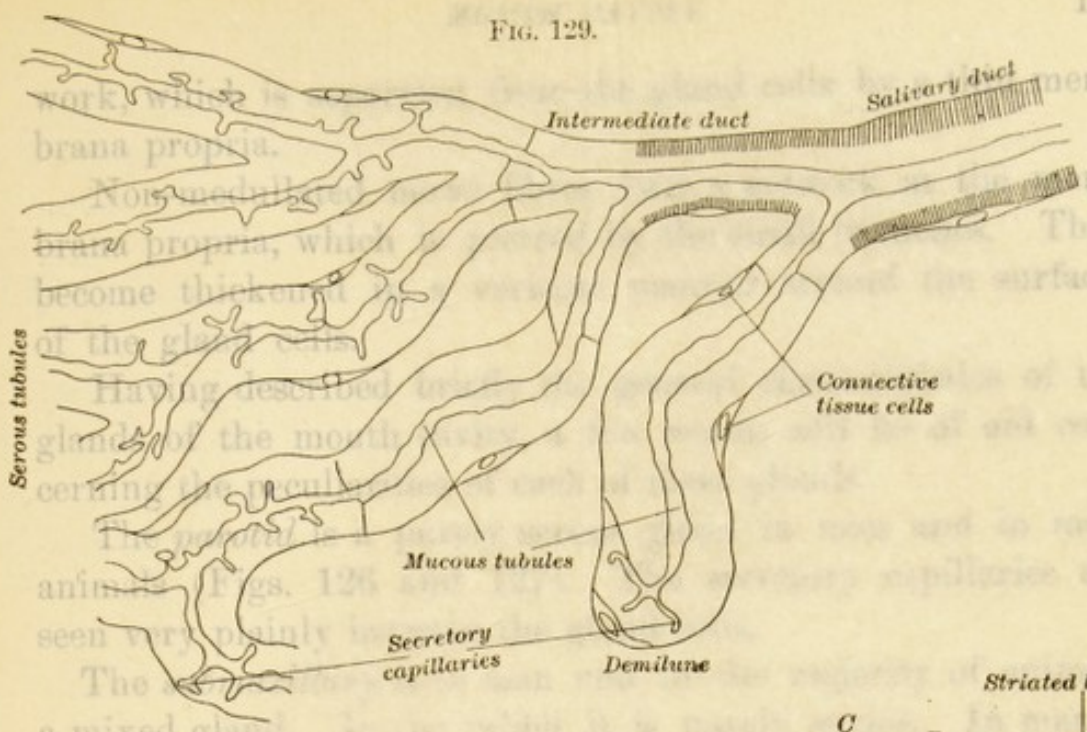
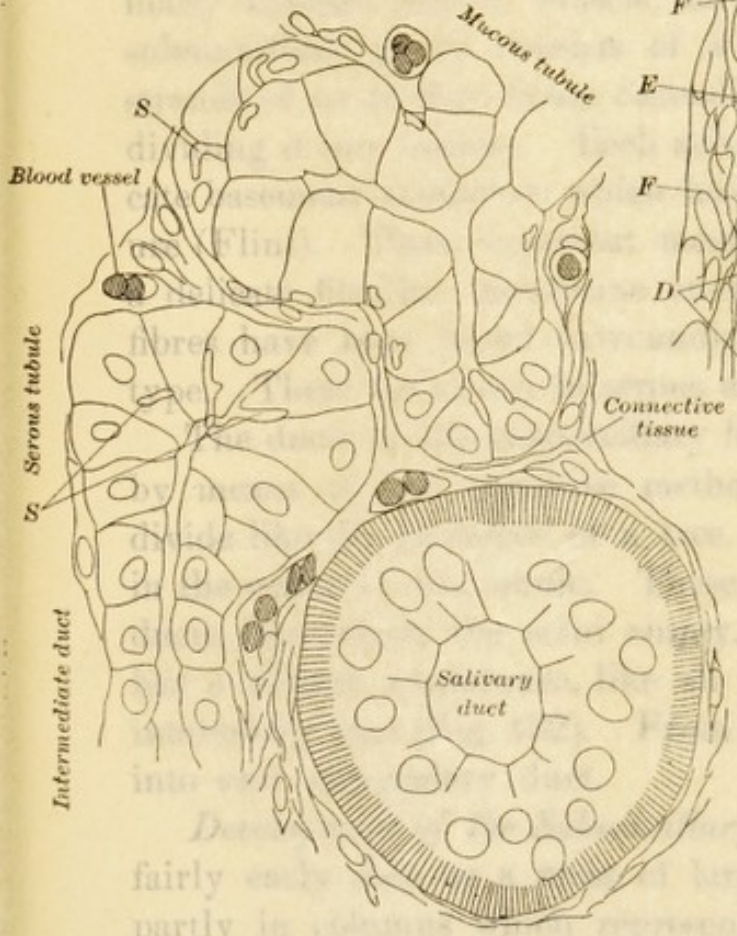


FIG. 130.



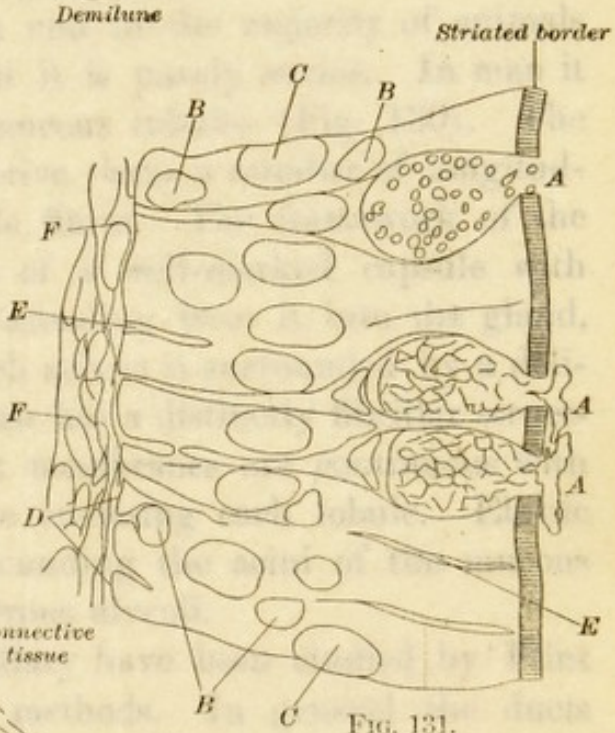


FIG. 131.

A = *Goblet cells*
B = *Wandering cells*
C = *Nuclei of epithelial cells*
D = *Basal membrane*
E = *Intercellular spaces*
F = *Cells of the reticular connective tissue*

FIG. 129.—Diagram of human submaxillary gland. After R. Krause.

FIG. 130.—From a section through a human submaxillary gland. Stained by Biondi's method. × 600. After a preparation by R. Krause.

FIG. 131.—From a longitudinal section through a villus of a cat's intestine. × 100.

FIG. 129.

FIG. 131.

FIG. 130.

A = Goblet cells
B = Wandering cells
C = Nuclei of epithelial cells
D = Basal membrane
E = Intercellular spaces
F = Cells of the reticular connective tissue

FIG. 129.—Diagram of human submaxillary gland. After R. Krause.

FIG. 130.—From a section through a human submaxillary gland. Stained by Biondi's method. × 600. After a preparation by R. Krause.

FIG. 131.—From a longitudinal section through a villus of a cat's intestine. × 100.

work, which is separated from the gland cells by a thin membrana propria.

Non-medullated nerve fibres form a network at the membrana propria, which is pierced by the small branches. They become thickened in a varicose manner around the surfaces of the gland cells.

Having described briefly the general characteristics of the glands of the mouth cavity, a few words will be of aid concerning the peculiarities of each of these glands.

The *parotid* is a purely serous gland in man and in most animals (Figs. 126 and 127). The secretory capillaries are seen very plainly between the gland cells.

The *submaxillary* is in man and in the majority of animals a mixed gland. In the rabbit it is purely serous. In man it contains more serous than mucous tubules (Fig. 130). The main duct has in the connective tissue a number of longitudinally disposed smooth muscle fibres. The framework of the submaxillary gland consists of a well-marked capsule with strands of connective tissue extending from it into the gland, dividing it into lobules. Each acinus is surrounded by a delicate basement membrane which has a distinctly fibrillar structure (Flint). These basement membranes are continuous with a delicate fibrillar membrane enclosing each lobule. Elastic fibres have been found surrounding the acini of the mucous type. These are absent in serous alveoli.

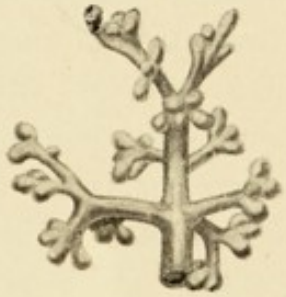
The ducts of the submaxillary have been studied by Flint by means of the corrosive methods. In general the ducts divide like the branches of a tree. The intralobular ducts lie in the centre of the lobule. These pass on into the intercalary ducts, into which the acini empty. The lumen of the acinus has a dilated appearance, like an ampulla, at the end of the intercalary duct (Fig. 132). From three to six ampullæ empty into each intercalary duct.

Development of the Submaxillary.—The gland appears at a fairly early date as a mass of large epithelial cells arranged partly in columns which represent the developing ducts and alveoli. At the ends of these columns there are knob-like

swellings showing numerous karyokinetic figures. A capillary plexus of blood-vessels develops around the masses of epithelial cells. The columns of cells divide many times, and a lumen is formed in them continuous with that of the duct. The interlobular connective tissue develops in connection with the ingrowing blood-vessels.

The *nerves* in the submaxillary are numerous. Some end in Pacinian corpuscles (Krause); some supply the blood-vessels; while most of them terminate in the secreting alveoli. These latter pierce the basement membrane and form a rich arborescence around the alveolar cells (Berkley).

FIG. 132.



Corrosion specimen of ducts of submaxillary gland of dog. (Flint.) The ducts were injected with celloidin injection mass, and the tissue dissolved away.

The *sublingual gland* contains no entirely serous tubules. It is a mixed gland, but in man is in large part mucous. The cells of the intralobular ducts are not striated, as in some of the other glands. The intercalary ducts are narrow, and are lined with a low cubical epithelium. The main ducts are clothed with cylindrical epithelium, and break into many small branches whose walls are made up of cubical cells. These lead to still smaller branches, which end at the demilunes of Gianuzzi in secretory capillaries (Fig. 128).

The *small glands*, which are distributed widely over the mouth and tongue, are tubular and branched, sometimes simple, and sometimes compound. The body of the gland is situated always in the submucosa, often extending down between the muscles.

According to their location, we have: glandulæ labiales, buccales, palatinæ, linguales, etc. According to their products,

we may distinguish serous, mucous, and mixed glands. They possess neither intercalary nor intralobular ducts. The ducts often are covered at their mouths with ciliated epithelium.

Serous glands are found only in the tongue, in the region of the circumvallate papillæ. These are called *v. Ebner's glands.* The ducts open in the furrows surrounding the circumvallate papillæ. In these glands also secretory capillaries may be present.

Small mixed glands have the structures described for the sublingual gland. Secretory capillaries are plainly to be made out. To these belong the labial and buccal glands, and those glands at the under side of the tip of the tongue, described by Blandin and Nuhn.

The palatine glands and the glands at the root of the tongue are purely mucous.

B. PHARYNX.

The *mucous membrane* of the pharynx resembles that of the mouth cavity. We find here also a stratified epithelium and a tunica propria with papillæ. The stratified epithelium of the nasopharynx is converted in the region of the nasal cavities into a many-layered ciliated epithelium, which is continuous above with the ciliated cylindrical epithelium of the nasal mucous membrane.

The *tunica propria* of the pharynx is supplied richly with adenoid tissue, which in places is collected to form the pharyngeal tonsils. Under the tunica propria there is a layer of elastic fibres running longitudinally, the *elastic limiting layer*, which is continued down to the œsophagus, where it gradually disappears. It lies, for the most part, on the inner surface of the pharyngeal muscles, and sends strong bands of elastic fibres into the intermuscular septa (J. Schaffer). In these places the submucosa is wanting, and the mucous glands extend down and branch between the muscle bundles. In the laryngeal part the elastic limiting layer is separated from the muscle, and here there is a distinct submucosa, in which the glands lie.

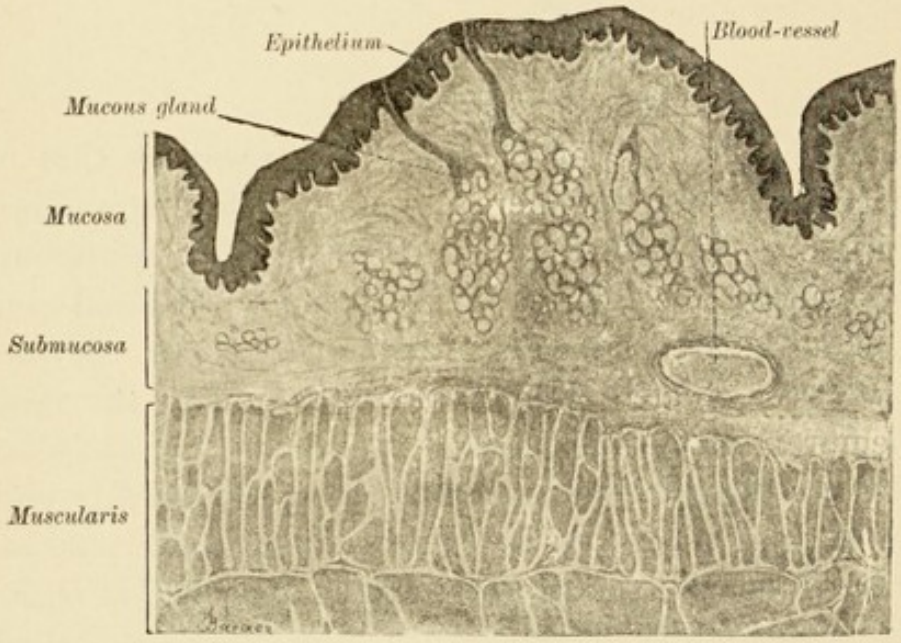
The outer muscle layer (the constrictors of the pharynx) consists of striated muscle.

C. ŒSOPHAGUS.

In the wall of the œsophagus can be distinguished: mucosa, submucosa, muscularis, and tunica adventitia.

The mucosa is similar in structure to that of the mouth cavity. It possesses, however, a thin layer not found in the oral mucous membrane, the so-called *muscularis mucosæ*. This lies at the edge of the tunica propria, between it and the submucosa, and consists of longitudinally disposed smooth muscle cells. Only in the lower half of the œsophagus is it a complete layer.

FIG. 133.



Part of a transverse section of the œsophagus of a dog. × 25.

The *submucosa* consists of firm connective tissue containing blood-vessels, nerves, and mucous glands. The latter do not differ from the mucous glands of the mouth cavity. They occur throughout the entire length of the œsophagus. The ducts pass through the muscularis mucosæ, and are lined for a short distance from their mouths with stratified cuboidal epithelium. Under the muscularis mucosæ there is usually a considerable dilatation of the lumina of the ducts. In the

tunica propria there is always a certain amount of adenoid tissue surrounding the ducts.

In the mucosa superficial to the muscularis mucosæ there are other glands distinct from the mucous glands. These occur in small groups situated mainly at the upper part of the œsophagus and near the junction of the stomach and œsophagus. They have been described by Rüdinger, and later by Schaffer. The subject has recently been worked over by A. W. Hewlett, who applied the term *superficial glands* to these structures. According to him, the glands are of the branched tubular type. The tubules show in many places cystic dilatations. The duct is lined with high columnar epithelial cells with oval nuclei. In the acini the cells are lower and the nuclei are more spherical and situated nearer the base of the cell. Besides these cells, there are in the acini cells identical with the parietal cells of the stomach. These vary considerably in number. The cystic dilatations are similar to those found in the mucous glands. According to Hewlett, the superficial glands differ from the œsophageal mucous glands in the following particulars: They are superficial to the muscularis mucosæ, and tend to occur in groups in certain places in the œsophagus. The ducts are lined with a single layer of columnar cells, and have no lymphoid tissue about them. They frequently contain parietal cells and do not stain deeply in the dyes used for mucin.

The *muscularis* consists in the upper part of the œsophagus of striated muscle; in the lower parts, on the contrary, there are two layers of smooth muscle. Of these, the inner is circular and the outer longitudinal. The striated muscle in the upper part is continuous with the inferior constrictor of the pharynx. It is found often extending down to the lower third of the œsophagus, where it is replaced gradually by smooth muscle.

The *tunica adventitia* consists of loose connective tissue binding the œsophagus to the surrounding structures.

The *blood-vessels* are arranged like those of the mouth cavity, the larger arteries and veins being situated in the sub-

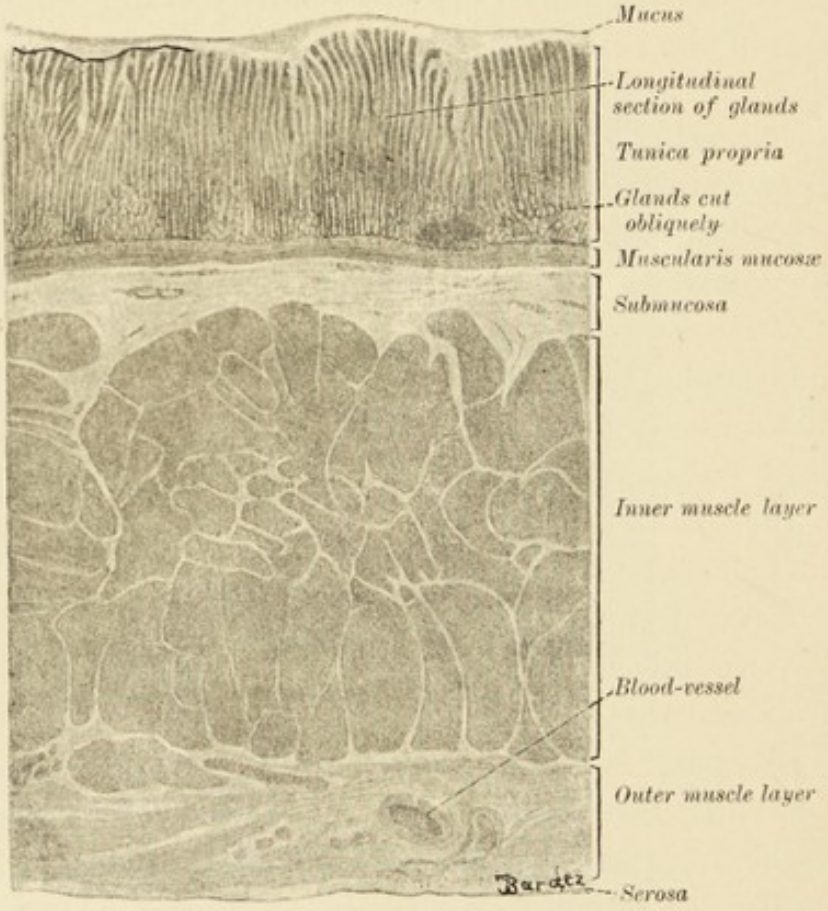
mucosa, with branches upward to the mucosa and down to the muscle.

The *nerves* are like those of the intestine, forming two large plexuses of sympathetic fibres, one between the muscle coats and one in the submucosa. The latter is derived from branches of the former, and from both plexuses finer branches are sent out to various parts of the wall. Medullated nerve fibres end in the striated muscles in motor end plates.

D. STOMACH.

The stomach wall is made up of mucosa, submucosa, muscularis, and serosa (Fig. 134).

FIG. 134.



Section through the stomach wall of man (pyloric region). × 14.

The gastric mucosa has in the recent state a gray or grayish-red color. The surface is uneven, and possesses certain small depressions, the *foveolæ gastricæ*, into which the gas-

PLATE XIV.

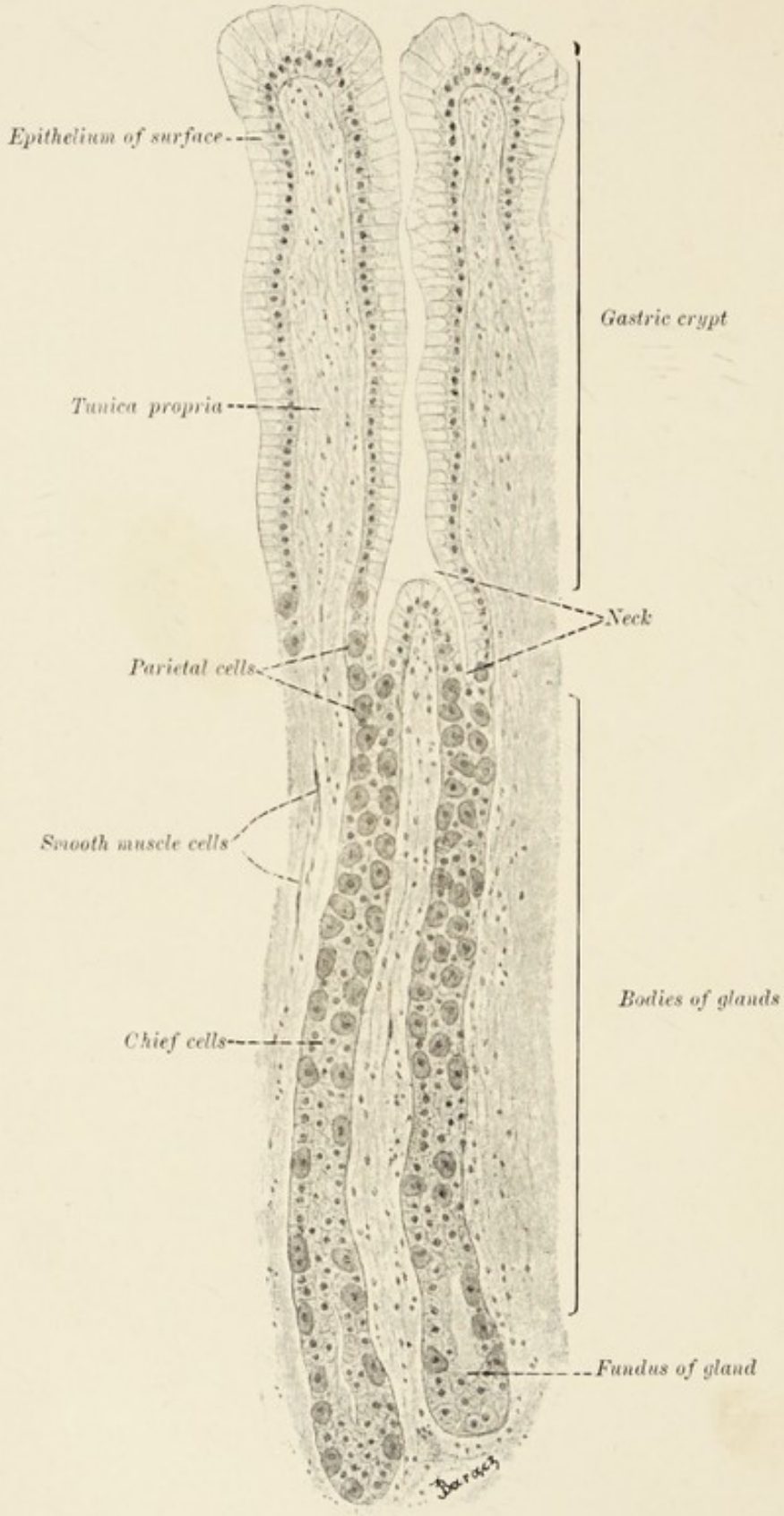


FIG. 135.—From a section through the human gastric mucous membrane in the region of the fundus. × 250.

tric glands open. In the region of the pylorus there are small folds, called the *plicæ villosæ*. Further, the whole surface often is divided by furrows into polygonal fields, which condition is known as the *status mamillaris*. This is said to be due to an unequal development of the gastric glands. The mucosa consists, as in the œsophagus, of epithelium, tunica propria, and muscularis mucosæ.

The *epithelium* covering the surface of the mucosa is a single layer of cylindrical cells. The protoplasm of that half of the cell toward the surface usually is clear or contains very fine granules, while that of the half next the membrana propria is made up of large, coarse granules. The oval or round nucleus lies generally in the coarsely granular part of the cell. The cells only exceptionally possess a cuticle as in the intestine.

At the cardiac end of the stomach the single layer of cylindrical cells passes abruptly over into the epithelium of the œsophagus.

Under the epithelium is the *tunica propria*, which is a loose connective-tissue layer containing a considerable number of leucocytes. The lymphocytes form in some places groups similar to the solitary follicles of the intestine. In the tunica propria are situated all the gastric glands, of which we distinguish three kinds:

Most widely distributed are the *true gastric glands* (*gl. gastricæ propriæ*). These are known also as fundus glands or peptic glands. They are distributed over the whole fundus and body of the stomach, and appear as simple tubular glands (Fig. 135). These often branch, take a slightly curved course, and traverse the whole thickness of the tunica propria as far as the muscularis mucosæ. Usually many of these open into one foveola, which is as deep as one-third the thickness of the mucosa, and which may be considered as the gland duct. In the glands one can distinguish a neck and a body. The latter ends blindly, and the lumen of the gland is everywhere quite narrow.

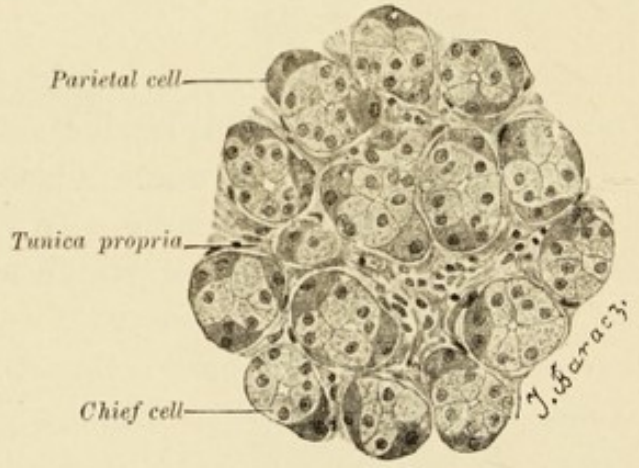
The epithelium lining the true gastric glands is made up of

two kinds of cells, the *chief cells* and the *parietal cells* (R. Heidenhain).

The chief cells, also called *adelomorphous cells* (Rollett), form the largest part of the gland. These are round or cubical, the form and size depending on their functional activity. During a period of fasting and at the beginning of digestion they are large, while after digestion has proceeded for a certain length of time they become much smaller. In the fresh condition they contain numerous highly refractive granules, which, as in other glands (pancreas, parotid, etc.), disappear in the outer zone of the cell during secretion. These granules are supposed by most authorities to consist of a substance, *pepsinogen*, which is converted into pepsin.

The parietal cells (*delomorphous*), also known as *oxyntic* cells, are larger and more conspicuous than the chief cells.

FIG. 136.



Transverse sections of glands from the fundus of a mouse. × 300.

They are not regularly arranged in the gland tubules, but are scattered here and there in the rows of chief cells. In the neck of the gland they are usually very numerous, and may lie in rows like the chief cells. They are generally only sparingly present in the gland body. Here they are pressed out by the chief cells against the membrana propria, so that they seem to be at the periphery of the tubule. A cross-section of the tubules gives an accurate idea of the relation of these cells to one another (Fig. 136). The parietal cells are round or

polygonal, finely granular cells, containing one or two spherical nuclei. They are smallest in fasting and increase in size during digestion. In the fresh state they are clearer than the chief cells, while in fixed preparations they are much darker and less clear than these. They show a special affinity for such stains as eosin, Congo-red, neutral carmine, etc.

Those parietal cells which are not situated directly on the gland lumen are connected with it by a secretory duct, which breaks up into a number of secretory capillaries. These surround the cells like a basket-work, and also project into its interior. The cells which are situated along the edge of the gland lumen do not possess a duct, as their secretory capillaries empty directly into the gland lumen (Figs. 137 and 138).

Fig. 137.



Longitudinal section of a fundus gland of a mouse. Golgi impregnation. × 125.

Fig. 138.



From the fundus glands of a mouse. Basket-shaped plexuses of capillaries are seen to surround three oxyntic cells and to open into the gland lumen. × 600.

Golgi's method is of special service in the investigation of these capillaries. During digestion they are wider, being filled with secretion.

It is supposed generally that the parietal cells have the property of secreting the acid contained in the gastric juice.

The *pyloric glands* (*gl. pyloricæ*) are distinguished from the

fundus glands by the facts that they branch more frequently; that they take a more curved course; and that the foveolæ into which they open are very deep. Besides these things, they consist entirely of chief cells. Between the fundus and the pylorus there is a *transition zone* or *intermediate zone* in which both forms of glands are present. This is not definite, for the parietal cells are found frequently in man even in the region immediately around the pylorus. In many cases no part of the stomach is free from them.

The so-called *cardiac glands* are present in that region of the stomach around the œsophageal orifice. They are compound tubular glands, whose elements closely resemble those of the pyloric glands. Parietal cells seldom are found. In this region, as well as in the pyloric area, there are found not infrequently cells resembling those of the intestine—*i. e.*, cells with a striated cuticle, and also goblet cells. These tubules, resembling Lieberkühn's glands, do not extend so deeply in the tunica propria as the cardiac glands.

The *membrana propria* which limits the epithelial layer of the mucosa, is a thin membrane on whose inner surface there are often to be observed flat branched cells. Where the glands lie close to one another the tunica propria is very inconspicuous.

Under the tunica propria is the *muscularis mucosæ*, which consists of smooth muscle cells crossing one another, but arranged usually in two or three layers parallel to the surface.

The *tunica submucosa* consists of fine connective tissue which contains a considerable number of elastic fibres. Fat cells, blood-vessels, and ganglion cells are seen also. The latter belong to the so-called Meissner's plexus, which is present throughout the alimentary canal.

The true muscle coat of the stomach, the *muscularis*, consists of three layers. The fibres of the innermost sheath run obliquely; the middle coat is circular, while the outermost layer is disposed longitudinally. A thickening of the inner and middle layers forms the *sphincter pylori*.

The serosa consists of a thin layer of connective tissue covered by a layer of endothelial cells (see Peritoneum).

PLATE XV.

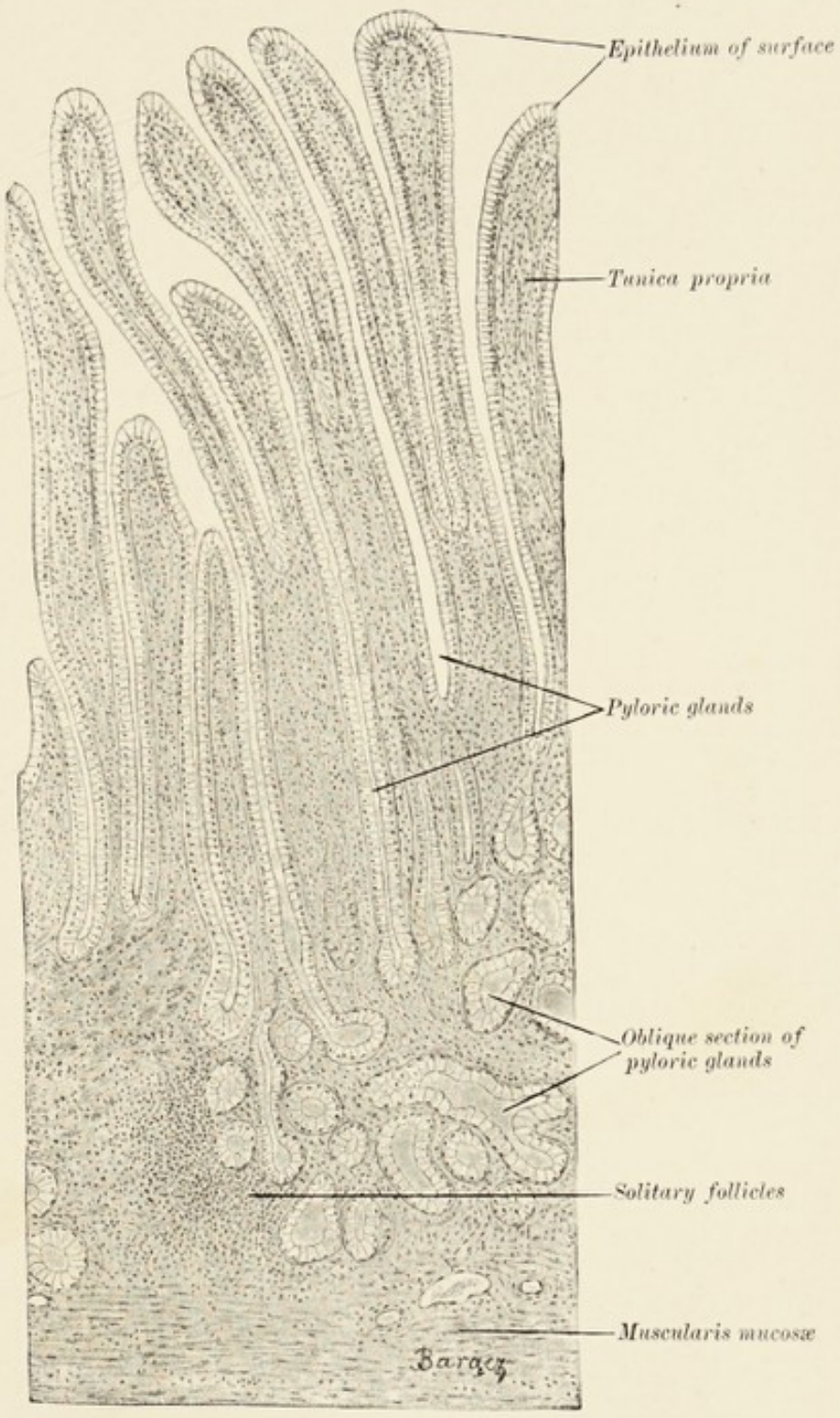


FIG. 139.—From a section through the human gastric mucous membrane in the pyloric region. × 100.

PLATE XVI.

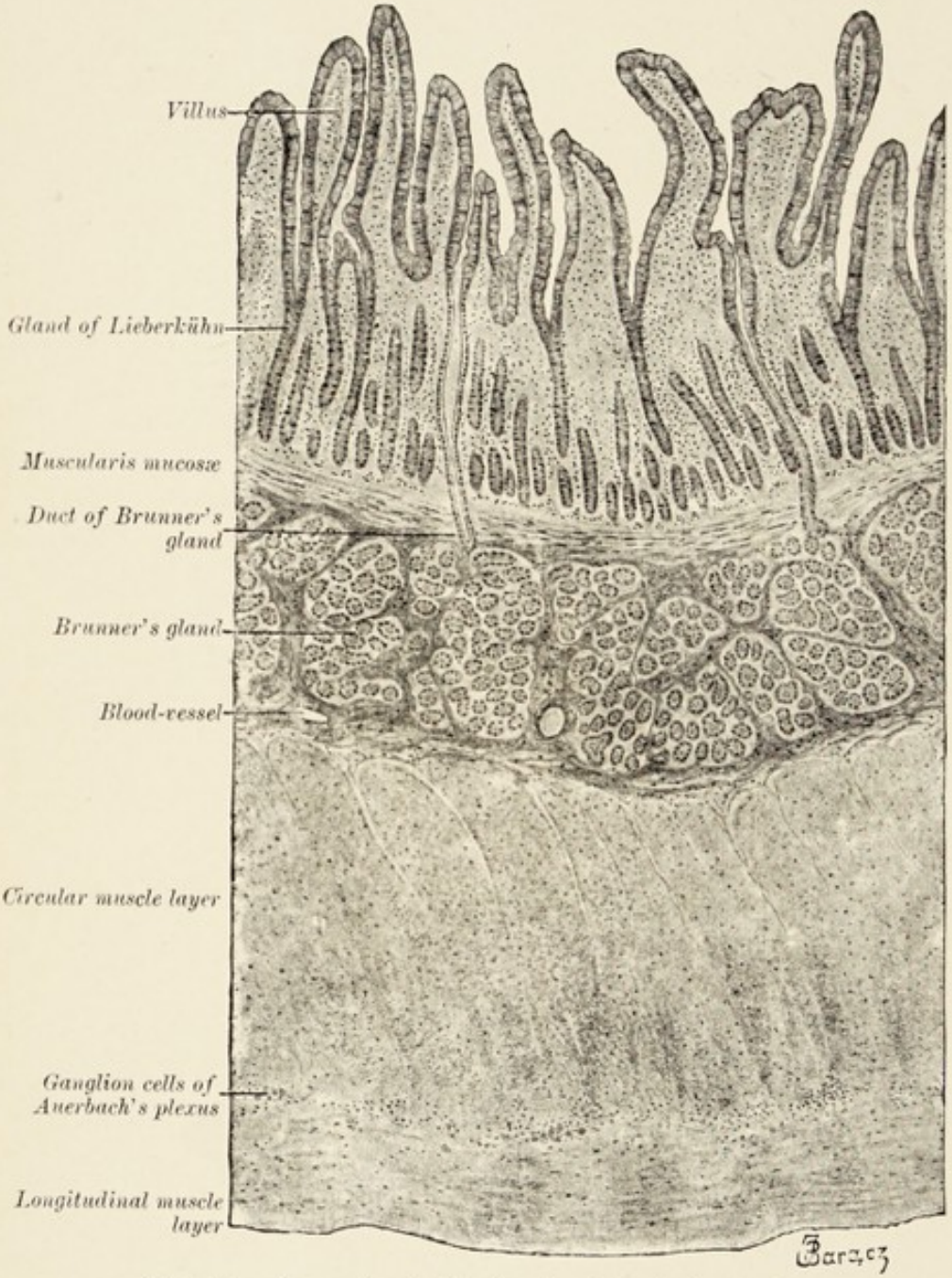


FIG. 140.—From a longitudinal section through the duodenum of a cat. × 34.

PLATE XVII.

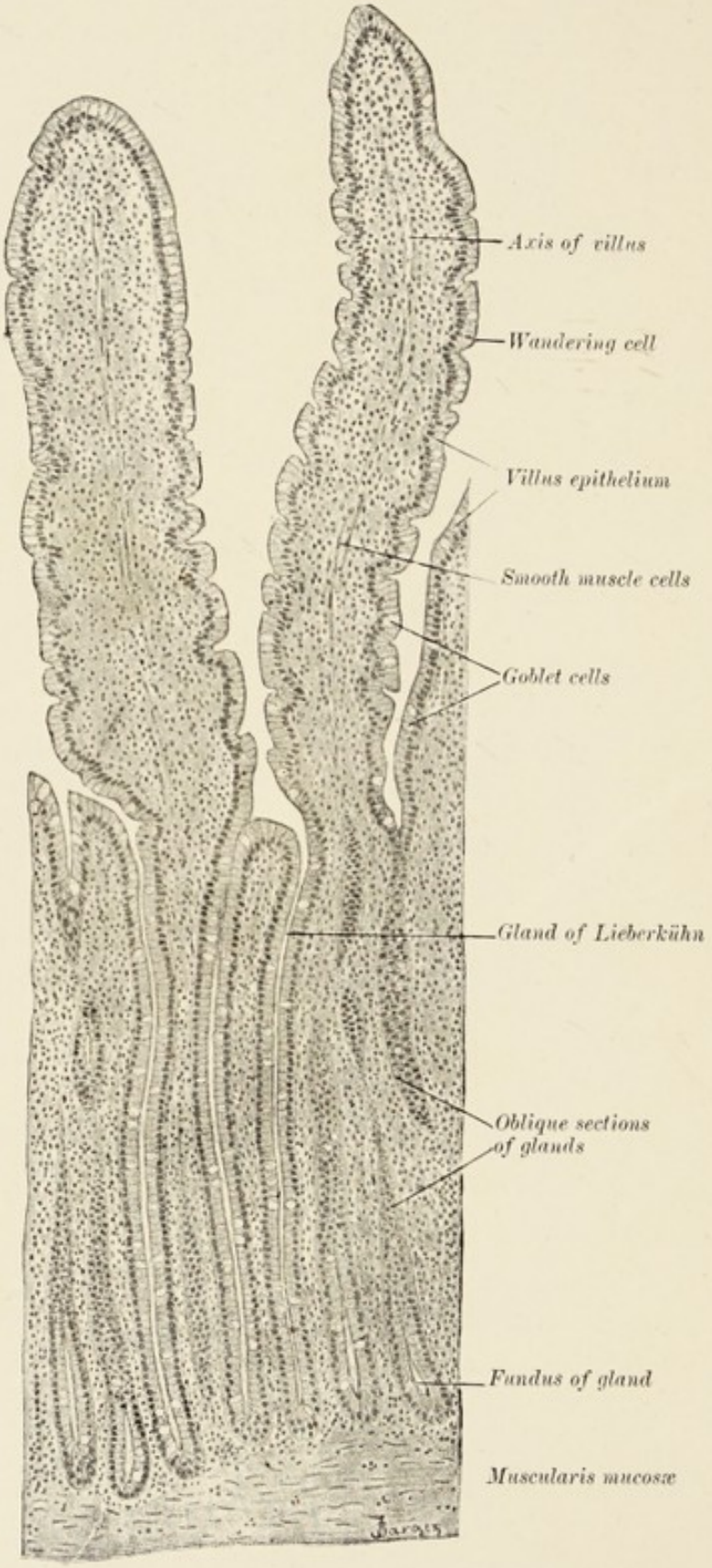


FIG. 141.—Section through the mucous membrane of a cat's jejunum. × 115.

E. INTESTINE.

In the intestine we can distinguish the same number of coats as in the stomach (Fig. 140), namely, mucosa, submucosa, muscularis, and serosa.

The surface of the *mucosa* is nowhere in the intestine smooth. It possesses two kinds of inequalities, whose function is to increase the area of the surface. There are ring-like folds of the whole mucous membrane, the so-called *valvulæ conniventes* (plicæ conniventes Kerkringii), which are developed especially in the upper part of the intestine. Besides these there are the *villi*, which are folds simply of the epithelial layer and the tunica propria, the muscularis mucosa continuing in a straight line below them. These are found only in the small intestine (Plate XVII.). They reach a height of 0.2–1 mm., and vary considerably in form according to the region of the small intestine in which they occur. In the duodenum they are leaf-like; in the jejunum and ileum cylindrical and somewhat thickened at the end. They lie more closely together in the duodenum than elsewhere.

We find also, in the intestine, cavities in the form of simple tubular glands (*Lieberkühn's glands*) which enter the depths of the tunica propria at the bases of the villi. These are longer in the large, than in the small, intestine.

The mucosa of the whole intestine consists of a single layer of epithelium, a tunica propria, and a muscularis mucosæ. The cells of the epithelial layer (Figs. 131 and 143) are cylindrical with a finely granular protoplasm, often containing many kinds of granular inclusions. The nucleus of each cell is oval and lies usually in the lower half. The sides of the cell show no definite cell membrane, while at its free surface it shows a characteristic finely striated border. These are known as border cells. The opposite end of the cell often runs to a point, and is separated from the underlying tissues by a thin homogeneous *basal membrane.*

The epithelium of the glands is not essentially different from that of the villi. The cells are somewhat lower and the striated border is not so well marked. Among these epithelial

cells we find both on the villi and in the glands mucus-producing cells, the so-called *goblet cells* (see under *Epithelium*). The cells full of secretion possess no true cell membrane, but only a thickened ectoplasm, which undergoes no mucoid change and corresponds with the crusta of F. Schulze (Fig. 131). These goblet cells are unevenly distributed, but are especially abundant in the large intestine.

It is not fully understood whether the goblet cells are a different kind of cell or a modified form of the cylindrical cells. Some authors claim that every young cylindrical cell has the power of changing into a goblet cell, and that a cylindrical cell is really a resting goblet cell. Most writers, however, believe that the two kinds of cells are separate and distinct, and that there is only a superficial resemblance between the resting goblet cell and the cylindrical cell. Many hold that mucus can be produced by any of these cells. In fasting, the number of goblet cells increases; likewise during active digestion, as also in poisoning with pilocarpine, they become more numerous. In connection with the regeneration of these cells, Bizzozero has observed that many karyokinetic figures are found in the glands, and almost none on the villi. Thus Lieberkühn's glands seem to be a place of regeneration for epithelium which has been destroyed by oversecretion. Bizzozero claims that these new cells are pushed up to the villi from the glands, and the differences in form of the cells is due to their age. On this theory may be explained the great abundance of goblet cells in the large intestine. Those on the villi are destroyed quickly, and must be replaced by cells formed in the glands. This condition is not present in the large intestine, owing to the lack of villi there, and the goblet cells accumulate.

The epithelial cells are joined together by protoplasmic bridges, which are best seen in horizontal sections of the epithelial layer—*i. e.*, cross-sections of the cells. Between the bridges are spaces which can be demonstrated by treatment with silver nitrate. They are filled with the so-called cement substance. The main function of the intestinal epithelium is

PLATE XVIII.

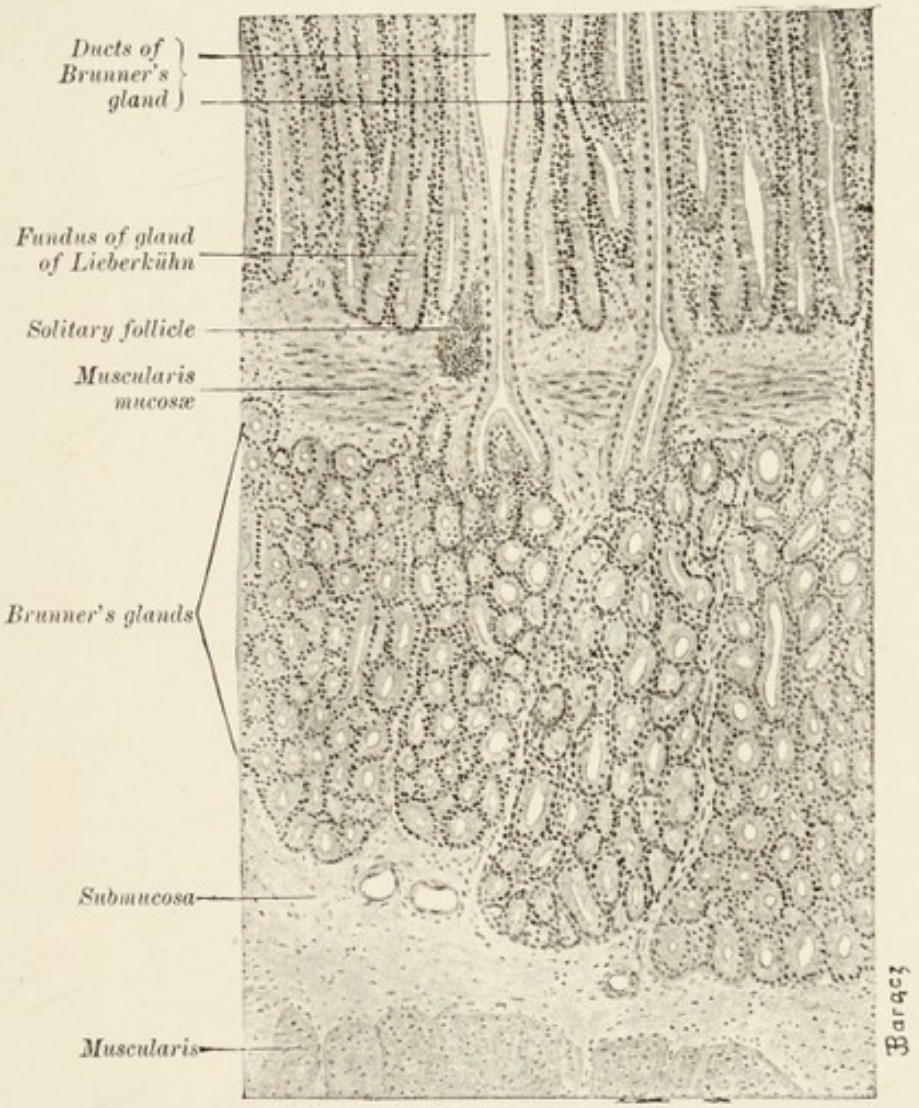
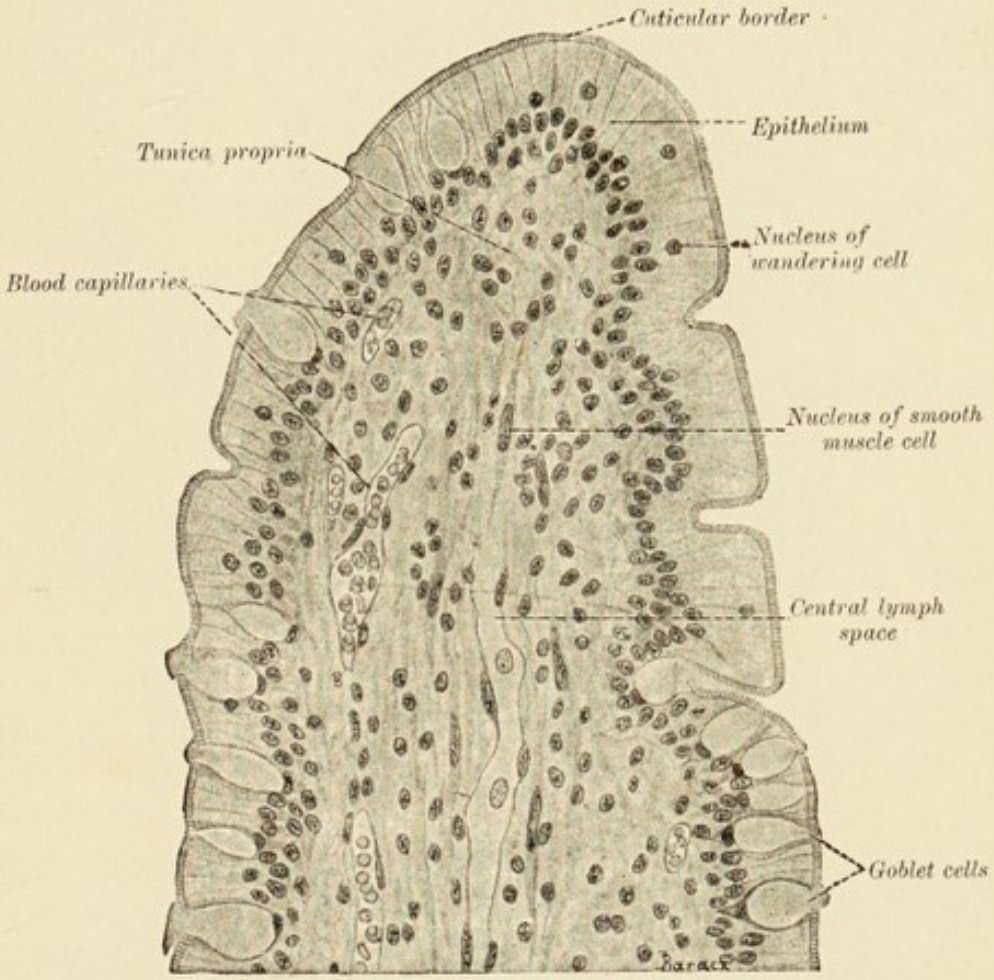


FIG. 142.—From a section through a cat's duodenum. The entire submucosa, Brunner's glands, and the adjacent parts of the mucosa, are shown. × 100.

that of *absorption*, which can best be observed in the digestion of fat. By treatment with osmic acid preparations can be made which show all stages of this process. In what form the fat enters the cells is unknown, but it is probable that it is not as an emulsion, but as fatty acids formed by combination with the bile salts. In the epithelial cells the fatty acids are converted again into neutral fats. It then appears in the intercellular

FIG. 143.



Longitudinal section through the end of a villus from the small intestine of a cat. × 450.

spaces in the form of fine globules which pass through the basal membrane. From here it reaches the lymph spaces of the parenchyma of the villus, and finally enters the central chyle vessel or lacteal. This power of fat absorption is not possessed by the epithelium of the large intestine.

The second important function of the intestinal epithelium, namely, that of *secretion*, is carried out in great part by the

goblet cells which produce mucus. It is probable, however, that the other cells of the glands of Lieberkühn secrete a specific substance which is a constituent of the succus entericus.

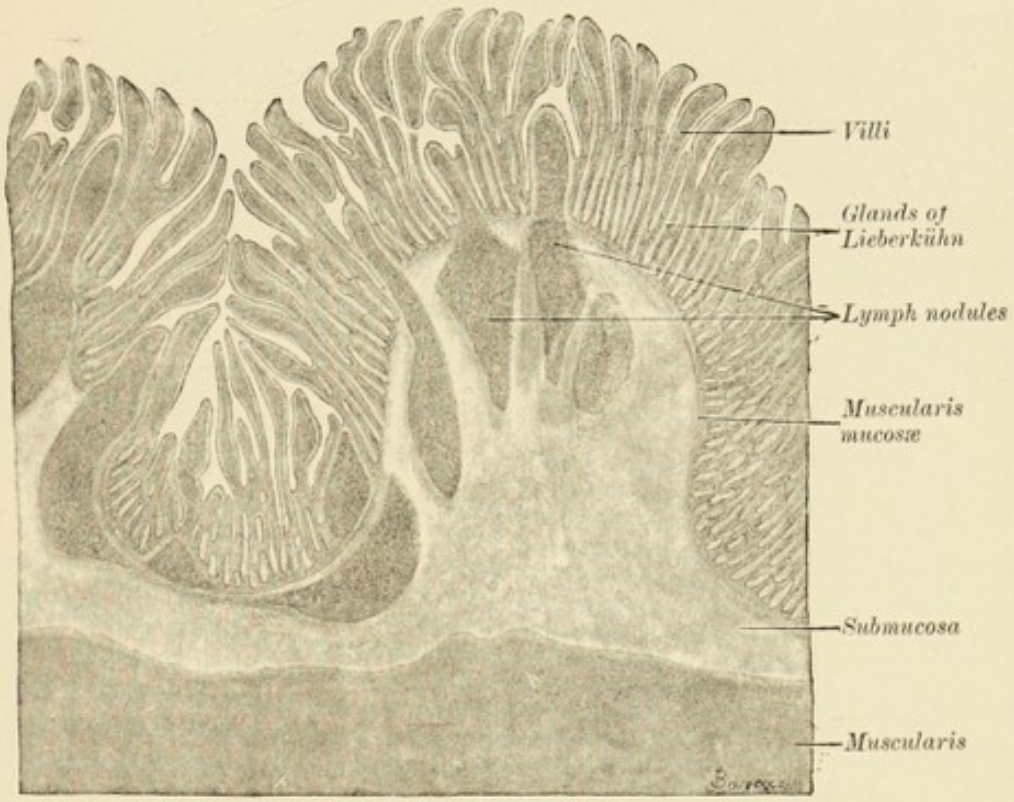
The *tunica propria* consists of a reticular connective tissue which contains a varying number of lymphocytes and other leucocytes. These are in some places collected in masses 1–2 mm. in diameter, which lie either singly (*solitary follicles*) or are grouped together (*Peyer's patches* or *agminated follicles*). The solitary follicles are distributed throughout the whole alimentary canal, but are found especially in the intestine. Their development begins always in the tunica propria and extends through the whole mucosa down to the muscularis mucosæ. They often cause a bulging on the surface of the epithelium, and not infrequently break through the muscularis mucosæ to enter the submucosa. The villi and glands usually are distorted in these regions. In the submucosa there is a smaller resistance to the growth of the follicle, and it comes therefore to have a flask-like form, with the large end in the submucosa and the neck in the mucosa. The structure of the solitary follicles is similar to that of the follicles of a lymph gland. A germinal centre is always present, and the newly formed lymphocytes proceed from this place out to the periphery of the follicle. There they enter the lymphatics or at the surface escape between the epithelial cells into the lumen of the intestine.

The Peyer's patches (Fig. 144) are met with in the ileum, more particularly near its junction with the jejunum. These are oval, and sometimes several centimetres in length. They may consist of as many as sixty follicles lying so close to one another that they usually are compressed and deformed. Often adjacent follicles coalesce, so that the follicle thus formed seems to have two or more germinal centres, as is seen in the appendix vermiformis. The follicles reach the surface of the intestine and are covered by the columnar epithelium, but there are seldom found villi immediately on them.

The submucosa is separated from the tunica propria by the muscularis mucosæ, which is a thin layer of smooth muscle

fibres, the innermost of which run circularly, while the outer fibres take a longitudinal course. From the inner layer muscle fibres run between the Lieberkühn's glands into the villi.

Fig. 144.



Transverse section through a Peyer's patch from a cat's small intestine. × 25.

These are supposed on contraction to shorten the villi and to aid in forcing the chyle, etc., from the villi to the large lymphatic vessels.

The *submucosa* consists of firm connective tissue, with glands only in the region of the duodenum. These are the so-called *Brunner's glands* (Figs. 140 and 142). They are branched tubular glands whose entire bodies are situated in the submucosa, and whose ducts pierce the muscularis mucosæ and open between, or into Lieberkühn's glands. These are occasionally found, not only in the duodenum, but also in the pyloric end of the stomach, just as pyloric glands are sometimes found in the duodenum. The Brunner's glands are recognized easily by the fact that they break through the muscularis mucosæ and into the submucosa. The cells of Brunner's glands are cylin-

drical, finely granular, and much like those of the pyloric glands. During secretion they are smaller and less clear than when no food is being digested. The blind ends of the gland tubules are dilated often like those of alveolar glands. Around the tubules there is to be seen a structureless basement membrane.

The *muscularis* consists of an inner circular and an outer longitudinal layer of smooth muscle fibres. In the large intestine the outer layer is very thin in general, but is thickened in three strong flat bands, which are called the *tæniæ coli*. In certain places the circular layer is thickened also, especially at the opening of the rectum, where it forms a strong circular band, the musculus sphincter ani internus.

The different regions of the intestine are distinguished easily from one another microscopically. The duodenum is characterized by the presence of Brunner's glands and leaf-like villi; the jejunum and ileum, by the absence of these and the presence of columnar villi. The ileum can usually be distinguished from the jejunum by the greater abundance of lymphoid tissue. The large intestine is characterized by the complete absence of villi, the abundance of goblet-cells, and the disposition of the external muscle coat.

Blood-vessels, Lymph-vessels, and Nerves of the Stomach and Intestine.

The arrangement and relation of the blood-vessels in the stomach and large intestine are so similar that they may be described together. In the small intestine the presence of villi causes a considerable difference.

The arteries enter the intestinal wall from the outside and pass through the outer layers to the submucosa. On the way small branches are given off to the peritoneum and the muscularis, to form capillary networks in these regions. In the submucosa the arteries break up to form a network of large vessels parallel to the surface. From these arteries branches pierce the muscularis mucosæ and form a second finer network in the tunica propria, which gives off branches to make up a capillary plexus

PLATE XIX.

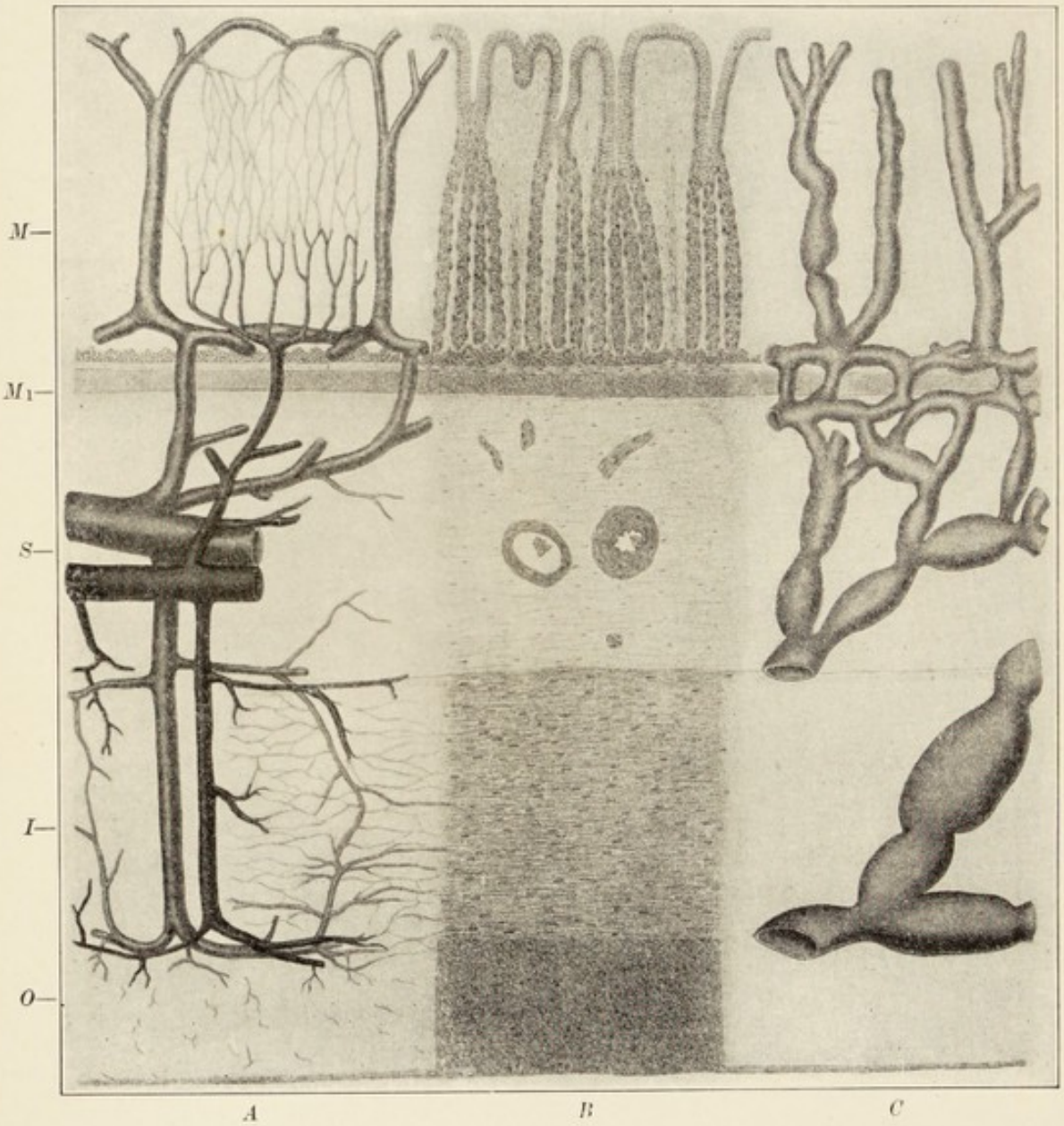


FIG. 145.—Blood-vessels and lymphatics of stomach. (F. Mall.) *M*, mucosa; M_1, muscularis mucosæ; *S*, submucosa; *I* and *O*, circular and longitudinal muscles. *A*, blood-vessels; *B*, microscopic anatomy; *C*, lymphatics. × 70.

PLATE XX.

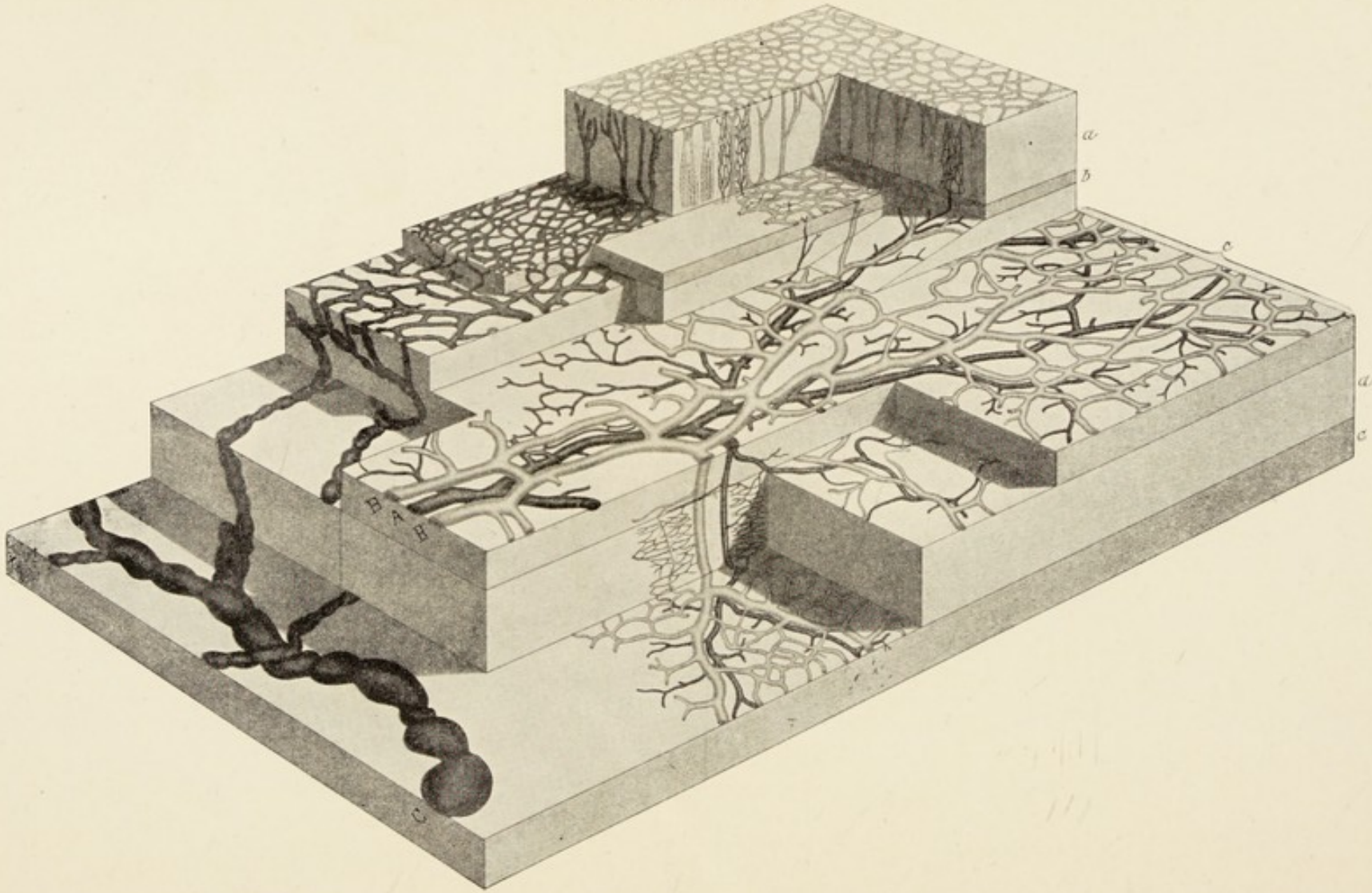


FIG. 146.—Reconstruction of a small part of the middle zone of the stomach. (F. Mall.) *A*, artery; *B*, vein; *C*, lymphatic; *a*, mucosa; *b*, muscularis mucosæ; *c*, submucosa; *d*, *e*, muscle coats.

which surrounds the gland tubules, and passes over into a venous network which is situated in the tunica propria. From here the veins enter the submucosa, where they join to form large vessels which leave the intestine by paths similar to that taken by the arteries in entering. From the submucosa also other branches from the large arteries pass downward into the muscular coats. The relations of the vessels of the stomach as demonstrated by F. P. Mall are shown in Figs. 145 and 146.

In the small intestine there are small arteries proceeding from the subglandular network to enter the villi. One or sometimes two arteries run in the centre of the villus to its end, giving out on the way side branches which form a capillary network. The branches of this network join near the periphery of the villus to form veins, which descend to join the subglandular plexus of veins.

The Brunner's glands are surrounded by a network of capillaries derived from the submucous branches. The lymph follicles gain their blood supply partly from the submucous branches and partly from the plexus in the tunica propria.

The beginning of the *chyle vessels* is between the glands in the stomach and large intestine, and in the axis of the villi in the small intestine. In the upper part of the villus the lymph-vessels end blindly and show a certain degree of anastomosis. These join to form the *central chyle vessel* or lacteal. Around the Lieberkühn's glands there are numerous lymphatics, which form a thick network below. This is in combination with a second coarser network in the submucosa. The efferent vessels pass through the muscularis, collecting the fluid from numerous lymphatics in the muscle and from a lymphatic plexus between the muscle layers. The lymph-vessels leave the intestine between the two layers of the mesentery. Around the follicles the lymph-vessels form a network with sinus-like dilatations.

The *nerves* of the alimentary canal arise mainly from the sympathetic system. The non-medullated fibres enter at the mesenteric border, pierce the external muscle layer, and form a peculiar plexus between this and the internal muscle coat. This is called the *plexus myentericus* or *Auerbach's plexus.* Where

the fibres making up the large meshwork come together, there are enlargements consisting of many multipolar ganglion cells, from which new non-medullated fibres proceed. These cells are to be observed in sections from any part of the alimentary canal, as large cells with much protoplasm staining brightly in eosin, and a large vesicular nucleus with well-marked nucleolus.

From this plexus branches are sent into the submucosa, where they form a second network, finer and more delicate than the first, known as *Meissner's plexus.* In this the meshes are smaller, the fibre bundles more delicate, and the cell groups not nearly so large. From this plexus fibres run throughout the submucosa, and end also in the muscularis mucosæ and the mucosa. They extend into the villi and end under the epithelium in small swellings.

F. PANCREAS.

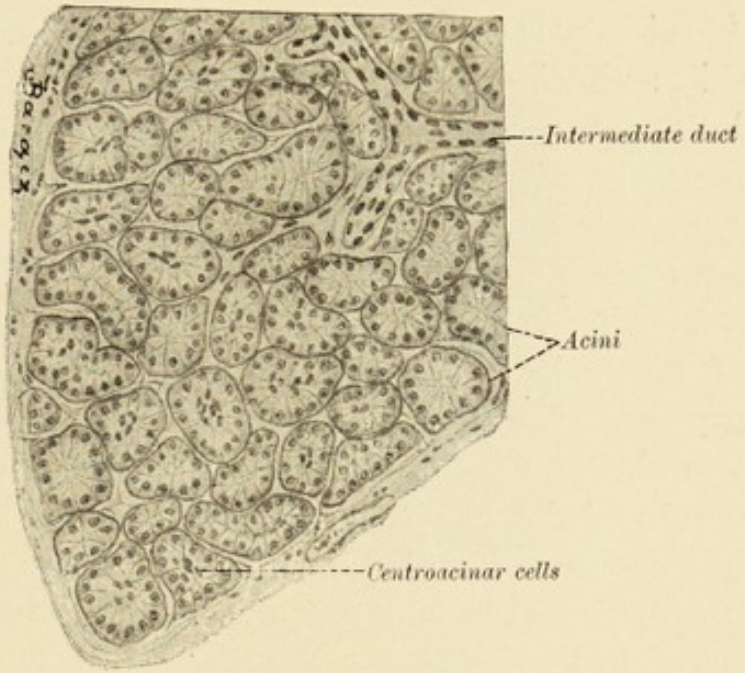
The pancreas is, like the salivary glands, a compound acinotubular gland divided by connective-tissue septa into lobules. Two ducts, the *duct of Wirsung* (ductus pancreaticus) and the *duct of Santorini* (ductus pancreaticus accessorius), conduct the external secretion to the intestine. These are lined with a single layer of cylindrical epithelium, which is surrounded by connective tissue containing small mucous glands. The interlobular ducts pass directly into narrow *intermediate ducts* (Fig. 147) lined with flat epithelial cells. The latter pass over into the secreting end tubules of the gland.

The glandular cells of these end tubules resemble those of the serous tubules, as, for example, in the parotid gland. They are rounded cells with highly refractile granules on the side toward the lumen of the tubule. These are called *zymogen granules.* The nucleus lies in the outer non-granular part of the cell. The number of zymogen granules, as well as the relation between the inner granular zone and the outer clear part of the cell, varies according to the condition of the gland. During digestion the granules gradually vanish and the cell becomes clear. In fasting, the granules, on the contrary, increase in number, and the granular inner zone takes up

more than half of the cell. The granules thus seem to be a stage in the formation of the secretion. Here, as elsewhere in serous glands, secretory capillaries are present.

In the secreting cell a structure has been described by M. Nussbaum, in amphibians, as the *Nebenkern* (paranucleus). This is a small body lying between the nucleus and membrana propria in the non-granular part of the cell. It is oval or twisted in form, and is stained easily. In animals that have fasted for some time it seldom is found. The function and significance of this structure are entirely unknown.

FIG. 147.



From a section of a dog's pancreas. × 175.

In the centre of the end tubules one often finds flat cells, the so-called *centro-acinar* cells (Langerhans). These must be considered as a continuation of the epithelium of the intercalary ducts into the lumen of the gland tubules (Fig. 148).

The tubules are surrounded by a membrana propria, which contains basket cells. The processes of these are intimately connected with the gland cells.

In the centre of each lobule there can be observed with low powers of the microscope light-staining areas. These were described first by Langerhans, and are known generally as the

islands of Langerhans. Their structure has been described by E. L. Opie. According to him, they are most numerous in the splenic end of the pancreas. He describes them as "composed of cells having the same origin as those of the glandular acini," and richly supplied with blood capillaries. In injected specimens the capillaries stand out from the surrounding tissues like a glomerulus. It has been shown fairly conclusively that the islands of Langerhans have to do with the internal secretion of the gland and the control of the storing up and excretion of sugar (Opie).

The *framework* of the pancreas consists of a network of white and elastic connective-tissue fibres. The interlobular septa contain blood-vessels and ducts, which, however, do not run side by side, as in the salivary glands, but enter the gland and the lobules at different points (Flint). The lobules are marked off by interlacing connective-tissue fibrils, and with these the basement membranes surrounding the acini are continuous. The lobules are polyhedral in shape, but do not possess a hilus, as in the salivary glands. The framework of the islands of Langerhans is made up of fine interlacing fibrils supporting the groups of cells and the capillaries. This structure is shown in a drawing by Flint (Fig. 149).

The nerves of the pancreas are almost entirely non-medullated. They enter the gland with the arteries and ramify between the epithelial cells of the alveoli. Small ganglia have been observed in their course.

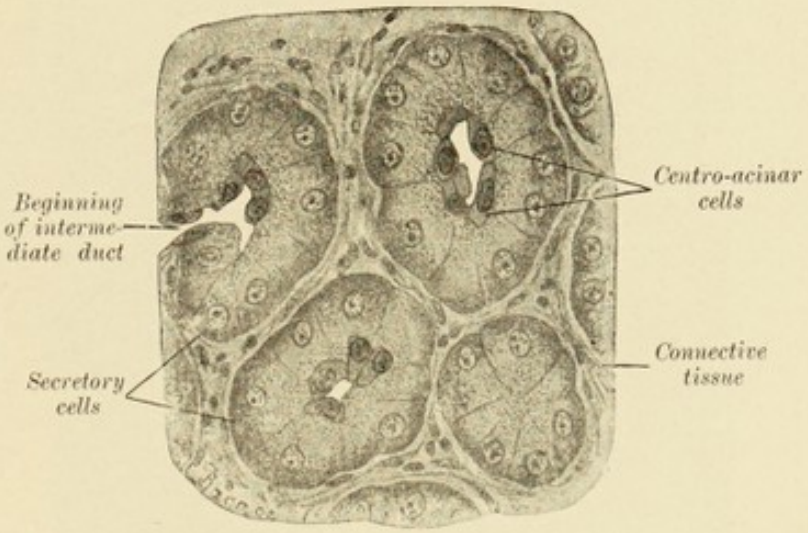
G. LIVER.

The liver is a compound tubular gland in which the tubules are joined by numerous anastomoses. It consists of many lobules, which are separated by a continuation into the gland of the connective tissue of the *capsule of Glisson*, which surrounds the whole organ. This is known as the interlobular connective tissue. The lobules have the form of rounded or polygonal prisms, and in section appear usually as polygonal fields, which in some animals (pig, camel) are marked off very definitely by a strongly developed connective-tissue framework (Fig. 150).

The lobules are usually to be seen plainly on the surface of the liver. Each lobule shows a radial arrangement of the liver cells. These columns of liver cells radiate from the central vein in the middle of the lobule, and are separated from one another by blood capillaries. Both the capillaries and the columns of cells anastomose frequently with one another.

The gland cells of the liver are polyhedral, membraneless structures, whose protoplasm is fibrillar and contains fine granules. In the periphery of the cell the protoplasmic network is dense and possesses small meshes, while near the centre the meshwork becomes looser and more open. The protoplasm often

FIG. 148.



From a section of a cat's pancreas. × 580.

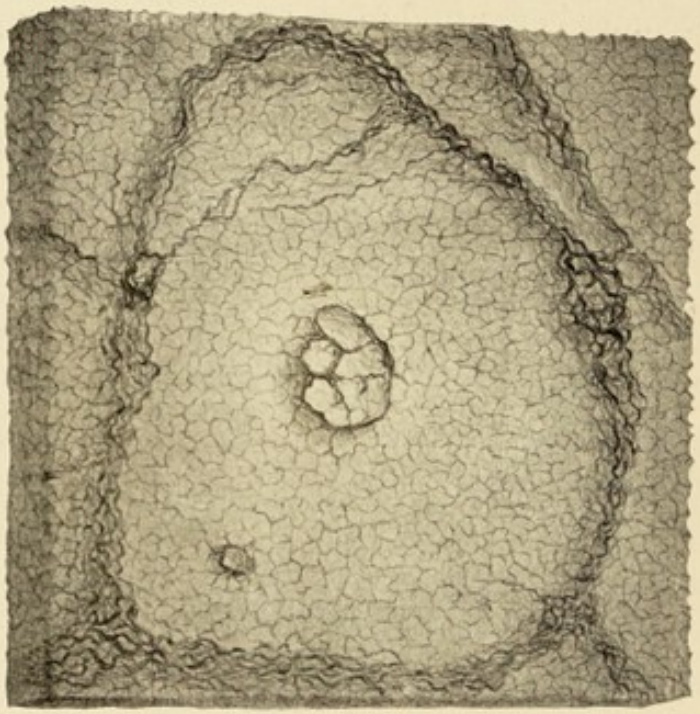
contains fat and bile droplets, glycogen, and pigment granules. The cells contain usually one, but often two, round nuclei.

Between the liver cells run the *bile capillaries* in such a manner that they touch always two or more cells (Fig. 151). There is thus always a part of a cell between each bile capillary and the nearest blood capillary. When many cells surround a bile capillary, it may be compared with the lumen of a salivary gland tubule. When the capillary is between only two cells, it appears as a small groove in each cell (Fig. 151). When more than two cells touch the capillary, the latter is situated at the angles of the cells.

The bile capillaries possess no distinct wall of their own,

except that formed by the liver cells between which they are situated. It seems that the bile capillaries begin in the interior of the cell in canals like those of the secretory capillaries in the parietal cells of the fundus of the stomach (Fig. 152). According to Browicz, the beginning is in the nucleus, for he succeeded in finding bile droplets there. In favor of the intra-protoplasmic origin of secretory capillaries is the fact that secretory vacuoles in the protoplasm are in connection with the bile capillaries.

FIG. 149.



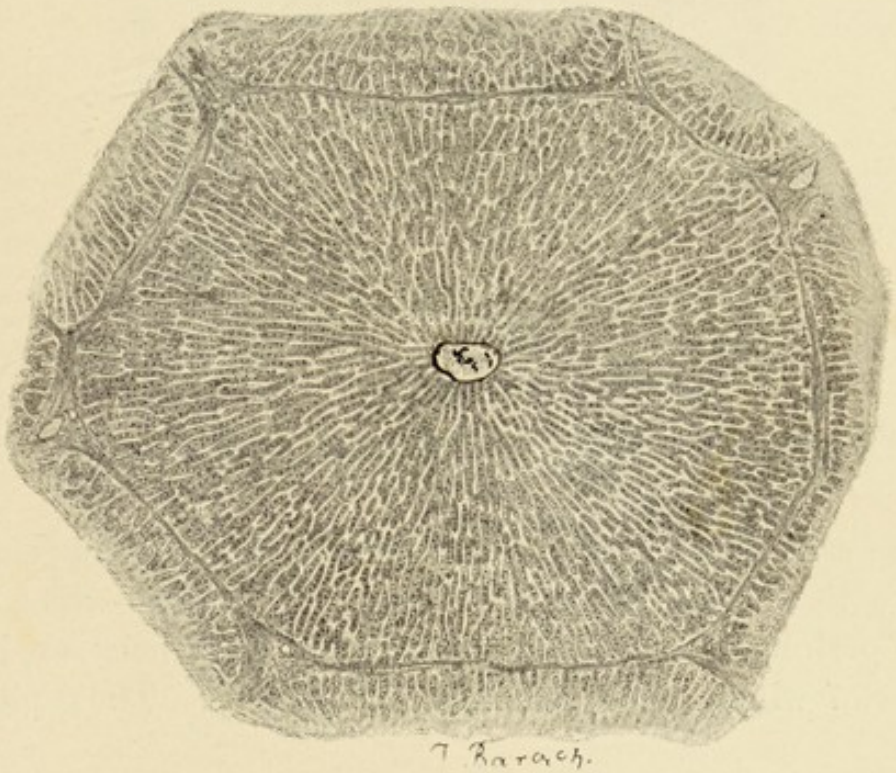
Framework of a lobule of the human pancreas, showing the connective tissue of an island of Langerhans. (Flint.)

By means of Golgi's method, it is possible to demonstrate the course of the bile capillaries and the presence of secretory vacuoles. The latter begin as small droplets of bile in the cell, which on reaching a certain size become discharged into the bile capillaries between the cells. They represent only transitory structures depending on the activity of the cell. Others hold that these are stable intracellular bile paths, which often contain bile and sometimes do not (Browicz).

In mammals the bile capillaries anastomose with one another, forming a network in which the liver cells lie. The

latter are surrounded by the capillaries, for these run along many surfaces of the cells. These capillaries join to form interlobular bile ducts, which are lined with low cubical epithelial cells possessing a refractile cuticular border. At the outside of these there is a homogeneous membrana propria. The wall of the large bile ducts consists of a single layer of cylindrical epithelium and a connective-tissue capsule.

FIG. 150.



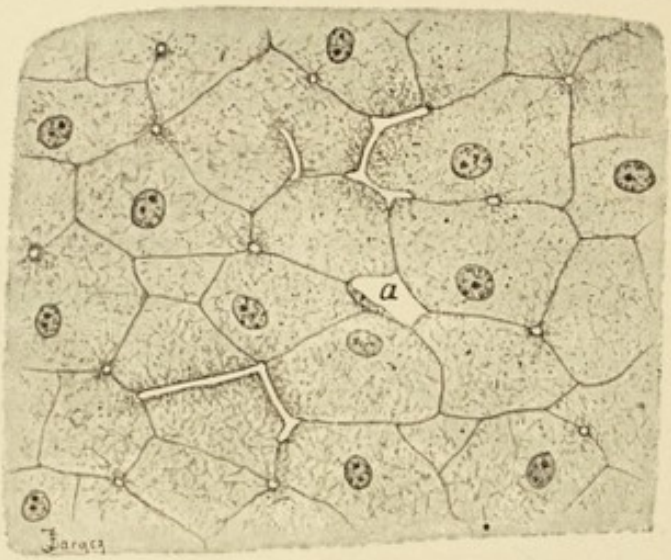
Transverse section of a lobule from a pig's liver, showing the vena centralis in the centre, and the interlobular connective tissue around the whole lobule. × 35.

The interlobular connective tissue is, as we have said, a continuation inward of the fibrous capsule of Glisson, which consists of fibrous and elastic connective tissue. Only a very little of this tissue enters the lobule itself. Here the framework is made up of the so-called "Gitterfasern" of Oppel. These are fine radially arranged fibrils surrounding the blood capillaries, and are entirely identical with the true reticulum described by Mall.

The liver contains blood-vessels from two sources (Fig. 156). The arterial blood from the hepatic artery forms only a small part

of the circulation. The larger part is venous blood entering the liver from the vena portæ. This blood not only brings the materials to be stored up in the liver, but also nourishes those parts of the liver not reached by the arteries.

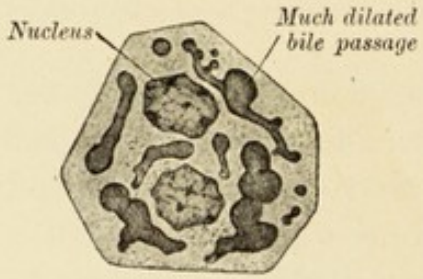
FIG. 151.



From a thin section through the liver of a siredon. *a*, blood capillary. The small passages are bile capillaries. × 325.

The *vena portæ* (Fig. 155) divides in the interlobular connective tissue into branches—interlobular veins—which form at the periphery of the liver lobule a capillary network, in the meshes of which lie the columns of liver cells. The capillaries

FIG. 152.



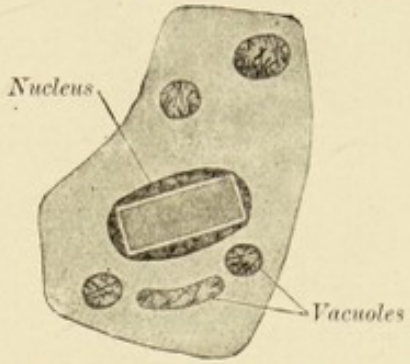
Liver cell with two nuclei, from a human liver in which there is a damming back of the bile. The intracellular bile passages are much dilated. (Preparation by Browicz.)

proceed from all sides of the lobule toward the central or *intralobular* vein. The central veins in turn open into the sublobular veins, which run along the bases of the lobules. Many

of these sublobular veins unite to form the hepatic veins which carry the blood into the inferior vena cava (Fig. 156).

The arterial blood supply of the liver is much smaller.

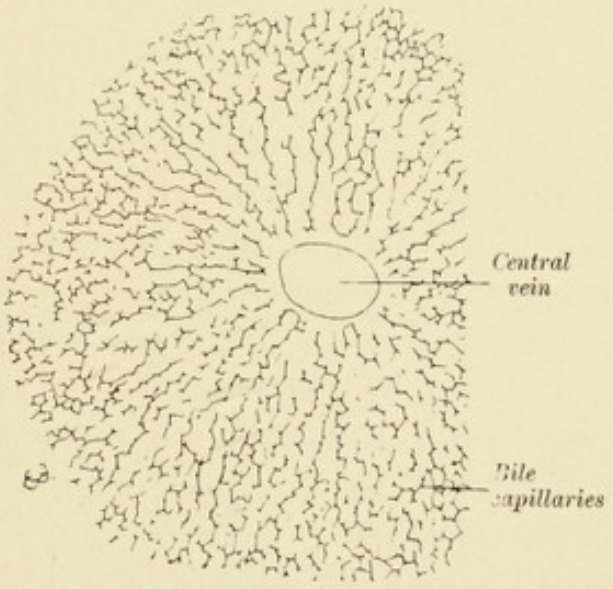
FIG. 153.



Liver cell from a dog. In the nucleus a hæmoglobin crystal is to be seen; in the vacuoles of the cell body brown needle-like crystals of methæmoglobin are found. The latter are due to the entrance of fluid hæmoglobin into the liver cells after intravenous hæmoglobin injection. (Preparation by Browicz.) × 700.

The branches of the hepatic artery break up in the interlobular connective tissue, and there form small networks around the larger bile ducts and enter the liver lobule in a direction similar

FIG. 154.



Bile capillaries in the liver lobule of a rabbit. (Chrome-silver method.) × 80.

to that taken by the venous capillaries. Some of these enter the venous capillaries and some proceed as far as the centre of the lobule to empty into the central vein. The capillary net-

work surrounding the bile ducts in the interlobular connective tissue forms veins which enter the interlobular veins.

It will be seen from the above descriptions that there are in the liver two units, a *secretory* and a *blood vascular unit.* The former is quite definite, and has for its centre one of the small interlobular connective-tissue spaces in which an interlobular bile duct is present. In these spaces there is also usually an artery and one or more veins. The periphery of the secretory unit varies considerably in outline, but can always be marked by lines drawn between all the nearest central veins. It thus takes in parts of at least three and sometimes several liver lobules. The bile capillaries of these lobules run in different directions toward the ducts into which they empty, so that those of one liver lobule may belong to many secretory units. The blood vascular unit is less definite, for the organ is built up around the venous system more than the arterial. Taking the arterial system as a centre, the vascular unit would be much like that described for the biliary system. With the veins, however, a much more definite unit is formed, which can be taken in two ways according as we consider the entry or the exit of the blood. Taking the interlobular veins as a central point, units can be mapped off which include parts of various liver lobules, as in the secretory unit. If, however, the central vein be considered as the centre, the unit would correspond exactly with what is known generally as the liver lobule. This is shown in Figs. 155 and 156. The liver lobule itself is a unit formed by the division of the organ by connective-tissue septa. The framework of the liver includes the parenchyma in the form shown by these lobules.

As shown in Fig. 153, the blood pigments contained by the body and nucleus of the liver cell may, under certain conditions, become crystallized.

In connection with the walls of the intralobular blood capillaries may here be mentioned the *stellate cells* of v. Kupffer. At first these were considered as perivascular connective-tissue cells, but in later years it has been determined that they belong to the endothelial coating of the intralobular blood capillaries.

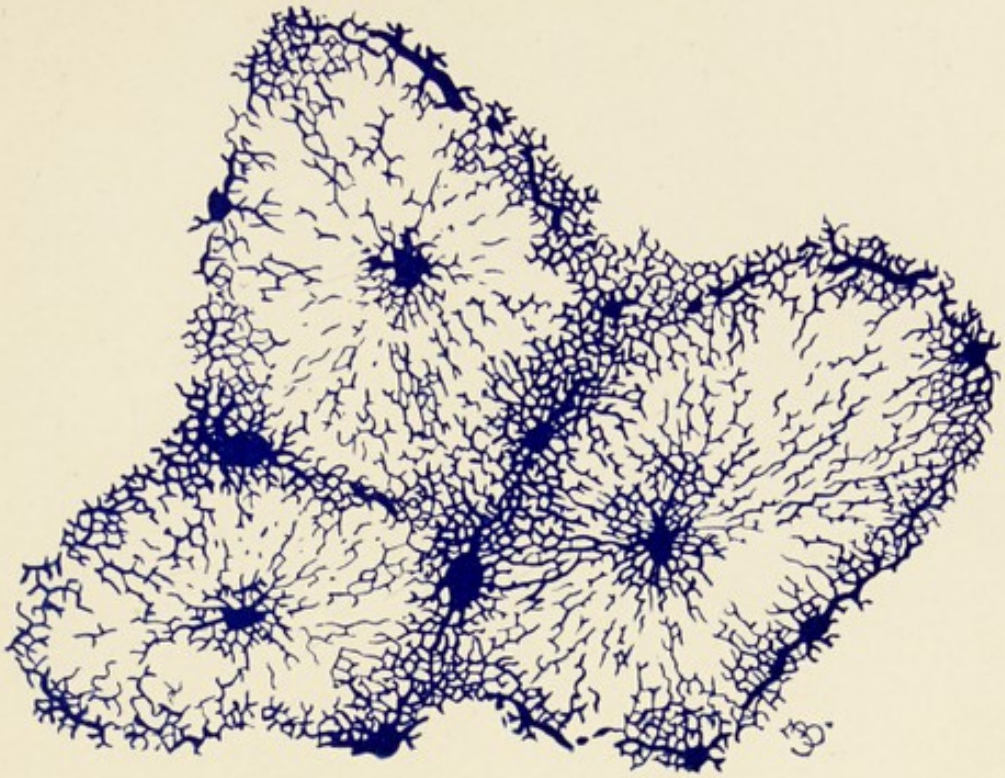


FIG. 155.—Blood-vessels of three liver lobules of a rabbit. In the centre of each lobule is a central vein; at the periphery, the interlobular veins. × 60.

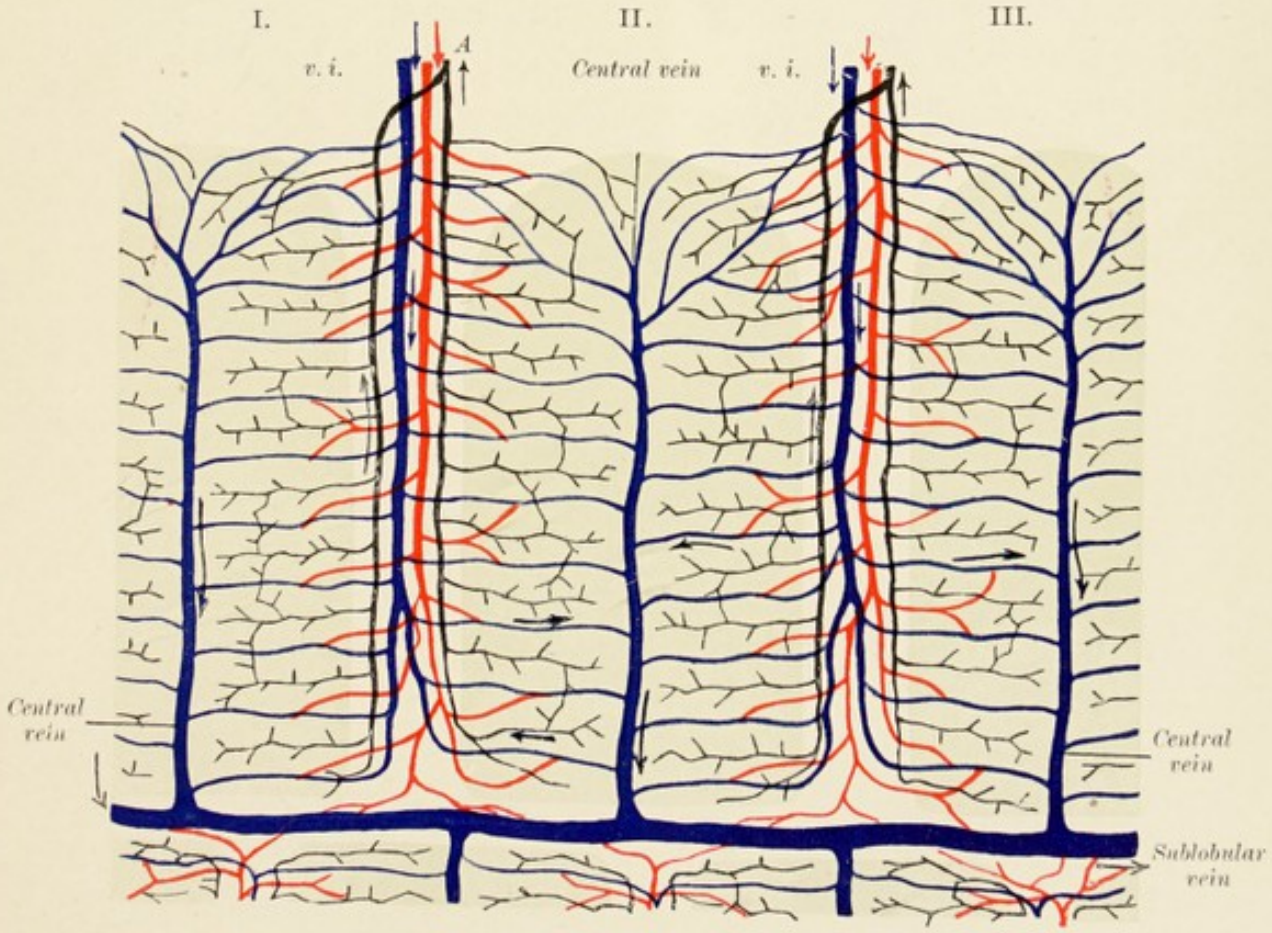


FIG. 156.—Diagram of the liver. Three lobules (I., II., III.) are to be seen. The bile passages are black, the arteries red, and the veins blue. *v. i.*, vena interlobularis; *A*, duct. The direction of the circulation is indicated.

They are large, finely granular cells, possessing phagocytic properties. They are found containing foreign materials, and red and white blood-corpuscles.

The *lymph-vessels* form a thick plexus in the capsule of the liver, which sends branches into the interlobular connective tissue. From between the lobules fine lymph-vessels proceed along the intralobular capillaries, not as closed channels, but as *perivascular lymph spaces.* These surround the blood capillaries and stand in close relation with them.

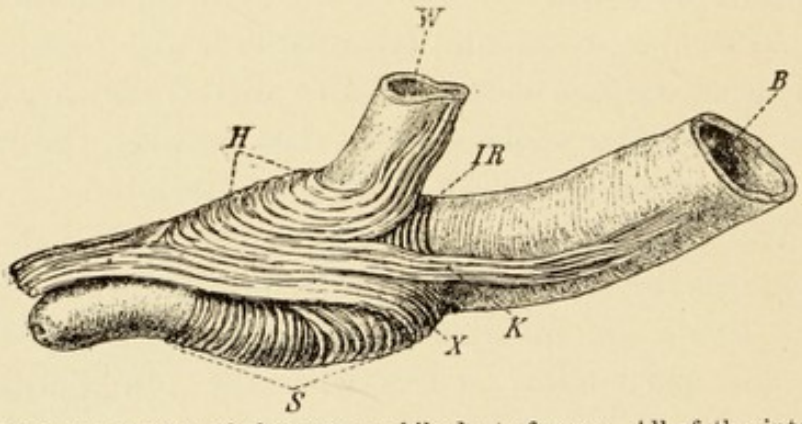
The relations of the lymphatics of the liver have been studied by F. P. Mall, upon whose description the following account is based: The forcing of a colored fluid into the bile duct causes an injection of the liver lymphatics. This is accomplished through the perivascular lymph spaces surrounding the blood capillaries. The walls of the blood capillaries consist of a layer of interlacing reticulum fibrils, upon which is placed an incomplete layer of the endothelial cells of v. Kupffer. The capillary walls are thus quite porous, and there is but little resistance to the passage of fluids from the capillaries into the perivascular spaces. By filling the blood-vessels of the liver with a colored injection mass, an injection of the perivascular spaces and lymphatics is also brought about. The perivascular space communicates directly with what Mall terms the perilobular space which exists between the liver cells at the periphery of the lobule and the interlobular connective tissue. The perilobular space in turn communicates with the lymph radicals by means of the interlobular connective-tissue spaces. "There are no direct channels connecting the perivascular and perilobular spaces with the lymphatics proper other than the ordinary spaces between the connective-tissue fibrils of the capsule of Glisson" (Mall).

The *nerves* of the liver are in large part non-medullated. They form plexuses in the interlobular connective tissue around the blood-vessels and bile passages. Some of the branches from these networks end in the interlobular structures, while others enter the lobules, to accompany the bile

capillaries and end between the liver cells. At their extreme ends the nerve filaments show varicosities (Berkley).

The *hepatic*, *cystic*, and *common bile ducts* are the larger channels concerned in the conduction of the bile to the intestine. They consist of a mucosa, submucosa, and muscularis. The mucosa consists of a single layer of columnar epithelium and a tunica propria which contains small saccular mucous glands and a few smooth muscle fibres. The submucosa is a thin connective-tissue layer. The muscularis has been studied in the whole extra-hepatic biliary system by Hendrickson. According to him, all these ducts possess a distinct transverse longitudinal and diagonal layer of smooth muscle arranged in a somewhat plexiform manner. In the folds of the cystic duct known as the *Heisterian valve*, muscle is also present. The transverse fibres of the cystic duct run in a circular direction in the valve, as though the wall at this level had been invaginated. Most of the longitudinal fibres continue down the duct, but a few turn into the valve almost at right angles. The diagonal fibres do not at all enter the valve. At the entrance

FIG. 157.



Macerated duodenal portion of the common bile duct of man. All of the intestinal coats have been removed. *S*, sphincter fibres. (Hendrickson.) × 5.

of the common bile duct into the intestine at the duodenal papilla an accumulation of the smooth muscle takes place, to form a *sphincter*. Fig. 157, taken from Hendrickson's work, shows the arrangement of the muscle fibres in the sphincter. At the junction of the duct of Wirsung (*W*) and the common bile duct (*B*) there is a circular disposition of the fibres forming the

sphincter (S). From this, certain fibres (X) run down along the sides of the intestine. Others (K) run from one side of the common bile duct to the other surrounding the duct of Wirsung.

Gall Bladder.

The gall bladder has been studied recently by M. T. Sudler, and the following account is based largely on the description given by him. The wall consists of the following coats: mucous, fibro-muscular, subserous, and serous.

The *mucous coat* is somewhat corrugated on its surface, the folds corresponding with ridges in the underlying fibro-muscular coat. They are covered by a single layer of columnar epithelial cells. No goblet cells are present. Fat droplets have been observed in these cells after chyle absorption. A few mucous glands are found in the tunica propria of the mucosa.

The *fibro-muscular coat* is composed of a framework of connective tissue in which bands of smooth muscle are laid down. According to Hendrickson, there are no definite layers of muscle in the gall bladder. Others have described three indefinite layers, of which the thickest runs transversely. The portion of the fibro-muscular coat just beneath the mucosa is made up almost entirely of connective tissue. It corresponds with the submucosa of many organs. In it there are solitary lymph follicles and many blood- and lymph-vessels.

The *subserous coat* is made up of interlacing bands of elastic tissue fibrils. The *serous coat* is the reflection of the peritoneum on the surface of the gall bladder.

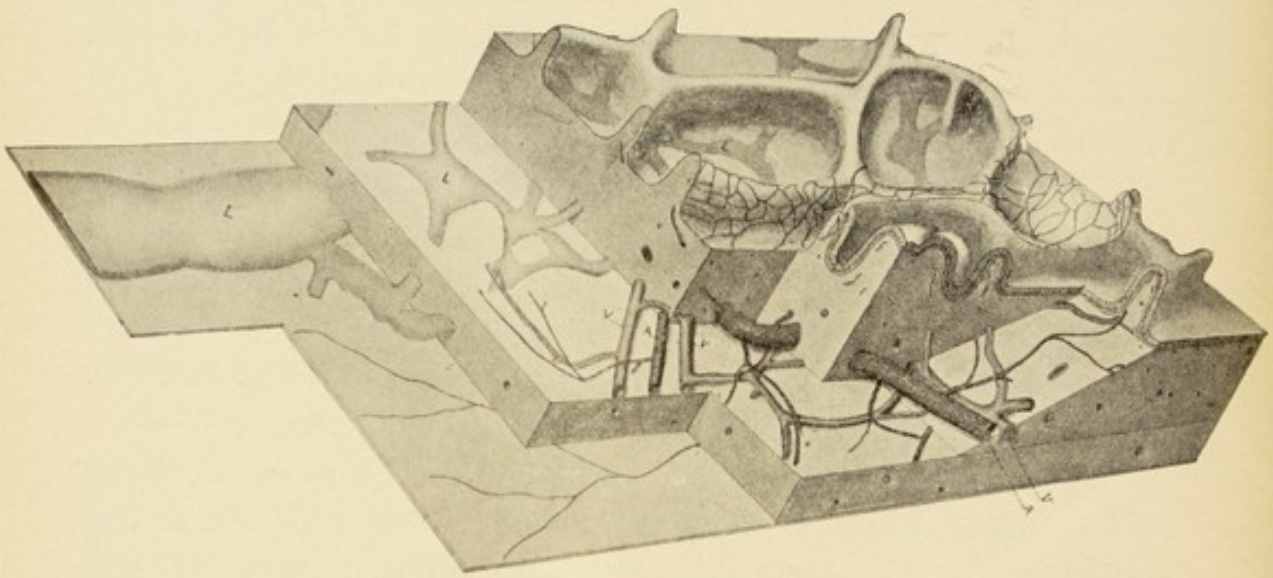
The *blood-vessels* penetrate the bladder wall and divide in the fibro-muscular coat near the subserous layer. Arterial branches are given off to the mucosa, in which there is formed a fine network. Fine branches run also to the subserous and serous coats. The veins collect in the fibro-muscular coat.

Over the surface of the gall bladder run large lymphatics, which are derived from the liver and from the coats of the gall bladder. In the subserous layer there is a network of irregular lymph channels which receive the lymph from a plexus of

smaller lymphatics in the submucous tissue (Sudler). These are shown in Fig. 158.

The *nerves* of the gall bladder are both medullated and non-medullated. Sympathetic fibres, according to Huber, supply the blood-vessels and smooth muscle of the wall. Dogiel has

FIG. 158.



Reconstruction of wall of a dog's gall-bladder. (Sudler.) A, artery; V, vein; L, lymphatic. × 60.

described ganglion cells in this situation. According to Huber, medullated sensory fibres are found near the large arteries and distributed to the mucous membrane.

The *development* of the various structures in the liver has not been worked out thoroughly. The lobule is formed late in the growth of the embryo. The portal and hepatic veins are at first at opposite ends of the organ, and the regions of tissue around them have nothing to do with one another. Later on, by a shifting of some sort, and a new formation of vessels, they come to have the intimate relation seen in the adult liver. Much of this change has taken place already in the human embryo by the fourth week.

As the diverticula grow out from the mid-gut of the embryo to form the first rudiments of the liver a primitive bile duct is established. By a branching of this the large ducts of the organ are formed, but it is uncertain whether the bile capil-

laries are formed from these or have a separate origin and later become connected with them. This subject was worked over by Hendrickson. According to this author, the capillaries cannot be demonstrated by the Golgi method in pigs' embryos less than 5 cm. in length. In these only a few appear immediately around the large branches of the portal vein. In human embryos 5 cm. in length the network of capillaries is considerably more extensive. In older embryos the main capillaries gain side branches, and those encircling different portal branches finally meet. The meshes of the network in the places where it first appears are smaller than where they are subsequently formed. This is due to the division of the older meshes by side branches. In some of the older embryos the capillaries are seen to be continuous with a larger vessel in the region of the interlobular vein, which probably represents the interlobular bile duct.

H. PERITONEUM.

The peritoneum lines the whole abdominal cavity and is reflected over the organs contained therein. As it passes out to the organs (*e. g.*, the intestine) it forms a double layer, known as the *mesentery*, and on the surface of the organs themselves it is spoken of as the *tunica serosa*.

The peritoneum is a thin membrane consisting of a connective-tissue layer and a single layer of flat endothelial cells. The latter cover the free surface, and are usually polygonal in outline. The cement lines between the cells can be made out readily in specimens treated with nitrate of silver; and by special methods, especially that proposed by Kolossow, structures which generally are understood to be protoplasmic bridges can be demonstrated. The outlines of the cells are often wavy or quite irregular.

The connective-tissue layer consists of interlacing connective-tissue bundles, containing numerous elastic fibres and connective-tissue cells. The peritoneum is bound to the underlying parts by means of a connective tissue rich in fat and elastic fibres. The so-called *subserous connective tissue* is developed more strongly in some places than in others. In the intestine and

liver it is so scarce that one cannot distinguish it as a separate layer, and the serosa seems to be a part of the organ upon which it lies.

The blood supply of the peritoneum is made up of an extensive capillary network. The lymph-vessels can be seen especially well in the mesentery of an animal which has recently had a fatty meal. Here they stand out as a white network of anastomosing vessels. The nerves are non-medullated, and end either freely or in the form of Pacinian corpuscles (see Nerve-endings).

III. RESPIRATORY SYSTEM.

A. LARYNX AND TRACHEA.

The *mucous membrane* of the larynx, like that of the trachea, consists of a ciliated epithelium, whose cilia move in the direction of the pharyngeal cavity. In the true vocal cords and on the posterior surface of the epiglottis is found a stratified pavement epithelium. In these places the tunica propria forms no papillæ.

The *tunica propria* is a connective-tissue sheath, containing elastic fibres and leucocytes, which vary in quantity in different places. Solitary follicles are not often seen. At the border of the epithelial cells is a *basement membrane* (membrana propria). This represents a thickening of the subepithelial connective tissue. In the tunica propria there are many smooth muscle cells, which in the posterior part of the tracheal wall are strongly developed and join together the ends of the C-shaped cartilage rings. The *submucosa* contains a number of branched tubular mucous glands, which are largest in the posterior wall of the trachea, and here often penetrate into the muscle layer.

The *cartilaginous framework* of the larynx and trachea is made up of hyaline cartilage, with the exception of the cartilage of Wrisberg and Santorini, and the median part of the thyroid cartilage, which are made up of elastic cartilage.

The blood- and lymph-vessels form wide networks parallel to the surface. The nerves show small ganglia in their course,

PLATE XXII.

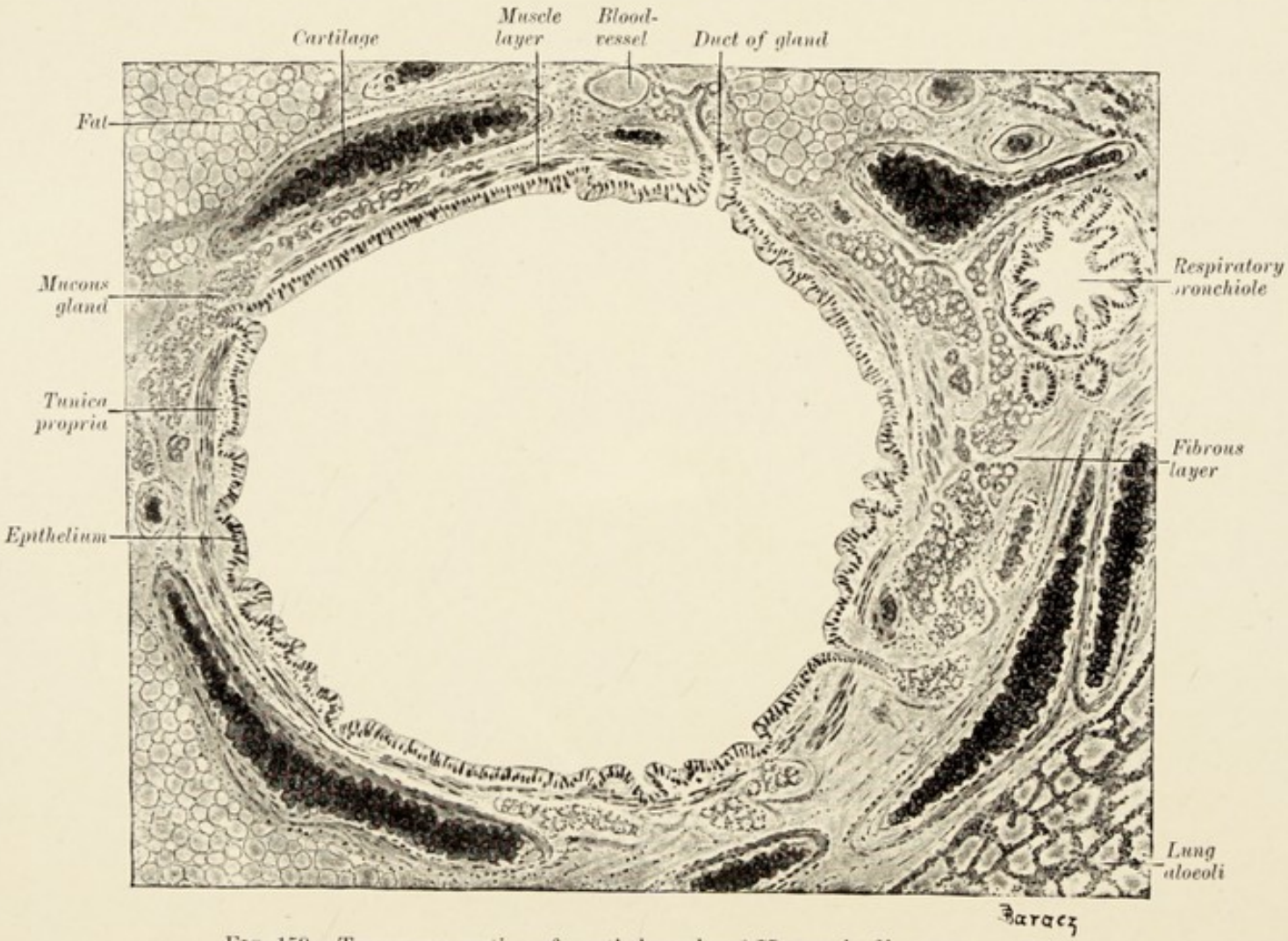


FIG. 159.—Transverse section of a cat's bronchus 1.75 mm. in diameter. × 40.

and end partly under and partly in the epithelium. On the lower surface of the epiglottis there are small taste buds present.

B. BRONCHI AND LUNGS.

The trachea divides to form the bronchi, of which the largest are quite similar in structure to the trachea.

The *mucous membrane* is thrown into longitudinal folds, and covered on the surface with a many-layered ciliated epithelium containing a considerable number of goblet cells (Fig. 159). The mucous membrane of the smaller bronchial branches consists of a single layer of ciliated epithelium. The *tunica propria* consists of connective tissue with elastic fibres and leucocytes. The smooth muscle cells here form a circular layer. The mucous glands break through this muscle layer, and are first absent in bronchial twigs as small as 1 mm. in diameter. This is also about the place where cartilage ceases to exist in the bronchi. In larger bronchi the cartilage has the form of half rings, while in smaller branches it usually appears as irregular plates which are arranged on all sides of the wall. Toward the outside the cartilage masses are surrounded by a fibrous membrane which contains elastic tissue, blood-vessels, and nerves.

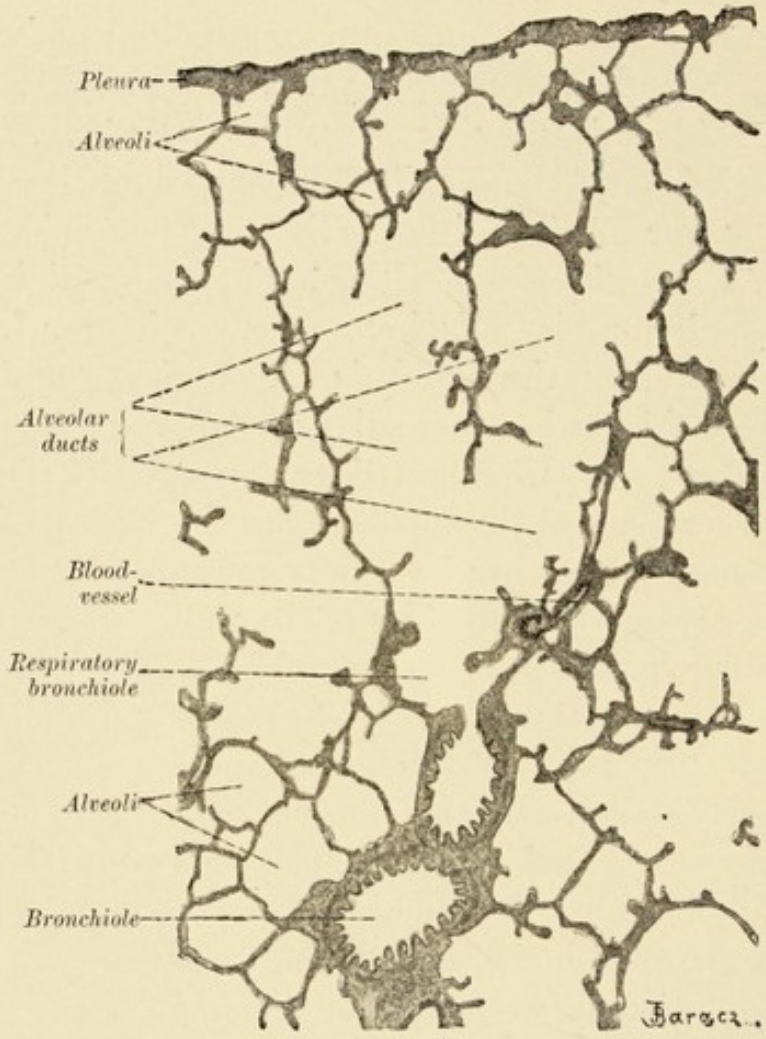
In *bronchioli* 0.5 mm. in diameter the cartilage and mucous glands are absent, and the mucous membrane consists of a single layer of ciliated epithelial cells, among which are mingled many goblet cells. The muscle layer surrounds these bronchioles as a circular sheath, and during contraction throws the surface into longitudinal folds.

By a division of the bronchioles there are formed the *respiratory bronchioles*, from which thin-walled diverticula, the *alveoli*, are developed (Fig. 160). These are covered by the so-called *respiratory epithelium*. The epithelium at the beginning of the respiratory bronchioles is ciliated, and becomes gradually cubical and then flat. The respiratory epithelium, which consists of flat non-nucleated cells, begins in the form of small islands among the low cubical epithelium of the respiratory bronchioles.

W. S. Miller has given us a new conception of the lobule

of the lung and its relation to the blood-vessels. The following notes are based on his work. He speaks of the last division of the bronchus before it breaks up into the lung parenchyma as the terminal bronchus. From this a number of other passages

FIG. 160.



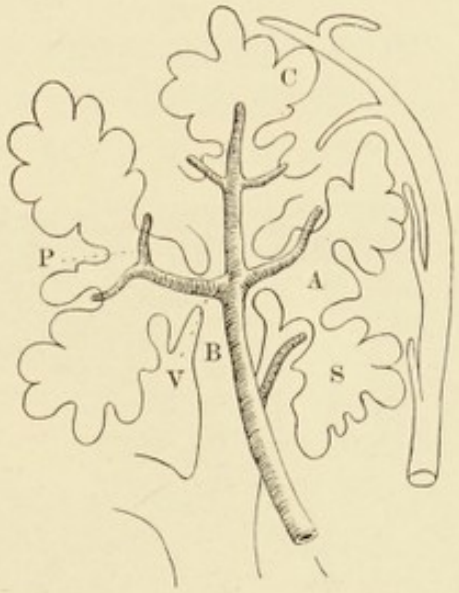
Section through the lung of a cat. The respiratory bronchiole divides to form two alveolar ducts. × 50.

lead, which are connected by a central chamber, known as the *vestibulum* (Fig. 161). These passages open into the *atria*, which communicate by means of the *air-sac passages* with the various *air sacs*. Around the periphery of the air sacs are the *air cells*. This can be seen in Fig. 161.

The terminal bronchus (average diameter, 0.4 mm.) contains smooth muscle cells in its walls. It is lined with columnar epithelium. Between this and the atria are the

vestibula, which are 0.2 mm. in diameter. Three to six of these arise from the end of each terminal bronchus. Smooth muscle fibres do not extend beyond the vestibule, but are found surrounding it like a sphincter. Several atria communicate with each vestibule. These are thin-walled chambers resembling the air sacs in their possession of a network of blood capillaries. Opening from each atrium are two or more air-sac passages, which average 0.143 mm. in diameter. The atria and air-sac passages contain no muscle cells. The air sacs are irregular in shape, with an average size of 0.511 mm. by 0.313 mm. The

FIG. 161.



Terminal bronchus of a mammalian lung. (Miller.) S, air sac; A, atrium; B, terminal bronchus; V, vestibule; P, air-sac passage. The artery is shaded and the vein is in outline.

walls are thin, and are made up of capillaries and a little connective tissue covered by flat epithelium. Irregular, thin-walled diverticula from the air sacs are the air cells. These are lined with cells of two kinds: delicate irregular cells lying over the blood-vessels, and small flat polygonal cells over the meshes of the capillary network. Similar air cells may arise from the bronchus and from the atrium. Those on the bronchi have an average diameter of 0.047 mm., and those on the atrium and air sac 0.113 mm.

The respiratory bronchiole of some authors leads into two

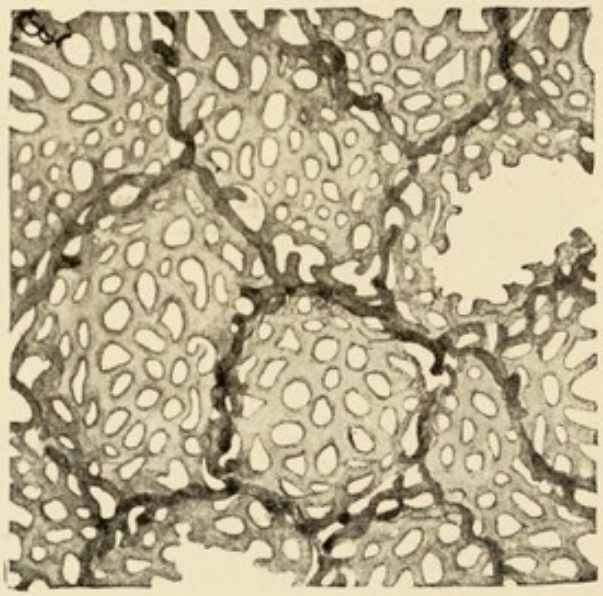
or more terminal bronchi, which are the same as the alveolar ducts. The alveolar sacs or infundibula correspond with Miller's air sacs. The term alveolus is applied to the air cells (Schulze, Kölliker).

The interlobular connective tissue contains many elastic fibres, and often a considerable amount of pigment, such as coal-dust breathed into the lungs. These foreign particles are carried away by the lymphatics to the lymph glands at the base of the bronchi, where usually they are retained.

The *pleuræ* consist of connective tissue containing a good deal of elastic tissue, and are covered on their free surface by flat endothelial cells.

The *pulmonary artery*, carrying venous blood to the lungs, breaks up into many branches, which accompany the bronchi.

FIG. 162.



Part of a section of an injected lung from a rabbit. × 300. The alveoli are seen from the surface; at *a* an alveolus is cut through.

The arterial end twigs form a capillary network which surrounds the alveoli (Fig. 162). One terminal twig usually supplies several alveoli. From this capillary network venous branches proceed to the bases of the bronchi and carry out the arterial blood to the *pulmonary vein*. During its passage through the capillary network surrounding the alveoli the venous blood absorbs the oxygen of the air through the walls

of the alveoli, and gives out in turn gases which are to be eliminated. The gases pass through the vascular epithelium, the connective tissue between the vessels and the wall, the basal membrane, and the respiratory epithelium.

The arterial blood supply to the lung is accomplished by the *bronchial arteries.* These break up into small branches, which supply the bronchi, the interlobular connective tissue, and the walls of the pulmonary vessels. There are numerous anastomoses between the bronchial and pulmonary systems of blood-vessels. A part of the blood of the bronchial arteries thus leaves the lungs through the bronchial veins, and a part through the pulmonary veins.

The branches of the pulmonary artery follow the bronchus to a point beyond the terminal bronchus. As has been described by W. S. Miller, the branches at this point divide to send twigs to each atrium. From these a capillary network is formed, which surrounds the air sacs and air cells. On the peripheral side of the air sacs and air cells the capillaries gather to form the veins, which remain at the outside of the lobule, as shown schematically in Fig. 161. The network which is shown in Fig. 162 is the richest capillary plexus in the body. It is thus seen that the lobule of the lung forms also a blood vascular unit, with the artery in the centre and the veins at the periphery. An exception to this is formed by two small veins arising from near the end of the terminal bronchus.

Lymphatics in the lung and bronchi have been studied by Miller. In the bronchus the lymph-vessels form a network which extends as far as the end of the terminal bronchus. Here branches are sent to the pulmonary artery, to the two small veins in this region, and to the veins that run to the pleura.

Nerves.—Nerve fibres follow the bronchi into the lung substance. These consist of both medullated and non-medullated fibres. The sympathetic fibres show small ganglia in their course. These nerves innervate the muscles and mucous membranes of the bronchi, and also the walls of the blood-vessels.

No nerve-endings have been found in the walls of the air sacs. Berkley has described arborizations of fine fibrils upon and between the cells of the alveoli.

IV. URINARY SYSTEM.

A. KIDNEYS.

The kidney is a compound tubular gland; but it may be considered as an alveolotubular structure, since the urinary tubules are dilated at their ends to form the capsules of Bowman. There can be distinguished in this organ a *medullary* and a *cortical* substance, a marked difference existing between the two parts, in the course and structure of their tubules (Figs. 163 and 164).

The medullary substance consists of a number of cone-like divisions, the so-called *Malpighian pyramids*, whose apices extend down into the pelvis of the kidney as papillæ. In man the number of these pyramids varies from seven to twenty. In many other mammals there is only a single pyramid and one papilla. These pyramids are made up of straight tubules extending radially from the apex of each papilla to the border of the cortex. From the medulla the straight tubules extend up into the cortex in conical masses, known as the *pyramids of Ferrein*, or *medullary rays*. It will be noticed that the Malpighian pyramids are many times as large as the pyramids of Ferrein, that their apices point in different directions, and that their bases are approximated. Further, the pyramids of Ferrein are situated in the cortical region, while the Malpighian pyramids make up the medulla.

Each tubule has its origin in the cortex in the region between the medullary rays, in a sac, the *capsule of Bowman*, into which is pushed a mass of blood capillaries, the *glomerulus*. The capsule of Bowman with the tubule may be compared with a rubber tube possessing at the end a bulb, the wall of which has been invaginated from the outside by a body representing the glomerulus. The space in the invaginated sac is the beginning of the lumen of the urinary tubule. The portion of the tubule next to the Bowman's capsule is known as the

PLATE XXIII.

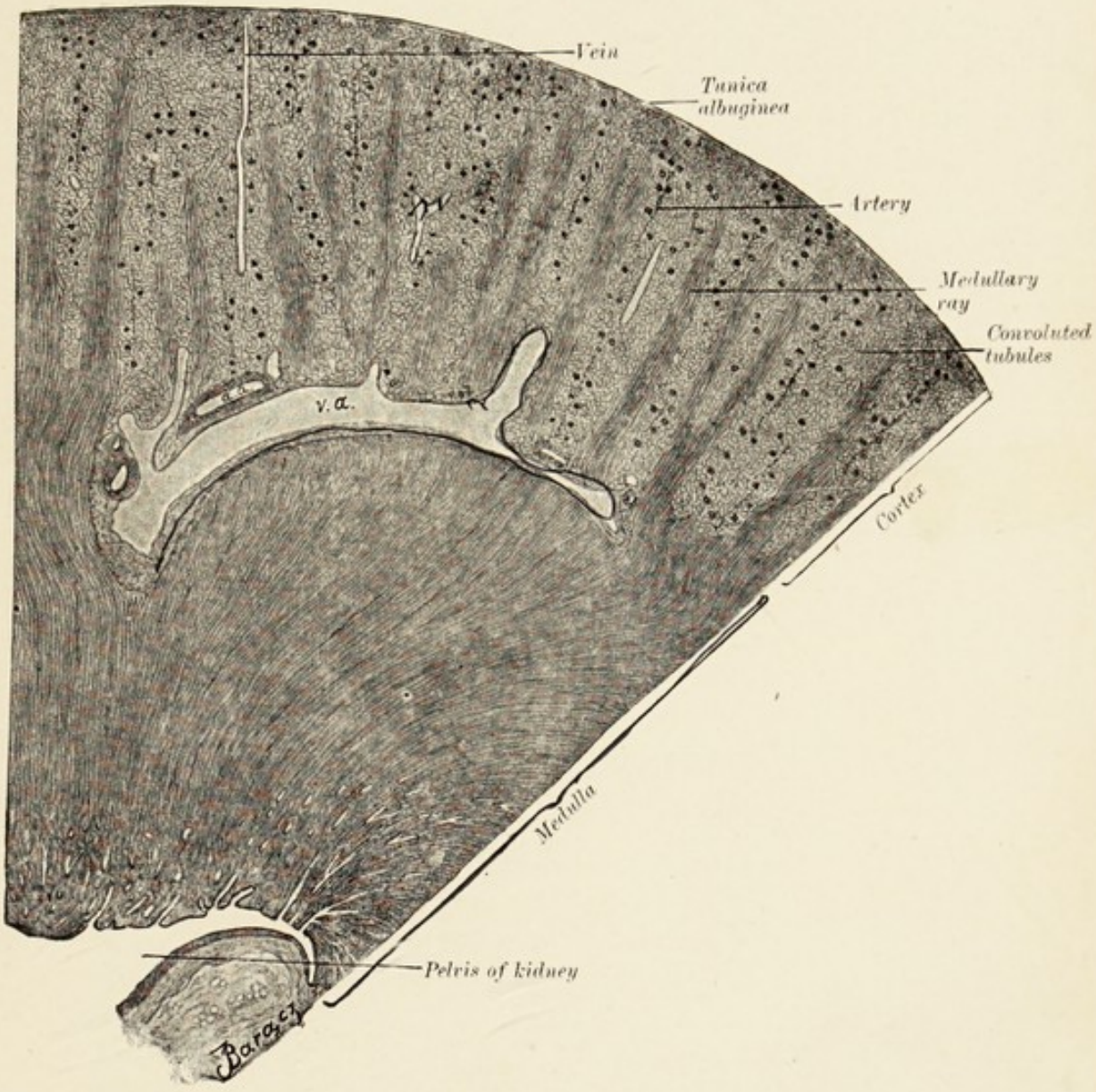


FIG. 163.—Longitudinal section through a part of an ape's kidney. × 13.

PLATE XXIV.

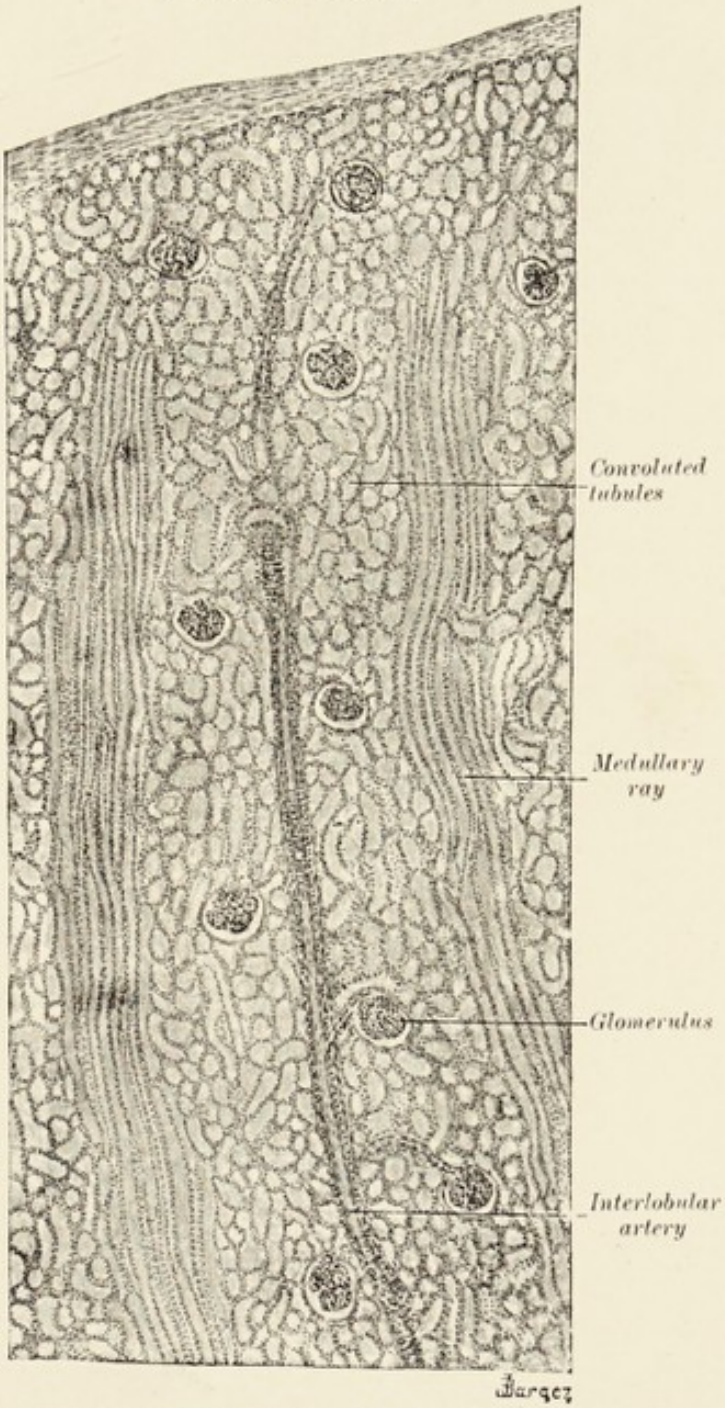


FIG. 164.—From a longitudinal section through the cortex of an ape's kidney. × 55. Two medullary rays are seen, and between them the Malpighian corpuscles and convoluted tubules. An artery runs through the centre.

PLATE XXV.

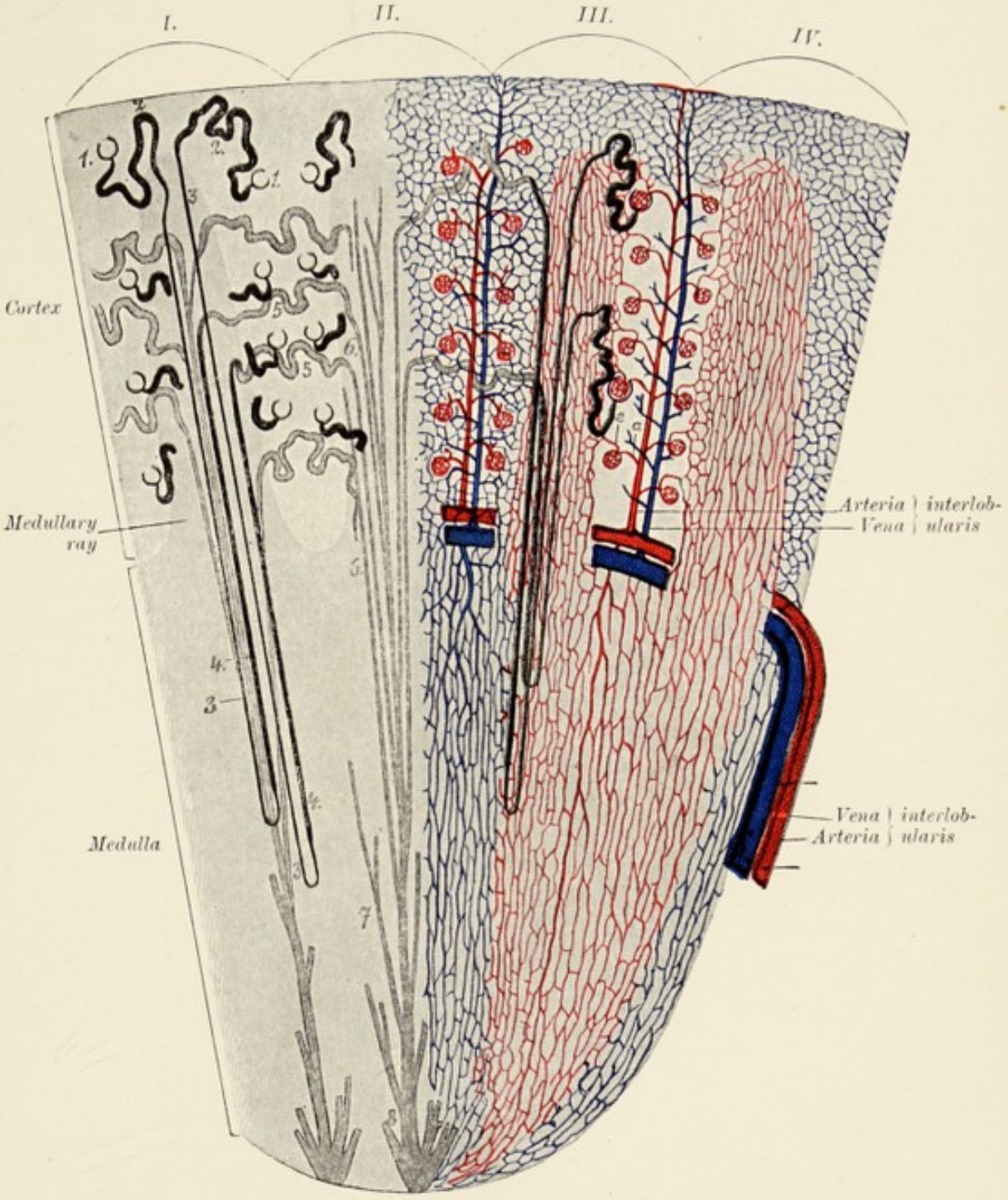


FIG. 165.—Diagrammatic representation of the course of the urinary canals (left) and the kidney vessels (right).

The arteries are red, the veins blue; capsules of Bowman, convoluted tubules I. order and loops of Henle are black; convoluted tubules II. order and collecting tubules, gray.

I., II., III., IV., four kidney lobules: *a*, vas afferens; *e*, vas efferens. 1. Bowman's capsule; 2, convoluted tubule I. order; 3, descending limb of loop of Henle; 4, ascending limb of loop of Henle; 5, convoluted tubule II. order; 6, 7, collecting tubules; 8, papillary duct.

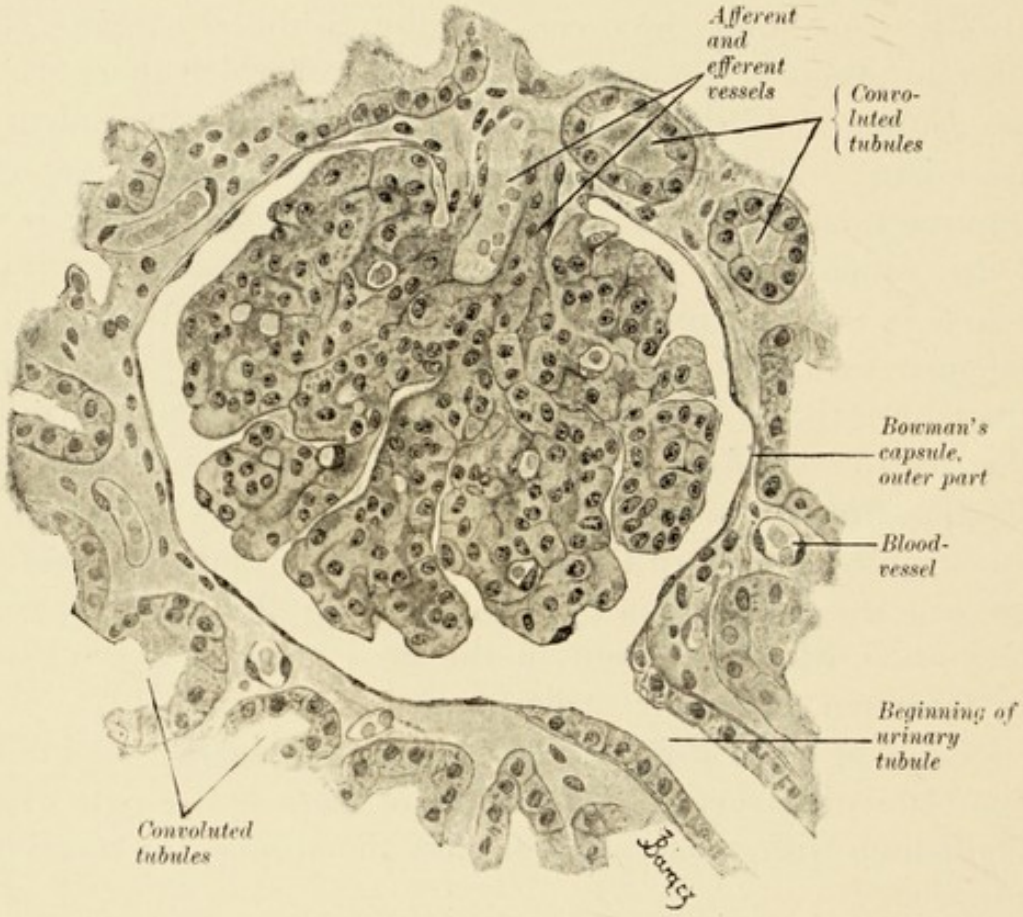
convoluted tubule of the first order. At the beginning of this there is a slight constriction. After taking a very tortuous course between the medullary rays, and forming what is called the labyrinth of the kidney, these convoluted tubules become much narrower and enter the pyramids of Ferrein. Here they take a straight course as far as the border of the medulla, and then turn abruptly on themselves, become considerably thicker again, and proceed upward toward the surface of the kidney, always remaining, however, in the medullary rays. This straight tubule is known as *Henle's loop*, of which there are the *descending* and the *ascending* arms (ramus descendens et ascendens). The ascending arm of Henle's loop passes over into the *intermediate tubule* or *convoluted tubule of the second order*, which leaves the medullary ray and takes a tortuous course in the labyrinth similar to but much shorter than that pursued by the convoluted tubules of the first order. From the labyrinth the canal passes back into the medullary ray as the *connecting tubule.* Similar tubules enter the pyramids of Ferrein from all sides and open into the larger *collecting tubules*, which run down through the medulla and join near the apex of the Malpighian pyramid to form the so-called *papillary ducts*, which open out in the *area cribrosa* of the papilla in from ten to twenty orifices.

Each of these different parts of the urinary canal has a characteristic structure. Everywhere there is a single row of epithelium with a fine structureless membrane, the membrana propria.

The capsule of Bowman is related to the glomerulus in such a way that the latter is covered closely by the inner wall of the capsule, while the outer wall passes over into the wall of the convoluted tubule of the first order (Fig. 166). The walls of the capsule are made up of a layer of flat epithelial cells with a membrana propria composed of reticulum (Mall). The capsule of Bowman, together with the glomerulus, forms what is known as the *Malpighian corpuscle*, which has a diameter of from 130 to 220 μ. A reconstruction of the glomerulus of a human kidney has been made by W. B. Johnston by the Born

wax-plate method. In this he found that the afferent vessel breaks up into five branches. These form a network of capillaries which anastomose in such a manner that three main groups are formed: a median and two lateral groups. Capillaries from these in leaving the glomerulus form two main branches, which join to make up the efferent vessel.

FIG. 166.



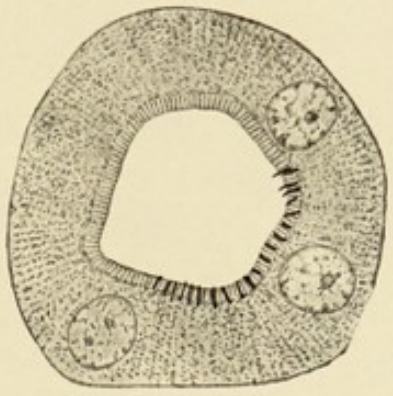
From a section through the cortex of an ape's kidney. A Malpighian corpuscle, together with the beginning of the urinary canal, is shown. × 350.

The convoluted tubule of the first order (38–42 μ in diameter) is lined with cubical epithelial cells. Near the capsule of Bowman we find a transition from flat cells to the cubical type. The protoplasm of the cubical cells is finely granular, and shows in the part of the cell toward the lumen a definitely striated appearance. In the rest of the cell the granules are arranged radially in rows. The borders between the epithelial cells usually cannot be made out (Fig. 167).

The part these cells take in the secretion of urine, and the changes that take place in them during this process, have not definitely been made out. In secretion the cells become lower and the lumen of the tubule wider than during rest. Secretory capillaries have not been demonstrated.

The descending arm of Henle's loop is a thin-walled tube made up of flat epithelial cells, whose nuclei bulge out into the lumen. The cells are so arranged in the tubule that in a longitudinal section they alternate on the two sides—that is, two cells are never opposite one another. In cross-section the canal is not unlike a blood capillary. The membrana propria usually

FIG. 167.



Cross-section of a convoluted tubule from the kidney of a rabbit. The boundaries of the epithelial cells cannot be seen. Only three nuclei are shown. The rod-like structure is plainly visible. × 1100.

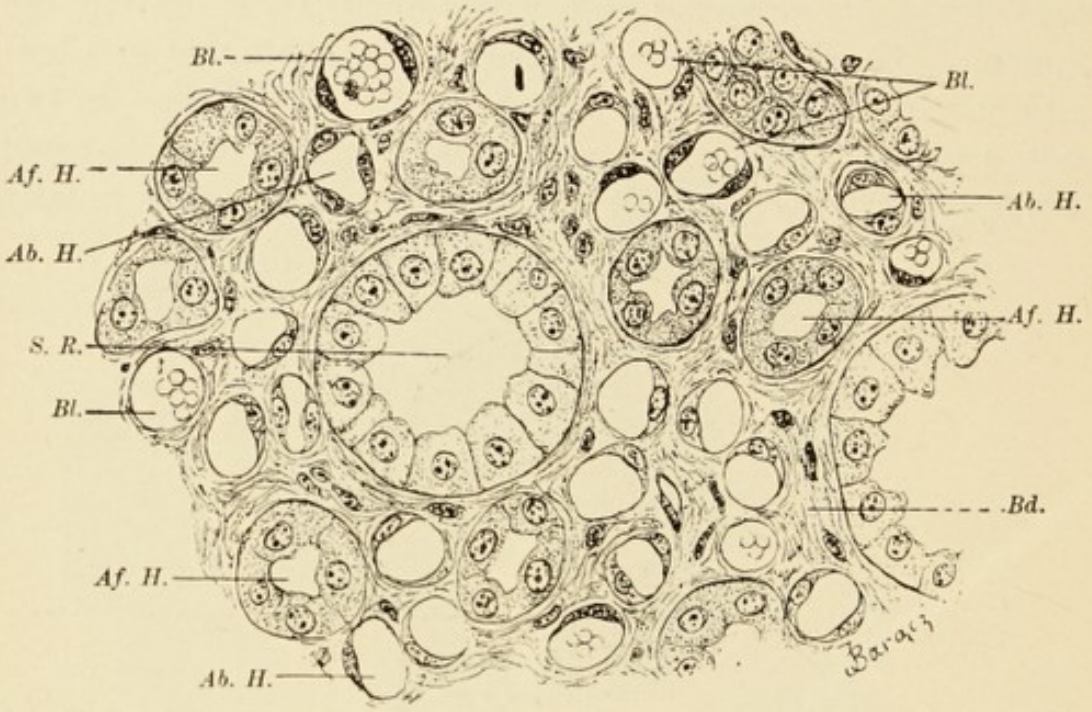
is seen distinctly, and the whole diameter of the canal is from 9 to 15 μ.

The ascending arm of the loop of Henle is considerably thicker, being 25 μ in diameter. The epithelial cells are cubical, and the size of the lumen narrow in relation to the thickness of the walls. The transition from the flat cells to the cubical takes place usually in the lower part of the descending arm of the loop. The cubical cells show the striation spoken of in the convoluted tubules.

The convoluted tubules of the second order are much shorter and have a wider lumen than those of the first order. The canals are 39–46 μ in diameter. The epithelial cells are low, and show a finely granular and striated appearance.

The connecting tubules, collecting tubules, and the ductus papillares have clear, transparent cells, showing no striated structure. In the beginning they are cubical, but as the canal widens into the papillary ducts they become columnar (Fig. 168). The nucleus is always spherical, and sharply

FIG. 168.



From a transverse section through the base of a pyramid of an ape's kidney. *S. R.*, collecting tubule; *Ab. H.*, descending limb of Henle's loop; *Af. H.*, ascending limb of Henle's loop; *Bl.*, blood-vessels; *Bd.*, interstitial connective tissue. × 500.

marked off. The diameter of the papillary ducts is as much as 100 μ.

Zimmermann found in the cells of all regions of the canal a double centrosome lying near the free surface of the cell.

The cortical substance may be divided into kidney lobules. These consist of all those Malpighian corpuscles and tubules which go to form one medullary ray. At the boundaries of each lobule there run the interlobular vessels. This is the secretory unit, and its periphery is formed by the beginnings—*i. e.*, the capsules of Bowman—of all the tubules which empty finally into the collecting ducts that run in the medullary rays (Fig. 165). There is more or less overlapping in this lobular division, and there is no definite separation of the lobules.

Besides this secretory unit, there is a blood vascular unit, which is made up of all those glomeruli and vessels which are connected with each interlobular artery and vein (Fig. 165).

The connective tissue of the kidney is not abundant, but is found in greatest quantity in the papillæ. It surrounds the membranæ propriæ of the urinary tubules and the capsules of Bowman, and carries with it the blood-vessels. The whole kidney is surrounded by the tunica albuginea, a fibrous membrane containing smooth muscle. Mall, some years ago, stated that the framework of the kidney is made up of interlacing connective-tissue fibres, which are differentiated at the borders of the tubules to form basement membranes. Such membranes appear in ordinary specimens to be homogeneous, but by methods of digestion (pancreatin) they can be shown to be fibrillar in structure. This has been confirmed by the work of Rühle, Disse, and v. Ebner. A later publication by Mall shows that the true basement membrane is destroyed by pancreatin digestion. This leaves only a framework of connective tissue, as stated above. Specimens were obtained by macerating in cold saturated sodium bicarbonate solution, in which not only this framework, but also a membrane closely associated with the epithelial cells was demonstrated. These membranes are neither elastic tissue nor reticulum. Mall suggests that they are possibly identical with the membranes of elastic fibres.

Blood-vessels of the Kidney.

The kidney derives its blood supply from the branches of the renal artery. The relations between these and the calyces and pyramids of the kidney have been described by Brödel. According to him, about three-fourths of the blood which enters the hilum of the kidney by four or five arterial branches, flows through the anterior subdivisions of these branches, while one-fourth is carried through the smaller posterior divisions. This is shown in Fig. 171. The anterior branches supply the anterior pyramids and the anterior part of the posterior pyramids; while the remainder of the organ is supplied through the posterior branches. The blood supply

of the two poles of the kidney is derived from the main artery. Single arteries run to each pole and break up into three branches: a posterior, an anterior, and a median branch. Between these large arteries there is no anastomosis; and it will be seen that at one place between the anterior and posterior arterial fields there is a comparatively non-vascular zone, marked by the dotted line in Fig. 171. Brödel has pointed out also the surgical importance of this fact.

The branches of these arteries run to the kidney substance between the pyramids as the *interlobar arteries.* At the boundary between the medulla and cortex these bend over and run for a short distance parallel to the surface of the kidney

FIG. 169.

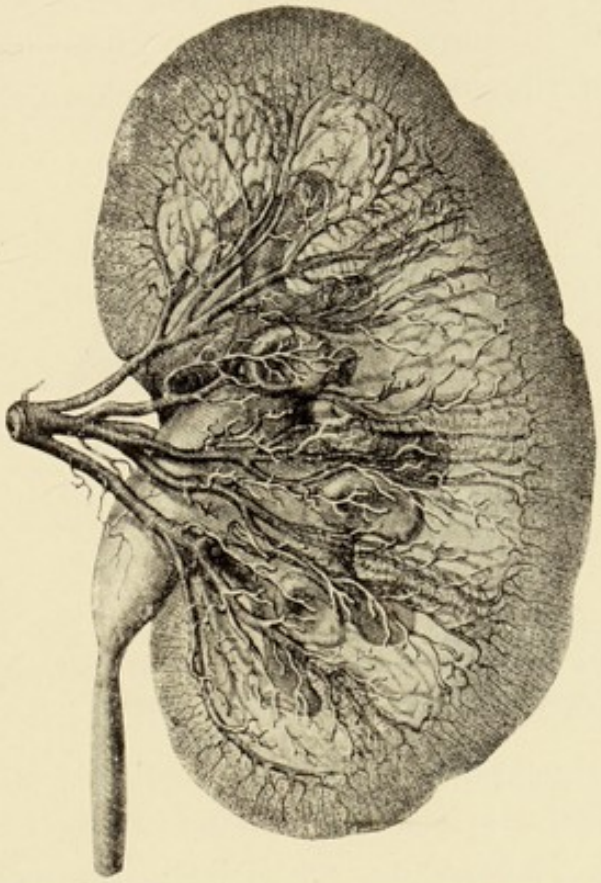


Glomerulus from an injected human kidney, showing vas efferens and vas afferens. × 160.

(Figs. 165 and 170). In this way an arterial arch is formed, made up of the *arcuate arteries.* From the convex side of these arteries small branches proceed radially toward the kidney surface. These are the so-called *interlobular arteries.* They give off in all directions lateral twigs, which carry blood to the Malpighian corpuscles (Fig. 165). These are the *vasa afferentia,* which enter the capsules of Bowman and break up into many branches to form the glomerulus (see above). The blood is carried away from each glomerulus through the *vas efferens.* Many vasa efferentia together break up to form a capillary network in the region of the medullary rays. The tubules of the medullary rays and the tubuli contorti lie in the

meshes of this network. From it arise small veins which open into the *interlobular veins*. These run parallel with the interlobular arteries, and at the boundary between the medulla and cortex open into the *arcuate veins*. Into the most peripheral

FIG. 170.



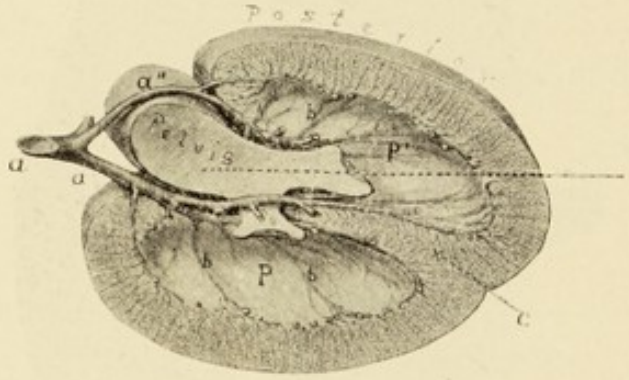
The renal artery and the distribution of its branches in relation to the pelvis. (Brödel.) Anterior view of a left kidney. There are six main branches seen entering the kidney substance. Only one of these (the third) passes posterior to the pelvis at the hilum; also small arteries coming from the upper and lower main branches are seen to pass posterior to the upper and lower calyces. All the rest of the arteries pass anterior to the pelvis and its calyces. The small branches to the cortex of the anterior portion of the kidney have not been drawn, in order that the large branches and the pelvis might appear more distinctly.

part of the interlobular veins there run small veins from the surface. These possess radial, star-like tributaries on the surface, and are known as the *stellate veins of Verheyn* (Fig. 165).

The medullary substance is supplied partly by capillary branches from the cortex, and partly from the *arteriolæ rectæ*. The latter are branches partly from the vasa efferentia of the

more deeply lying glomeruli, and partly from the interlobular or arcuate arteries. The meshes of the capillary network which arises from these two sources and supplies the medulla are elongated and surround the collecting tubules. The capillaries collect to form the *venulæ rectæ*, which end in the arcuate veins. It must be noted also that the vessels of the kidney parenchyma are in communication with those of the perirenal fat by means of the vessels of the kidney capsule. A collateral

FIG. 171.



Transverse section through the middle of the same kidney (Fig. 170), seen from above. (Brödel.) The anterior branch of the artery supplies about three-quarters of the kidney substance, while the posterior branch supplies only one-quarter.

circulation is thus possible. There are also direct communications between the arteries and veins of the kidney (Hoyer, Steinach, etc.). According to Brödel, the collecting veins form anastomoses around the bases of the pyramids and around the necks of the calyces.

The *lymphatics* form a superficial plexus in the capsule and a deep plexus, the vessels of which leave the kidney at the hilum. Anastomosing lymphatic spaces have been observed connecting the two plexuses.

The *nerves* accompany the blood-vessels into the kidney, where they form plexuses around the uriniferous tubules. According to Azoulay and Berkley, they penetrate the membrana propria, and end by knob-like thickenings on the surfaces of the epithelial cells.

PLATE XXVI.

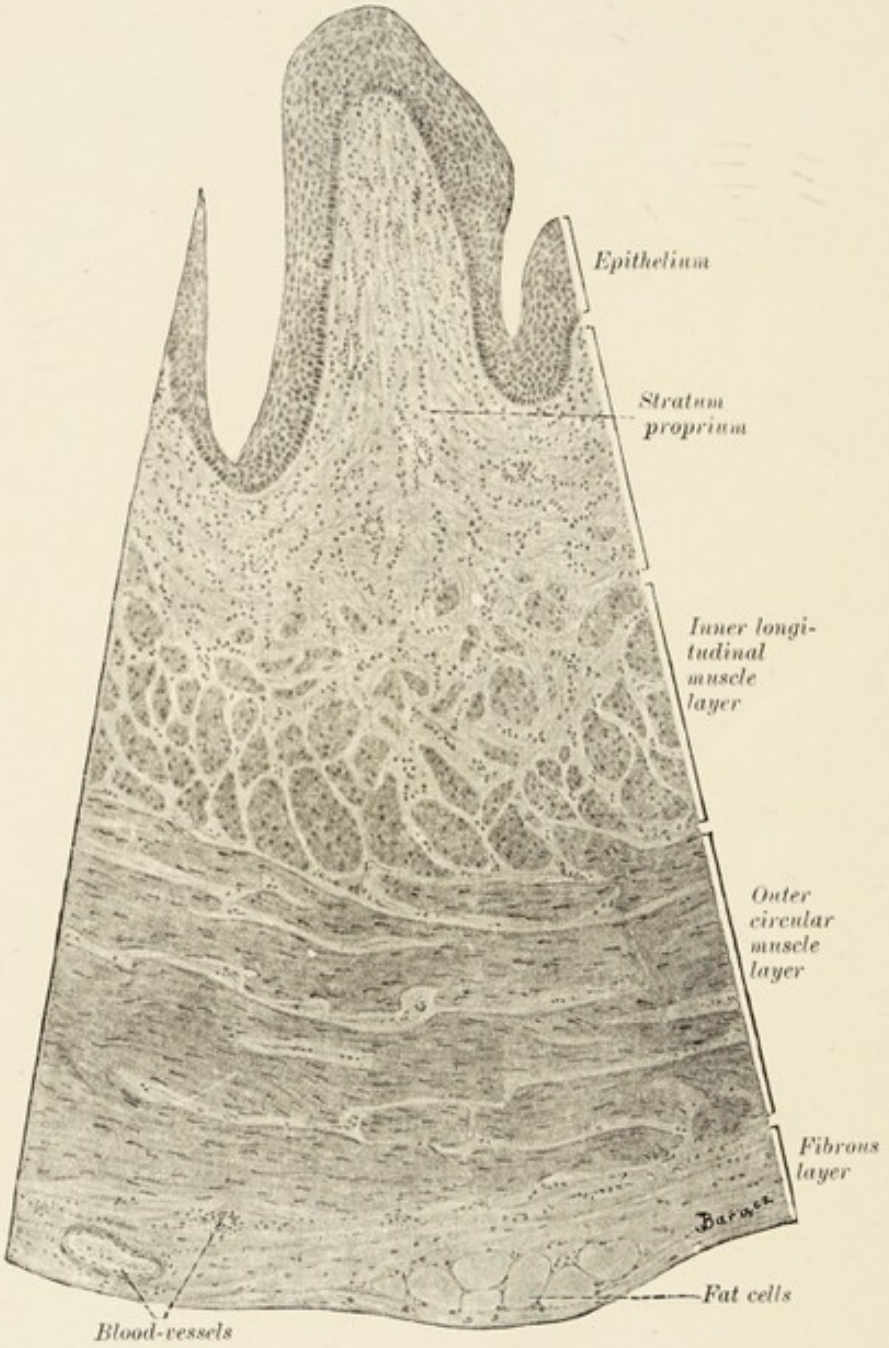


FIG. 172.—Part of a transverse section of a dog's ureter. × 110.

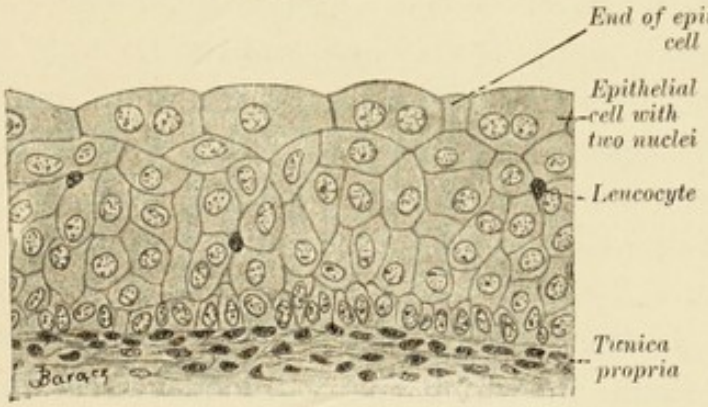
B. URINARY PASSAGES.

(*a*) Kidney Calyces, and Pelvis; Ureter and Urinary Bladder.

In all of these parts of the apparatus which conducts urine from the kidney we find the walls made up of the following layers: 1, mucosa; 2, submucosa; 3, muscularis; 4, fibrosa.

The *mucosa* consists of an epithelium and a tunica propria. The former is the so-called *transitional epithelium*, and is quite similar in all parts of the canal, so that in pathological conditions of the tract where the cells appear in the urine it is difficult to say from what part these cells are derived. The cells differ, however, in the various layers. The uppermost layer consists of large cubical or somewhat flattened cells; the middle layers of cylindrical, pyriform, spindle-shaped, or polygonal cells; and the deepest layer of relatively small cubical or irregularly oval cells. The cells of the first two layers often possess processes which extend between neighboring cells. Those of the outer row may contain more than one nucleus (Fig. 173).

FIG. 173.



From a section through the mucous membrane of an ape's urinary bladder. × 300.

The epithelial layer is considerably thinned at the place where the calyces of the kidney pass over to the kidney papillæ, and usually consists of only a single layer of cubical cells. The mucosa of the ureter is thrown into longitudinal folds (Fig. 172). In the bladder also the surface is much folded in many directions on account of the contraction of the muscularis and submucosa. In the distended bladder most of these folds dis-

appear, and the epithelial sheath itself becomes thinner and the cells flatter. The *tunica propria* consists of fine connective tissue which contains leucocytes, and small collections of lymphocytes which sometimes form solitary follicles. This layer passes over gradually into the *submucosa*. Here glands are wanting. In sections infoldings of the mucosa are sometimes cut across, and were formerly thought to be glands in the submucosa.

The *muscularis* consists of two layers of smooth muscle cells, one longitudinal, and the other circular (Fig. 172). In the lower third of the ureter there is outside the circular coat a third layer, which consists of bundles of muscle fibres running longitudinally. In the calyces of the kidney there is no longitudinal muscle coat whatever; the circular coat forms an annular muscle around the base of each papilla.

In the urinary bladder of man we can distinguish three layers of muscle, of which the inner and outer are longitudinal, and the middle circular. These layers cannot be separated definitely, for there is a manifold anastomosis between the bundles of the different layers. Two fixed points of the bladder give a basis for the study of the musculature. These are the point at which the urachus is attached, and the triangle formed by lines drawn between the openings of the ureters and the urethra—*i. e.*, the trigone. Remembering that the bladder is developed from the inner third of the allantois, which is a more or less tubular structure, these two points represent the two ends of the tube.

The *fibrous sheath* of the urinary tract consists of fine connective tissue in which many blood-vessels and nerves are found.

The blood- and lymph-vessels form a capillary network in the tunica propria.

The nerves are spread out mainly in the muscle coat, with a certain number of fibres reaching as far as the epithelium.

(*b*) Urethra.

(1) *Male.*—The urethra consists of a mucosa, submucosa, and muscularis, somewhat differently arranged in the different regions of the canal. In the *pars prostatica* the *epithelium* is quite similar to that of the bladder; in the *pars membranacea* there is a stratified cylindrical epithelium, which in the *pars cavernosa* is converted into two rows of cylindrical cells. The last segment, the *fossa navicularis*, is lined with flat stratified epithelium.

The *tunica propria* contains numerous elastic fibres and forms papillæ in close contact with the epithelium. These are developed most strongly in the fossa navicularis. The *submucosa* contains a rich plexus of veins, and in the whole canal there are here present branched tubular glands—*glandulæ urethrales* (Littré)—which are more numerous in the posterior part. They are lined with cylindrical glandular epithelium and extend into the submucosa.

The *muscularis* in the prostatic and membranous urethra shows two layers of smooth muscle fibres, an inner longitudinal, and an outer circular coat. The circular coat is wanting in the pars cavernosa, and the longitudinal layer becomes very thin.

The whole urethra is highly vascularized (see Corpus cavernosum urethræ). The nerves form networks of fibres, which end freely or in various end organs (see Nerve-endings).

(2) *Female.*—In the female the urethra is considerably shorter and not so definitely divided into sections. We can distinguish a wall made up of the same layers as in the male. The *epithelium* in the upper part is like that of the bladder, but lower down becomes a single or double layer of columnar cells, and finally passes over at the lower end into a stratified pavement epithelium.

The *tunica propria* forms papillæ at its junction with the epithelium. These are highest in the region of the urethral opening. Littré's urethral glands are present here also, but are not so numerous as in the male. The *muscularis* consists of an inner longitudinal and an outer circular coat of smooth muscle

fibres, separated by connective tissue containing elastic fibres. Outside the circular coat, especially in the upper part of the canal, are strands of striated muscle fibres, forming the musculus compressor urethræ. The mucosa is supplied richly with blood-vessels, of which the veins form a thick plexus in the submucosa.

V. GENERATIVE (REPRODUCTIVE) SYSTEM.

1. MALE SEXUAL ORGANS.

A. Testes.

The testes are branched tubular glands. The whole organ is surrounded by a fibrous capsule, the so-called *tunica albuginea s. fibrosa*, which consists of firm connective tissue. The outer surface of this is attached closely to the visceral layer of the *tunica vaginalis propria* (tunica adnata). Both the visceral and parietal layers form a process of the peritoneum, and enclose between them a space which is a part of the body cavity. They are thin connective-tissue membranes with a layer of flat epithelium covering the free surface. Between the visceral layer of the tunica vaginalis propria and the next layer, the *tunica vaginalis communis*, there is a layer of smooth muscle cells which form the internal cremaster muscle (Fig. 174).

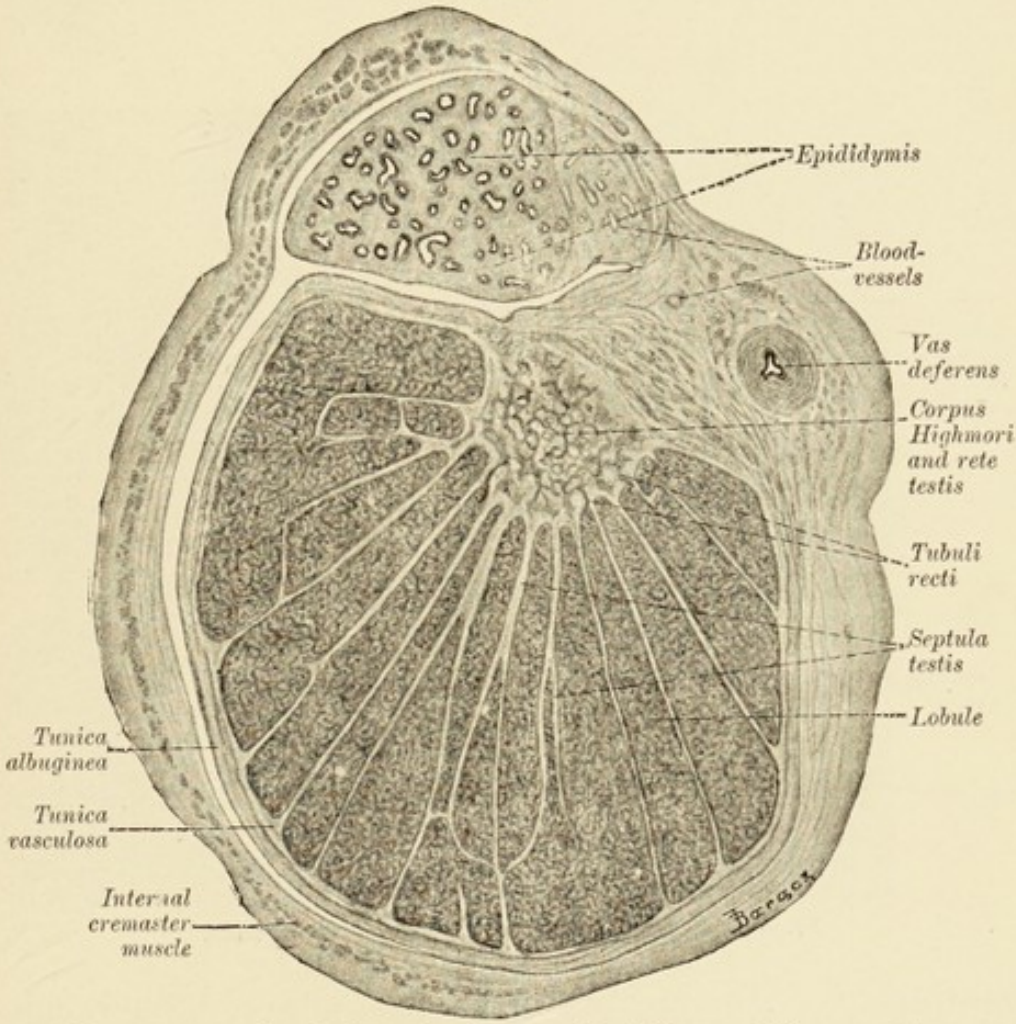
Toward the inside the tunica albuginea borders on a sheath of loose connective tissue, which, on account of its richness in blood, is called the *tunica vasculosa*. This rests directly on the parenchyma of the testis.

In the posterior upper part of the testis there lies a collection of firm connective tissue in the form of an oval hillock. This is the so-called *mediastinum testis* or *corpus Highmori*. From it there are sent, in a radiating direction, into the organ many bands of connective tissue, the *septula testis*. These pass through the testis as far as the tunica vasculosa, and at the same time divide the organ into lobules (*lobuli testis*), which have the form of pyramids with their bases toward the outside and their apices toward the centre of the organ (Fig. 174).

The whole of the parenchyma contained in a lobule consists

of canals, the *seminiferous tubules*, which, on account of the different course they take in different regions, are divided into three parts. The part lying toward the periphery of the organ forms the much-convoluted *tubuli contorti*. These join with one another and make up the *tubuli recti*, which near the mediastinum break up to form a network, the *rete testis* (Halleri).

FIG. 174.



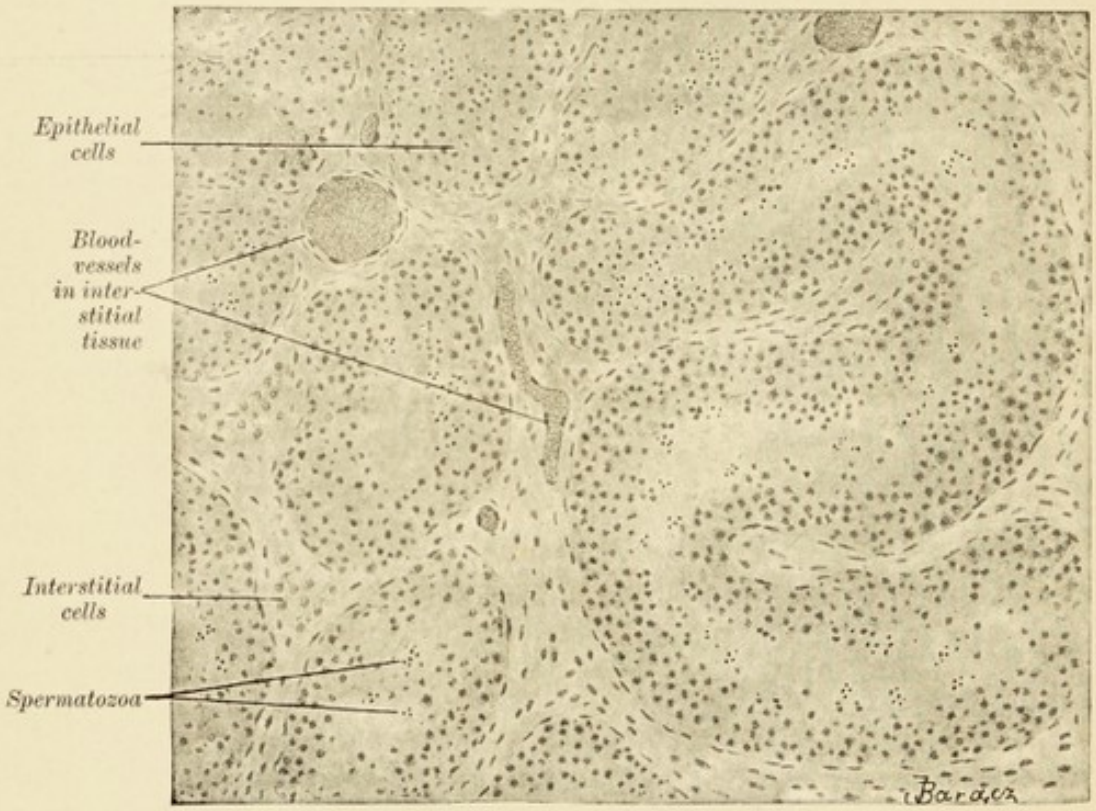
Transverse section of the testis of a two and a half year old boy. × 7.

The *tubuli contorti* in the human adult are very long canals, about 140–250 μ in diameter, and form the most important part of the testis parenchyma, inasmuch as they give rise to the spermatozoa. At the periphery of the testes many of the tubules anastomose and form a closed system. Others, on the contrary, begin blindly. The walls of these convoluted tubules consist of several layers of epithelial cells,

a membrana propria, and a layer of connective tissue. The appearance of the tubules, especially of the epithelial layer, differs markedly according to the condition of functional activity (spermatogenesis).

The tubules join together, decreasing in number, and finally pass over into the *tubuli recti*. These are distinguished from the tubuli contorti by their straight short course and by their small diameter (20–50 μ). Their structure is simple, the walls

FIG. 175.



From a transverse section of a human testis. × 125.

consisting of a membrana propria and a layer of low cylindrical epithelial cells. They are interposed between the tubuli contorti and the rete testis.

The *rete testis*, which is contained in the corpus Highmori, consists of canals of an unequal thickness, lined merely with a single layer of cubical or flat epithelial cells. The tubules of the rete testis pass over into the epididymis.

Between the convolutions of the tubuli contorti there lies a loose connective tissue which is in connection with that of

PLATE XXVII.

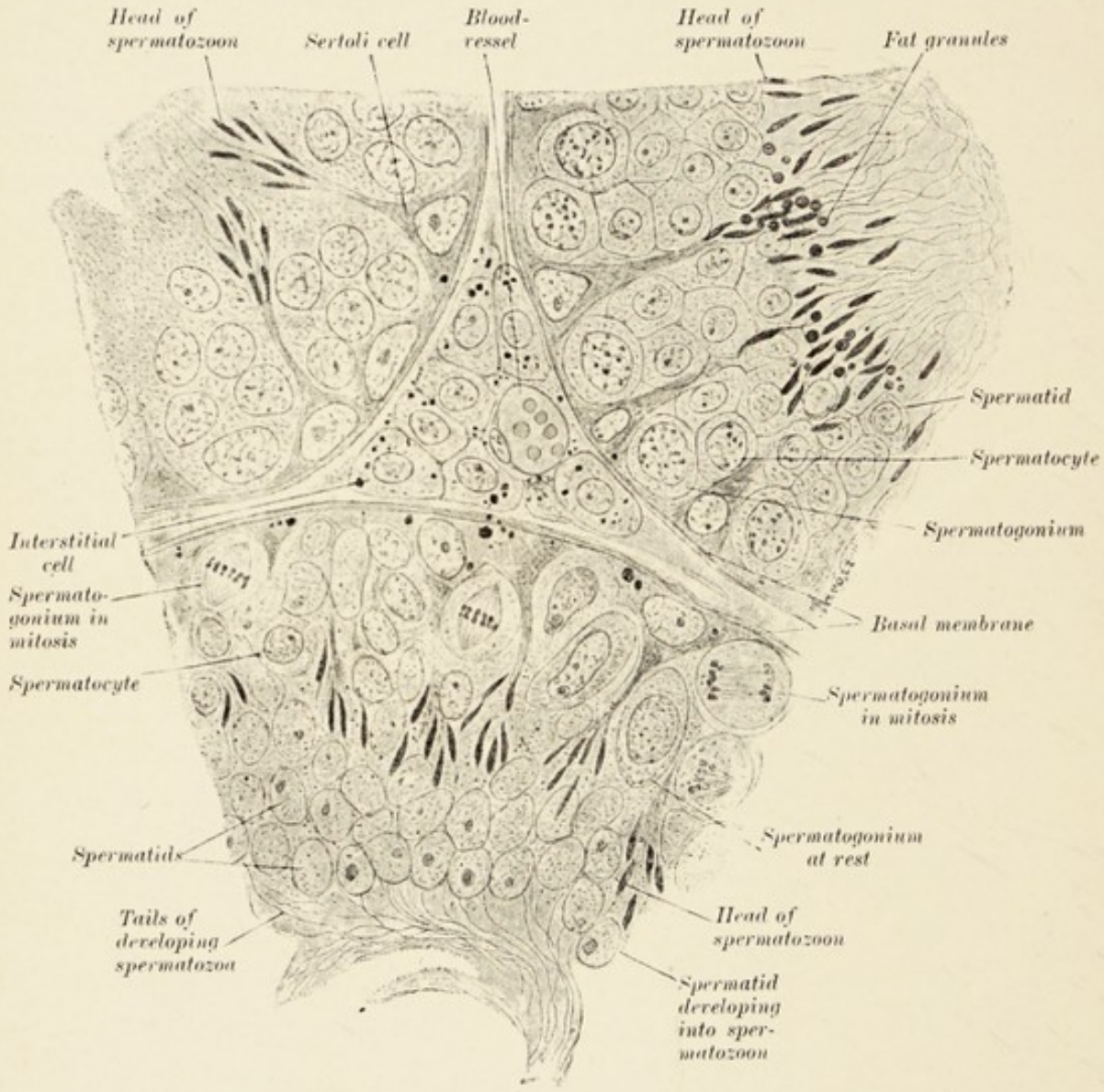


FIG. 176.—Part of a transverse section of tubules from the testis of a white mouse. × 600.

the septa. This *interstitial* connective tissue is characterized by the presence of numerous large cells, known as *interstitial cells* (Figs. 175 and 176). They are rounded, coarsely granular cells, with abundant protoplasm, containing fat droplets, pigment granules, or crystalline bodies. They lie usually in groups or columns situated in the spaces between adjacent seminiferous tubules. The origin and significance of these cells are not known definitely. It is to be assumed that they are of connective-tissue origin. A few authors hold that they are derived from epithelial cells. J. Plato ascribes to them a trophic function, claiming that the fat-like inclusions wander through pores in the membrana propria to reach the cells of Sertoli, and thus serve as a nourishment for the spermatozoa that are in process of formation.

The testes are supplied with blood by branches of the internal spermatic artery, which enter the septa partly from the mediastinum and partly from the tunica vasculosa. They form networks of capillaries around the seminiferous tubules, and send off branches to the interstitial cell group. The veins collect in the interstitial tissues and leave the organ by the path taken by the arteries in entering.

The lymph-vessels run partly superficially in the tunica albuginea, and partly in the deeper parts, where they form plexuses surrounding the seminiferous tubules.

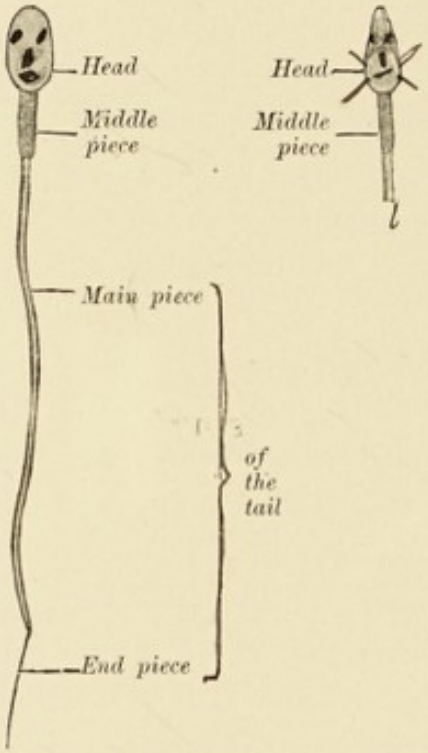
The nerves accompany the blood-vessels, and send fine branches between the epithelial cells, where they end in small enlargements.

The semen consists of a fluid part produced mainly by the accessory sexual glands and the spermatozoa, which are a product of the testes themselves. There are about 60,000 spermatozoa in 1 cu. mm. of semen.

The *spermatozoön* of man may be divided into three parts: the head, the middle piece, and the tail (Fig. 177). The *head* (Fig. 178, *h. Sk.*) is flattened, 3–5 μ long, and 2–3 μ wide. Its flat surface is oval, and shows depressions in its anterior part. Seen from the side, it is pear-shaped. The whole head consists of chromatin substance (nuclein), and represents the cell nucleus.

Behind the head is the connecting part, *body*, or *middle piece* (*Vst.*), which is a cylindrical structure of about the same length as the head, and 1 μ wide. By means of special stains we may distinguish in it an axial part and a *capsule* surrounding it (H_{I}, *Sph.*, and H_{II}). The axis has a fibrillar structure (*axial threads*), and begins in a thickening, the so-called *terminal globule* (*Ekn.*). According to Meves, there are in man two such bulbs closely connected with the head. Both on account of staining reactions, and from histogenetic reasons, this end

FIG. 177.



Spermatozoa of man. (After Retzius.) At the left a surface view is shown; at the right, a lateral view. × 1200.

bulb is believed to represent the centrosome of the cell. In the process of fertilization also it plays this rôle. The capsule is applied directly to the axial threads, and is continued along the axis (H_{I}) to nearly the end of the tail. In many animals this capsule has a spiral form, and is connected behind with an annular thickening (*Ss.*). The outer capsule (H_{II}) shows in one place a swelling and throughout its whole length a spiral thickening (*Sph.*).

In the *tail* we may distinguish two parts: the *main segment*

(*Hst.*), which is 45–60 μ long; and a thinner *end segment* (*Est.*), 6–10 μ in length. The axis runs through the whole length of the tail, and a finely fibrillar structure can be recognized throughout. The capsule is lacking in the end segment, but is considerably thickened in the rest of the tail. Some authors have described an undulating membrane running the whole length of the tail. In many animals the spermatozoön shows a much more complicated structure than that described.

By means of a lashing, waving motion of the tail, the spermatozoa can change their location with considerable rapidity. They are quite resistant to low temperature, although their motility becomes very slight in temperatures much lower than that of the body. They can, however, regain their activity even after a considerable period of cooling. Alkaline fluids tend to increase the motility, while acids inhibit the activity and finally kill the spermatozoa.

The *development of the spermatozoa* is fairly well known in some animals. The process in mammals has been studied especially by Ebner, v. Leuhossék, Hermann, Meves, v. La Valette, and others. In the walls of the seminiferous tubules there are two kinds of cell elements: the *essential gland cells*, which play a direct rôle in the formation of the spermatozoa, and the so-called *supporting cells* (*cells of Sertoli*). The latter are large membraneless cells, which lie always with their bases on the membrana propria and processes extending inward between the essential cells. They possess a large, clear, flattened nucleus, which is somewhat triangular on section. They are supposed by many authors to assist in the nourishment of the developing spermatozoa (v. Ebner, Benda, Plato, K. Peter, and others).

The gland cells, which finally give rise to the spermatozoa, are arranged in many layers, those nearest the lumen being the youngest and most nearly related to the spermatozoa themselves (Fig. 176). The whole process of spermatogenesis begins in the most peripherally lying cells, the so-called *spermatogonia*. These are low columnar cells lying on the basement membrane. They increase in number by mitotic division, and give rise to new spermatogonia, which become situated in a row by them-

selves, not touching the membrana propria. Such modified spermatogonia containing much protoplasm are known as *spermatocytes of the first order*. Mitotic changes occur in the nuclei of these, and a double division takes place. By the first division there are formed the *spermatocytes of the second order*, and by the second division the *spermatids* arise. According to many authors, there is a short resting stage between these two divisions. The first is spoken of (Flemming) as *heterotypical*, and the second as *homotypical*. The difference between the two is in the fact that in the diaster stage of the first there is a repeated longitudinal splitting of the chromosomes, while in the homotypical division this does not occur. It is in this period of division that the reduction of chromosomes takes place (see Fertilization).

The spermatids are small cells bordering on the lumen of the tubule. They represent the last generation of the sexual cell, and are converted into the spermatozoa. During this process of changing, the cells of Sertoli become modified. Their processes extend into the lumen, and the spermatids, which are to be converted into the spermatozoa, group themselves around each process to form what are known as the *spermatoblasts* (v. Ebner). In this way they become nourished, and after a certain time the combination becomes looser, and finally the newly formed spermatozoa move away.

Numerous investigations have been carried on in late years to arrive at the exact method of transformation of the spermatids into the spermatozoa, but the entire process is still by no means clear. Since it is not possible here to discuss the various views that are held with regard to this, we shall confine our description to the process as it occurs in man and the other mammals, and follow in the main the investigations of Meves. In all mammals the process is very similar. Observing the parts of Fig. 178, which represents the transformation of human spermatids into spermatozoa, we notice that the chromatin matter of the spermatid nucleus shows a progressive increase in density and a more and more homogeneous appearance. The nucleus is originally round and centrally placed, but

PLATE XXVIII.

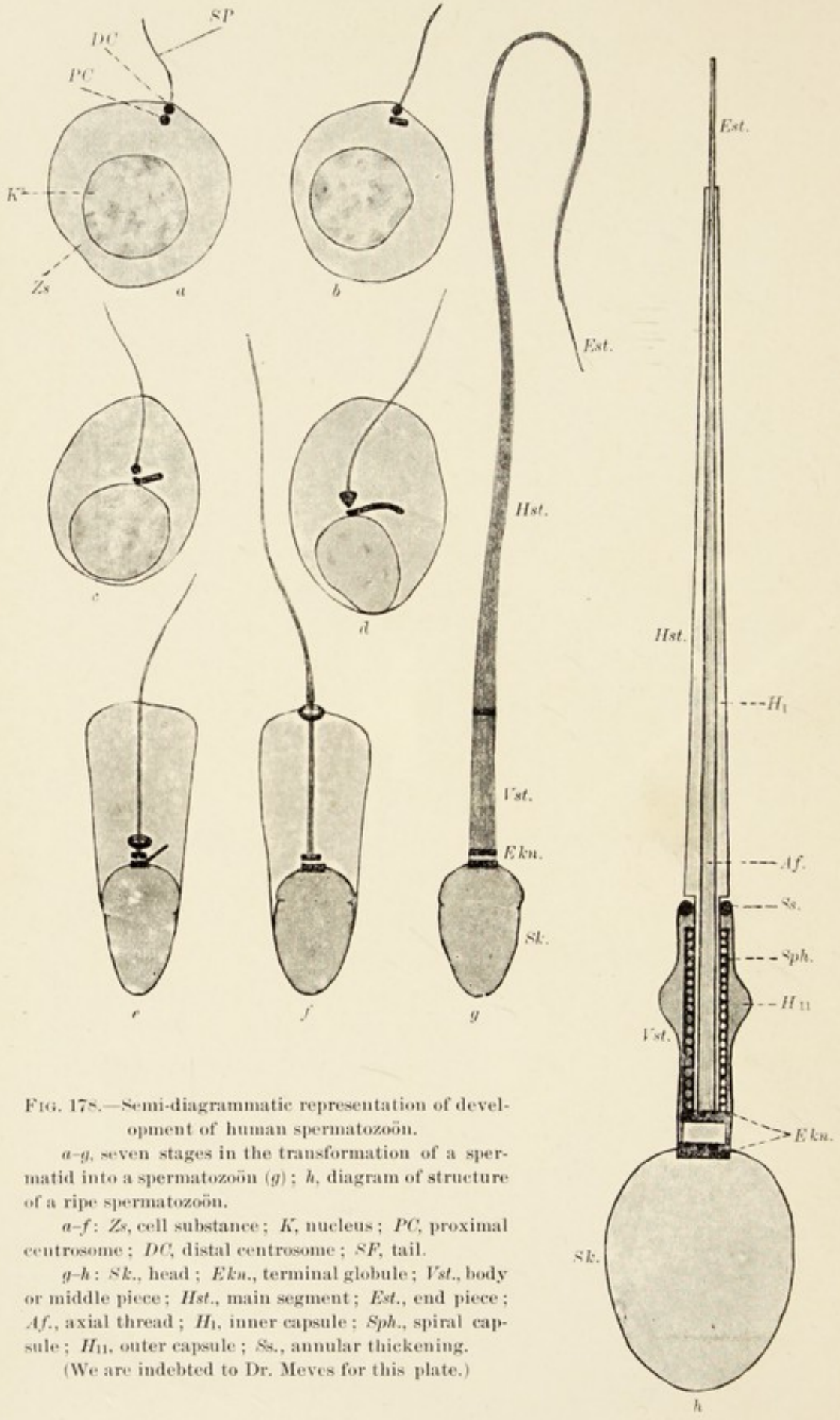


FIG. 178.—Semi-diagrammatic representation of development of human spermatozoön.

a–g, seven stages in the transformation of a spermatid into a spermatozoön (*g*); *h*, diagram of structure of a ripe spermatozoön.

a–f: *Zs*, cell substance; *K*, nucleus; *PC*, proximal centrosome; *DC*, distal centrosome; *SF*, tail.

g–h: *Sk.*, head; *Ekn.*, terminal globule; *Vst.*, body or middle piece; *Hst.*, main segment; *Est.*, end piece; *Af.*, axial thread; H_I, inner capsule; *Sph.*, spiral capsule; H_{II}, outer capsule; *Ss.*, annular thickening.

(We are indebted to Dr. Meves for this plate.)

becomes gradually excentric and assumes a long, oval form. In the early stages of the change the spermatids contain two centrosomes which have a quite superficial situation. From the more superficial (distal) of these there grows out from the cell a delicate thread of protoplasm, which is the very beginning of the tail (Fig. 178, *a*). The centrosome lying nearer the nucleus (proximal) becomes rod-shaped, while the one outside assumes a conical form. Both centrosomes approach the nucleus and the proximal one unites with it. The distal conical centrosome is differentiated into two structures, a bulb and a ring (Fig. 178). The ring moves back along the tail axis until it reaches the periphery of the cell. This divides the middle piece from the chief segment of the tail (Fig. 178, *f* and *g*). The significance of the capsule is not clear. In the middle piece it probably represents the remains of a part of the cell protoplasm. From this last stage the fully formed spermatozoa may readily be traced (Fig. 178).

B. Spermatic Ducts.

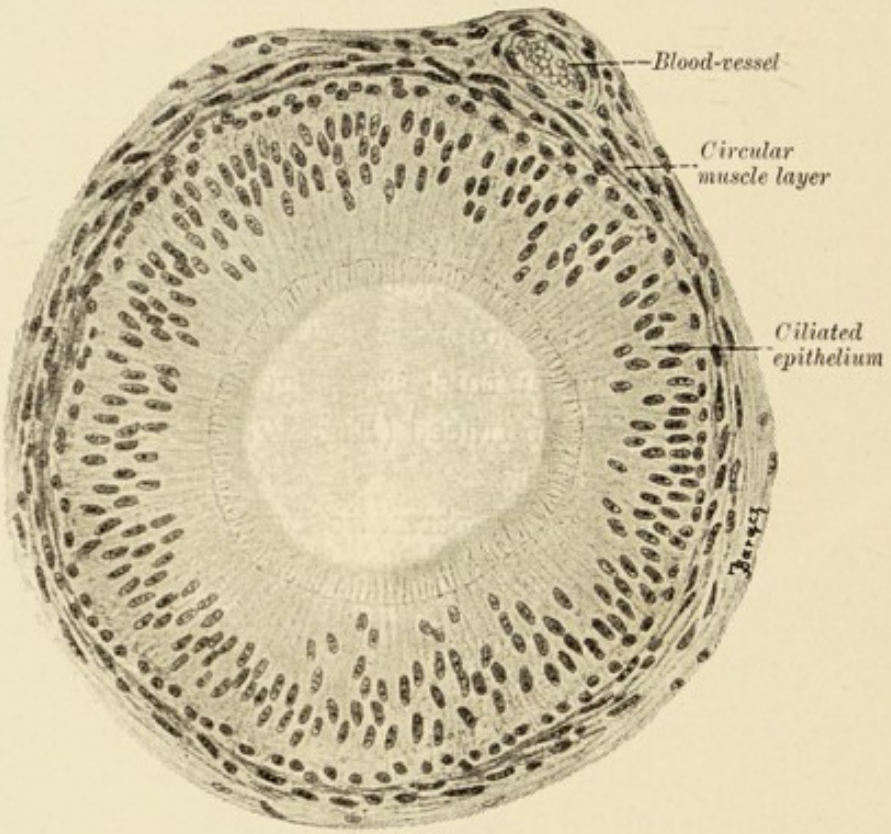
From the rete testis proceed the *ductuli efferentes testis*, or *vasa efferentia*, which break through the tunica albuginea and form a part of the epididymis. There are from nine to fifteen of these, and each forms by its tortuous course a lobule surrounded by connective tissue (*lobuli epididymis, coni vasculosi Halleri*). All the lobules together form the head of the epididymis. The vasa efferentia join to form the *vas epididymis*, which takes a very complicated, coiled course and makes up the body and tail of the epididymis, finally opening into the *vas deferens*.

The vasa efferentia are lined with two kinds of epithelium, one composed of high columnar ciliated cells containing yellow granules, and the other made up of cubical non-ciliated cells. These are arranged in rows and concentrated in groups. The groups of cubical cells form swellings among the cylindrical cells, and have the appearance of intra-epithelial alveolar glands. Outside the membrana propria there are smooth muscle cells arranged in circular layers. Some authors have

described glandular cells among the non-ciliated epithelium, and have observed evidences of secretion in them.

The walls of the *vas epididymis* are lined with a ciliated epithelium in a single row, with, however, the nuclei at different levels. Outside this are a membrana propria, a circular muscle layer, and a connective-tissue coat (Fig. 179). The

FIG. 179.



Transverse section of a human epididymis. × 300.

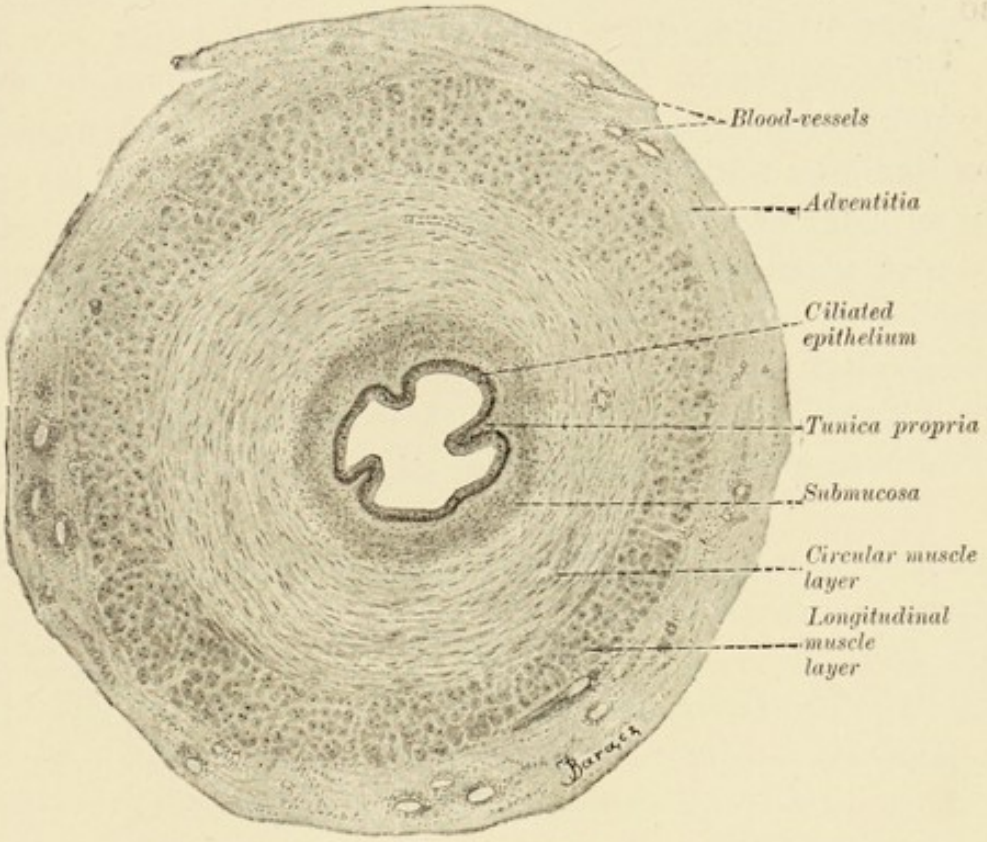
coils of tubules of the vas epididymis and vasa efferentia are joined together by fine loose connective tissue.

The *vas deferens* (Fig. 180) is lined with an epithelium which is thrown into longitudinal folds. In the upper part the epithelium is like that of the vas epididymis, but lower down passes over into a stratified cylindrical epithelium. The tunica propria is a thin fibrous layer. Outside this is the submucosa, which consists of connective tissue with blood-vessels, etc. Three coats of muscle surround the tube, a very thin longitudinal layer next to the submucosa, a middle circular coat, and an outer longitudinal layer. Outside these there is a

layer (adventitia) of connective tissue containing elastic fibres and longitudinal smooth muscle cells (m. cremaster internus).

The terminal part of the vas deferens is dilated to form an *ampulla*, which is lined with stratified columnar epithelium, containing branched gland tubules with cubical or cylindrical epithelium.

FIG. 180.



Cross-section of a human vas deferens. × 37.

The structure of the *seminal vesicles* (vesiculæ seminales) is not essentially different from that of the ampulla. These are glandular sacs, and may be considered among the accessory sexual glands.

The *ejaculatory duct* (ductus ejaculatorius) is lined with stratified cylindrical epithelium. Like the vas deferens, its walls show two main coats of smooth muscle, as well as a thinner layer inside.

Certain other structures must be mentioned, which are only remains of embryonic organs. The *paradidymis* (organ of Giraldè), which consists of a few blind tubules lined with a

layer of ciliated epithelium, lies between the blood-vessels of the spermatic cord in the neighborhood of the testis. In the epididymis we distinguish side branches, the *ductuli aberrantes.* These are spoken of as the ductulus aberrans Halleri (which is a branch of the vas epididymis), the ductulus aberrans capitis epididymis, and the ductulus aberrans in the rete testis. All these end blindly, are lined with ciliated cylindrical epithelium, and arise from the Wolffian body.

The *appendix testis* or *hydatid of Morgagni*, is made up usually of a vascular connective tissue and lined with ciliated epithelium. It often has a stalk of considerable length, and may itself be a large sac containing fluid. It is situated in the upper part of the head of the epididymis. It is probably a rudiment of Müller's duct. The *appendix epididymis* is a somewhat similar structure similarly situated, and lined with small cubical epithelial cells. It is usually a saccular structure, and is supposed to be a vestige of the Wolffian body.

C. Accessory Glands of the Male Sexual Organ.

1. Prostate.

The prostate consists of from thirty to fifty branched tubular glands converging toward the base of the colliculus seminalis. Many ducts join with one another and open into the ureter in the region of the colliculus seminalis by from fifteen to thirty orifices. The epithelium lining the tubules is cubical, and only in the larger ducts do we meet with transitional epithelium, such as is present in the prostatic urethra. The secretion of the prostate—*succus prostaticus*—is a serous fluid containing no mucus. In old individuals the gland tubules form so-called prostatic stones, round concentrically built-up structures about 1 mm. in diameter, very hard, and often calcified.

A considerable part of the prostate is formed by the *interstitial tissue* between the glands. This is made up of a firm connective tissue containing many bundles of smooth muscle cells. It forms at the outer surface of the organ a well-developed capsule, and on the inner surface next the urethra it is

collected into a thick layer, from which there proceed in the region of the colliculus seminalis strands of connective tissue running radially toward the capsule. The interstitial tissue increases with age, while the opposite is the case with the gland tubules. The hypertrophied prostates of old age are due largely to increased connective-tissue growth.

The *nerves* are derived from the hypogastric plexus. Medullated and non-medullated fibres, with ganglion cells, are present.

Blood-vessels of the Prostate.—The prostate gland derives nearly all of its blood supply from the inferior and superior vesical arteries. These vessels also anastomose with the internal pudic. Branches of the arteries enter the connective-tissue septa between the lobules, and send off fine twigs to the substance of the lobules. Here the capillaries are associated closely with the secreting cells. This subject has been worked out carefully by G. Walker, from whose results these notes have been taken.

The prostate contains the so-called *utriculus prostaticus* (vesicula prostatica, sinus prostaticus, uterus masculinus) in the form of a blind sac with its mucous membrane thrown into folds. It represents the remains of the caudal end of the fused ducts of Müller, and is lined with a double-rowed ciliated epithelium containing small tubular glands.

2. *Cowper's Glands.*

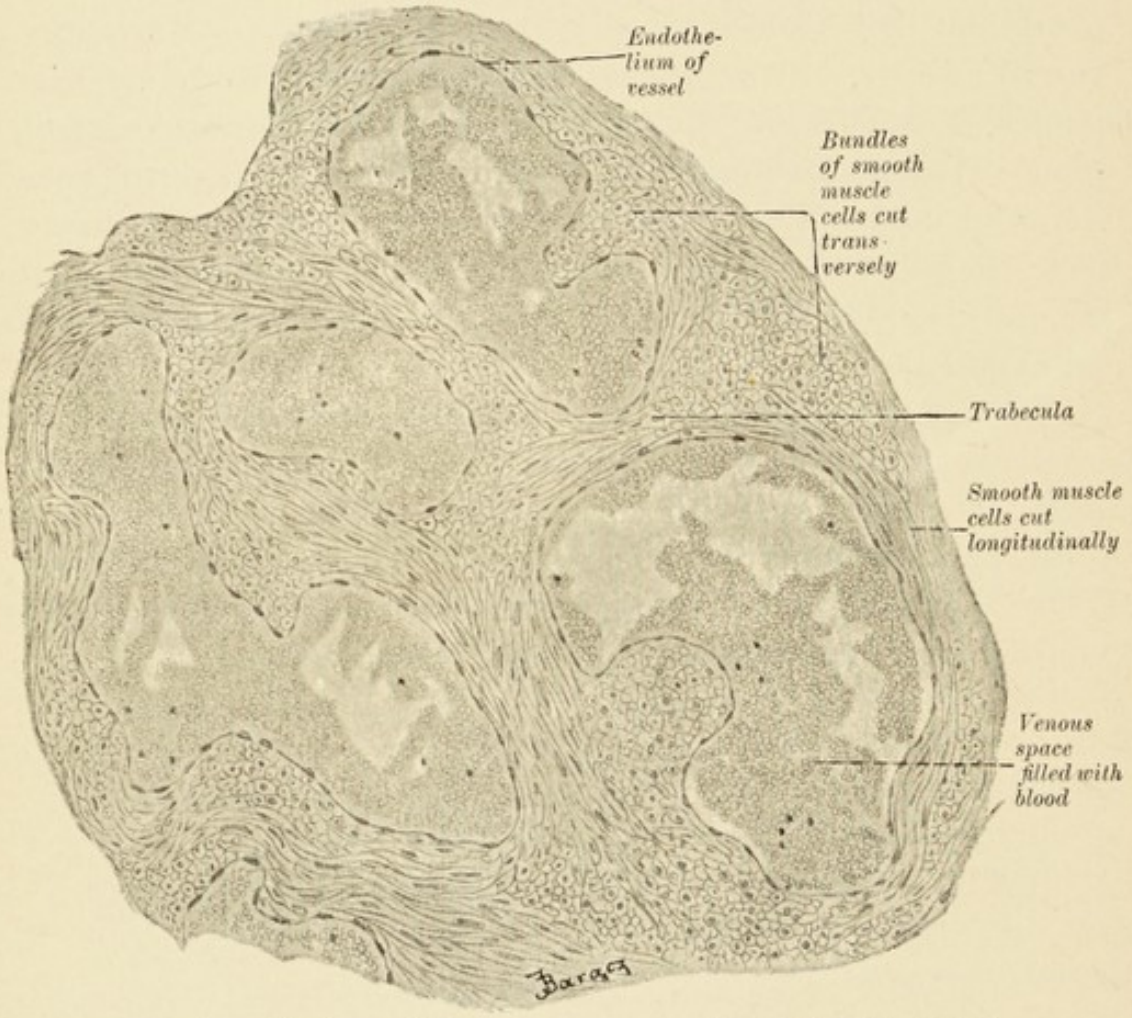
Cowper's glands (*glandulæ bulbo-urethrales Cowperi*) are compound tubular mucous glands, the gland tubules of which are lined with a single layer of cubical epithelium, and the ducts with two or three layers of similar cells.

D. The Penis.

The main part of the penis is formed of *erectile tissue*, which is collected into three cylindrical erectile bodies, the two *corpora cavernosa penis*, and the *corpus cavernosum urethræ*, or *corpus spongiosum*.

The *erectile tissue* (Fig. 181) consists of connective-tissue strands containing many elastic fibres and smooth muscle cells, and joined with one another to form a network. In the meshes of this network there are spaces which form an anastomosing system, lined with a single layer of flat epithelium. Contained in this cavernous system is venous blood. The erectile tissue of each corpus cavernosum is surrounded by a fine connective-tissue sheath, the *tunica albuginea.*

FIG. 181.



Spongy (erectile) tissue of the corpus cavernosum of an ape's penis. × 200.

The corpora cavernosa penis are supplied with blood in the following way: the afferent arteries, branches of the arteriæ profundæ et dorsales penis, pass in part into the veins by means of capillaries, and in part open directly into venous spaces. In the first case the capillaries form a fine cortical network under

the tunica albuginea, which passes over into the deeper-lying venous cortical network. This is connected in turn with the large central venous spaces of the erectile bodies. In the second case the arteries pass directly over into the veins, opening into the deep venous cortical network or directly into the cavernous venous spaces.

The efferent veins (*venæ emissariæ*) collect partly from the deep cortical network, partly from the central cavernous spaces. The veins from the interior of the corpora cavernosa pass through the meshes of the cortical network. This arrangement is of great importance in the process of erection. When the cortical network is well filled, the venæ emissariæ are compressed, so that the exit of the blood cannot keep pace with its entry. This condition is increased by the direct connection of some of the arteries with the cavernous spaces. The veins pass through the tunica albuginea and join to form the vena dorsalis and the venæ profundæ penis.

In the corpus cavernosum urethræ (c. spongiosum), which is surrounded also by a thin tunica albuginea, we may distinguish two regions. The deep region is formed by a rich development of venous networks in the submucosa urethræ. The peripheral part is composed of erectile tissue which is like that of the corpora cavernosa, except for the fact that its meshes are smaller and the connective-tissue strands more delicate. The arteries here never open directly into the venous spaces, but always break up into capillaries before reaching the veins.

The *glans penis* consists of much-branched and convoluted veins, which are held together by an abundance of firm connective tissue.

The tunica albuginea of the cavernous bodies and the glans penis are supplied richly with nerves (see Nerve-endings).

2. FEMALE SEXUAL ORGANS.

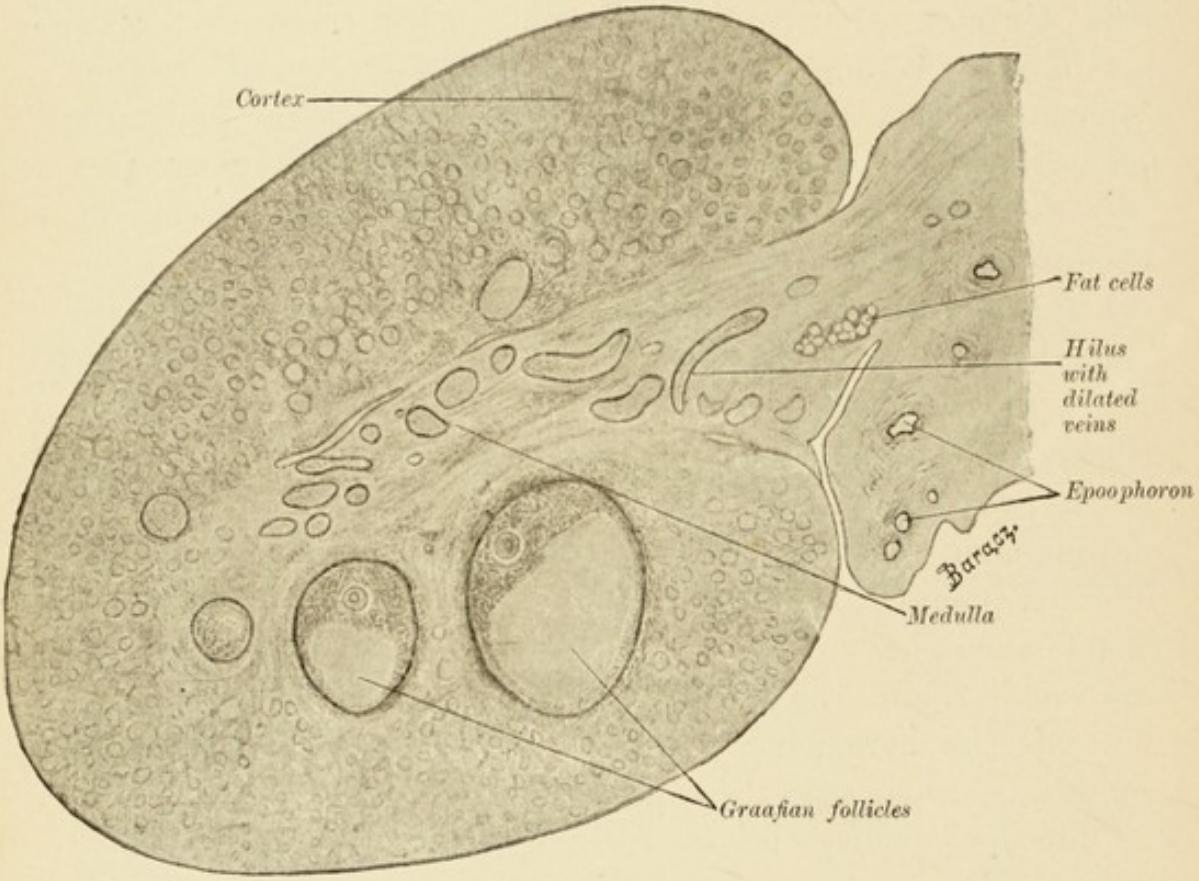
A. The Ovaries.

The ovaries are alveolar glands possessing no ducts. Their product—the egg cell—is secreted in a special way, to be

described later. In the ovary we can distinguish a *medulla* and a *cortex* (Fig. 182).

The medulla, also called the *zona vasculosa*, is characterized by its richness in blood-vessels. It consists of connective tissue, which contains elastic fibres, strands of smooth muscle cells, and the larger vessels of the ovary. These vessels enter the hilus and take a characteristic much-convoluted course.

FIG. 182.



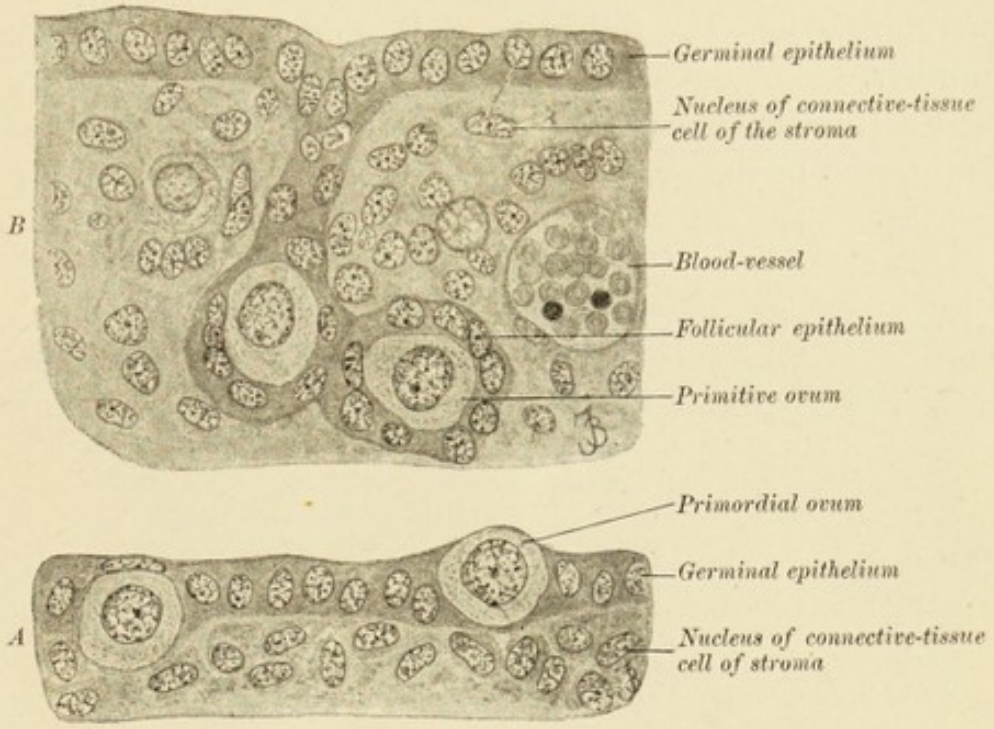
Transverse section of the ovary of an ape. × 26.

The *cortex* contains, besides the connective tissue, the essential glandular tissue, which is present in the form of so-called *follicles*. In these there are present the *egg cells*. The connective tissue separating the gland elements is directly continuous with that of the medulla, and is known as the *stroma*. It forms on the surface of the cortex a compact layer, the *tunica albuginea* of the ovary. The whole surface of the ovary—*i. e.*, the whole tunica albuginea—is covered by a single layer of

cubical epithelium (*germinal epithelium*), which is a modification of the peritoneal covering.

The stroma of the cortex consists of fibrillar connective tissue, which in young individuals is rich in cells whose nuclei have a characteristic appearance. They are long and oval, with a distinct nuclear membrane and a well-marked chromatin network. They are larger than the ordinary connective-tissue nuclei, and resemble more in outline those of smooth muscle (Fig. 183).

FIG. 183.



From a section of the ovary of a human embryo in the third month. × 540.

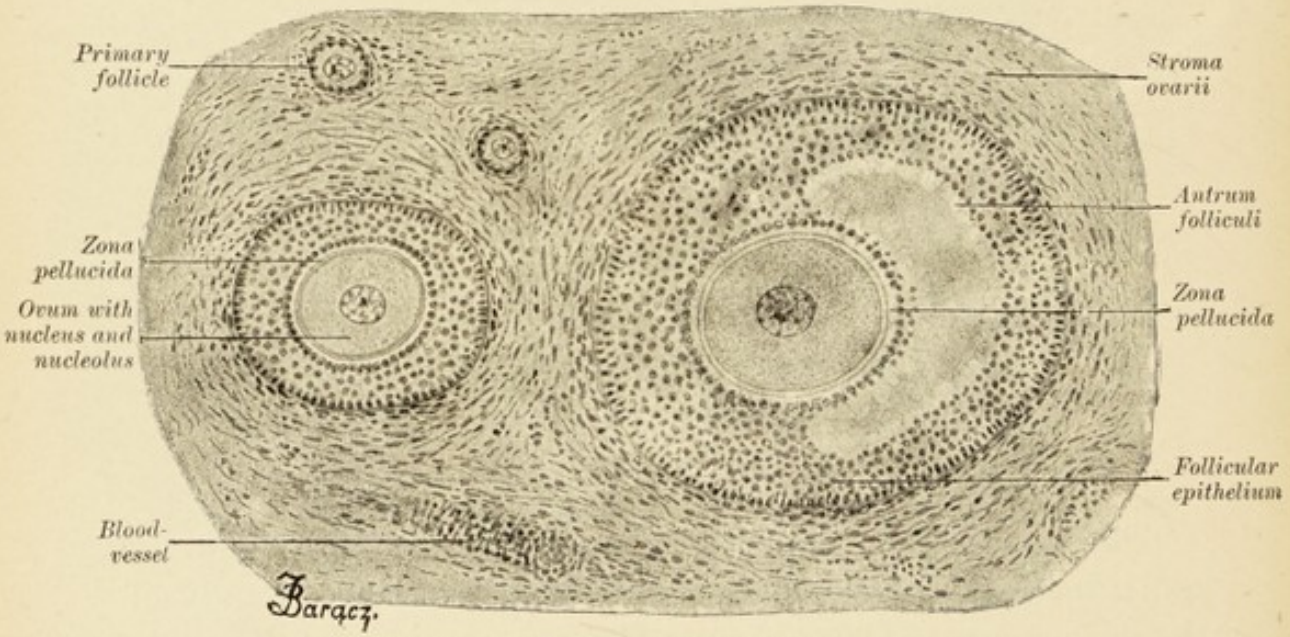
The structure of the glandular part of the organ and the individual egg follicles can best be understood by a study of the development of the ovary. The egg follicle arises from the germinal epithelium. The first part of the development occurs in embryonic life, while the ripening of the egg does not take place until puberty. The cells of the germinal epithelium increase by division, and some of them develop into large cells rich in protoplasm, with large nuclei and nucleoli. These are called the *primordial ova* (Fig. 183, *A*). The germinal epithelium grows together with the primordial ova into the underlying stroma (Fig. 183, *B*), and gives rise to the column-like

structures, the *Schläuche* of Pflüger. The primordial ova are thus collected into groups, called *egg nests* (*Eiballen*).

The egg nests are divided into smaller cell groups by the ingrowth of connective tissue. In each of these *primordial follicles* we find at least one ovum, and often three or four, which are surrounded by a layer of germinal epithelium cells, the *follicular cells.* Later, each primordial follicle contains only one ovum, partly because the others disintegrate, and partly because a follicle containing more than one ovum is usually split up by connective tissue into as many follicles as there are ova. The follicular cells tend to increase greatly in number.

Further changes which usually occur in post-embryonal life consist in the great increase in the follicular cells by karyo-

FIG. 184.



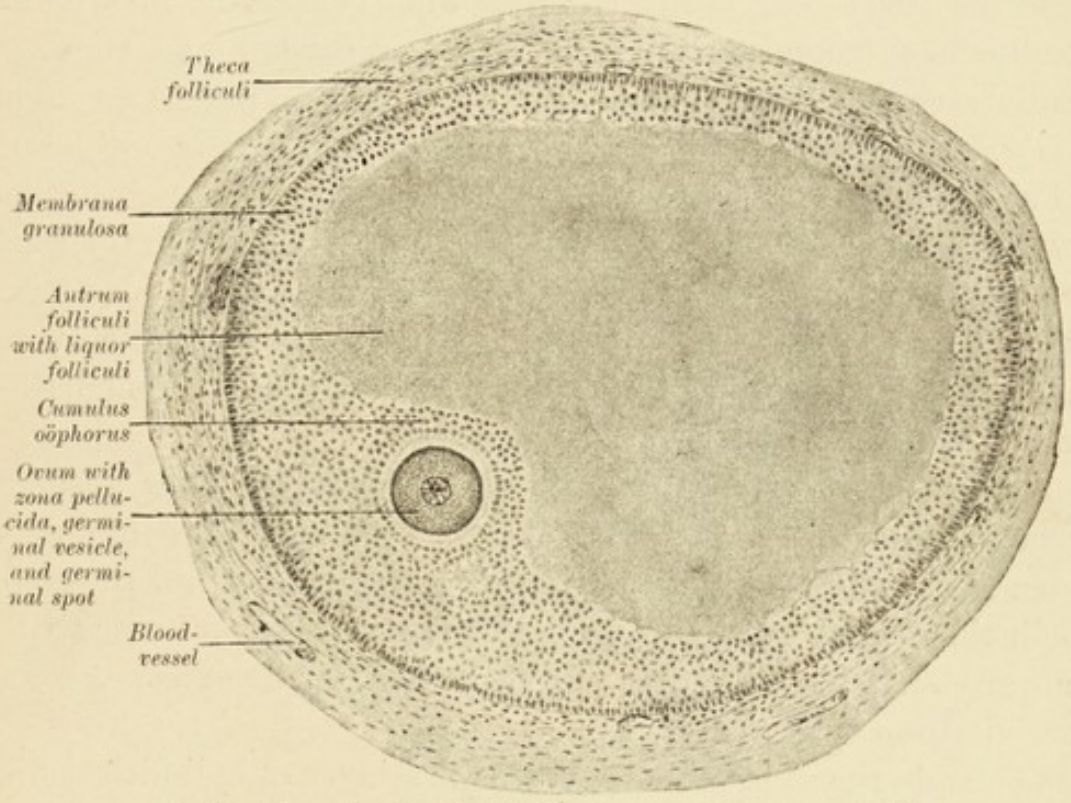
From a section through the cortex of an ape's ovary. × 150.

kinesis and the production by these of several layers around the ovum (Fig. 184). In the layers of follicular cells there occur during the growth of the follicle certain changes. The ovum increases in size and there is developed around it a delicate membrane—the *zona pellucida*—which, according to some, is a product of the follicular cells, while others hold that it arises from the ovum itself. At the same time the egg proto-

plasm stores up in itself nourishing material in the form of a granular substance, so that the greater part is converted into the so-called *deutoplasm*. Thin layers around the nucleus and at the periphery of the ovum remain unchanged. The deutoplasm and protoplasm together form the *yolk*.

The excentrically lying nucleus of the ovum is spherical, clear, and vesicular, and possesses a distinct nuclear membrane with a double contour. On account of this structure, the nucleus is known also as the *germinal vesicle* (*vesicula germinativa*). In the chromatin network is present a distinct nucleolus, which is called also the *germinal spot* (*macula germinativa*), and in which amœboid movements have been observed (Nagel).

FIG. 185.



Section through a Graafian follicle from an ape's ovary. × 90.

At the same time, changes take place in the follicle, beginning in a collection of serous fluid between the follicular cells (*liquor folliculi*). This is contained in a cavity, which gradually becomes larger, and is known as the *antrum folliculi*. The fluid is due partly to a transudation from the vessels surround-

ing the follicle, and partly to a liquefaction of certain of the follicular cells. In consequence of the increase in this fluid the ovum is pushed to one side (Fig. 185), and the whole *Graafian follicle* (folliculus oöphorus vesiculosus) becomes as large as 5 mm. in diameter, and is seen bulging from the surface of the ovary.

The follicular epithelium lining the interior of the follicle in many layers is known as the *stratum granulosum* (membrana granulosa). At one place it forms a hill-like mass, which contains the ovum (Fig. 185), and is known as the *cumulus oöphorus* or *discus proligerus*. At this period the membrana pellucida surrounding the ovum becomes thicker and shows a radial striation, which was at first thought to be due to a system of pores running through the membrane. Later investigators (Paladino and Retzius) claim that the striation is caused by the passage of fine processes of the follicular cells through the zona pellucida, after the manner of protoplasmic bridges. In this way there is established a close connection between the ovum and the follicular cells, which is of importance in the nourishment of the egg cell.

Between the ovum and the zona pellucida there is a small space, known as the *perivitelline space*. Thus the ovum may turn inside the zona pellucida. Sabotta has described the zona pellucida in the mouse as a quite homogeneous membrane without any striation whatever, and disputes also the existence of a perivitelline space.

Outside the zona pellucida there is a layer of cylindrical follicular cells arranged radially. These form the so-called *corona radiata*. The whole Graafian follicle is surrounded by a connective-tissue capsule, the *theca folliculi*. Between this and the follicular epithelium there is a structureless basal membrane (membrana propria folliculi, Glashaut). In the theca folliculi there are to be distinguished two layers: the *tunica interna*, consisting of round or spindle-shaped cells; and the *tunica externa*, which is made up of circularly disposed connective-tissue fibres.

The formation of the Graafian follicle begins before puberty,

and often some stages are found to have been completed in the newborn and in fœtuses. The above-described ovum, however, is not yet capable of being fertilized. In order to reach this stage, it must undergo the *ripening processes*, which consist in the so-called reduction of chromosomes. The extrusion of both polar bodies in lower animals has been discussed in treating of fertilization in general. In higher animals (including man) the ripening takes place in the ovary. The second polar body is extruded shortly before the bursting of the follicle and the escape of the ovum.

The theca folliculi come in contact with the tunica albuginea of the ovary as the follicle moves to the surface. The coverings of the follicle become gradually thinner, but the true reason for the rupture of the follicle is not clear. It is probable that many forces act simultaneously. The increase in the liquor folliculi, the marked congestion which is characteristic of the tissues in ovulation, the swelling of the ovary, and possibly the contraction of smooth muscle contained in the stroma, may help in this process. At the same time the walls of the follicle at the place of bursting become thin and atrophic on account of the obliteration of blood-vessels by pressure. Meanwhile the connection between the ovum and the cells of the discus proligerus and membrana granulosa becomes looser, and finally disappears, so that the ovum comes to lie in the liquor folliculi. During the bursting of the follicle the liquor folliculi as well as the ovum is cast out into the peritoneal cavity.

After the ovum has escaped, there is always a certain amount of blood which fills up the empty follicle. This becomes a closed cavity containing a blood-clot, which begins to undergo organization. This is known as the *corpus hæmorrhagicum*. The organization takes place by a formation of fibrin, and the ingrowth of the so-called *lutein cells* from the periphery of the follicle. The origin of the lutein cells is not clearly understood. They were described first in 1827 by v. Baer, who considered them as a derivative of the theca interna cells. Later on, Bischoff studied this subject, and came to the conclusion that they were derived from the fol-

licular epithelium making up the membrana granulosa—*i. e.*, from the epithelium. There are many adherents to each of these views, but the balance of evidence seems to be in favor of v. Baer's theory. Other theories have been advanced, but have gradually been abandoned. J. G. Clark has studied the subject, and believes that the lutein cells are specialized connective-tissue cells derived from the theca interna. According to him, they appear in the inner layers of the follicle wall when a differentiation into theca interna and externa is beginning.

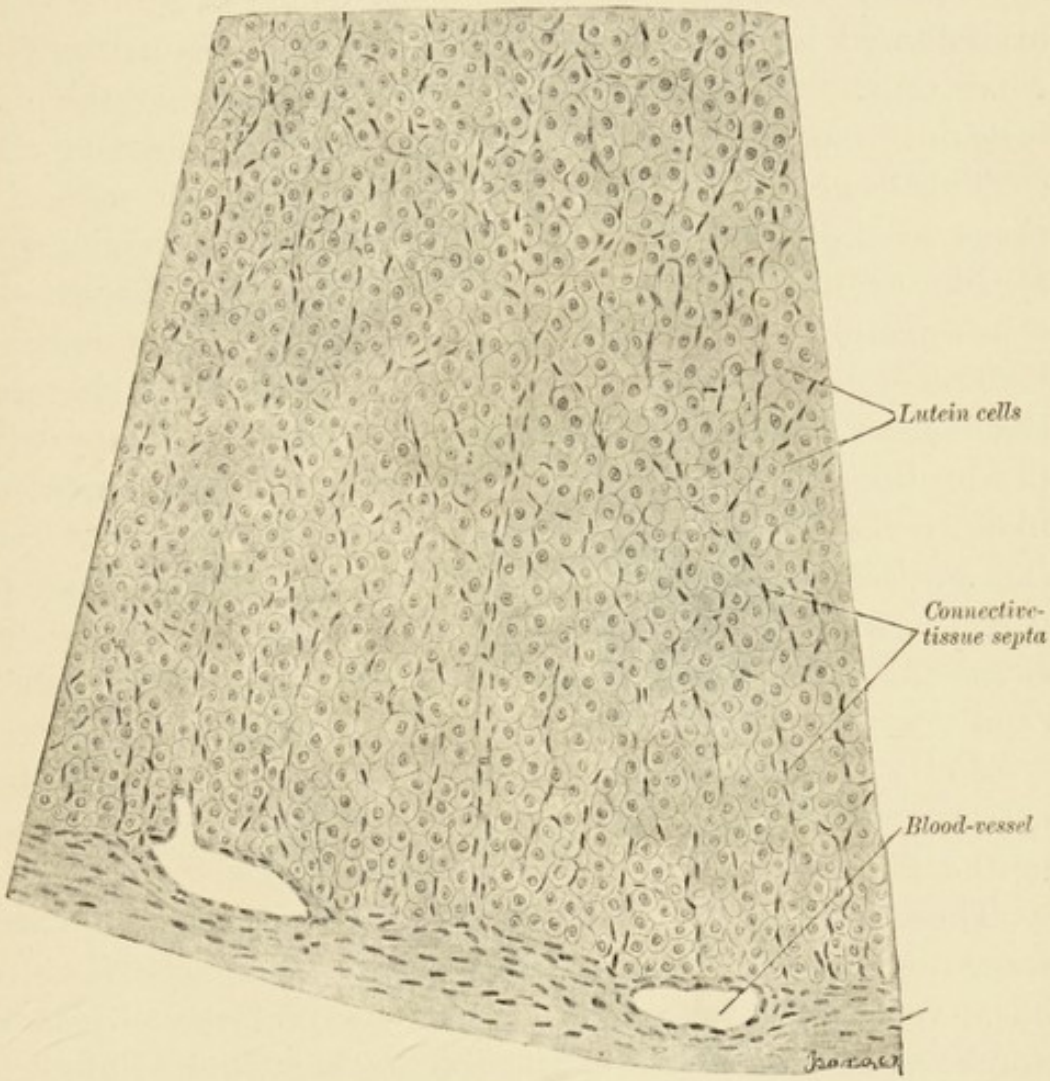
Whatever the origin of the lutein cells may be, it is certain that the corpus hæmorrhagicum is invaded on all sides by large yellow cells containing fatty granules (*lutein*); and that by this invasion the blood-clot is replaced by a definite cellular tissue, the whole making up the *corpus luteum* (Fig. 186). The lutein cells give to the body a yellowish color, and often there are found orange-red hæmatoidin crystals, which are the remains of the blood-clot.

According to Clark, the lutein cells in the growing follicle increase at the expense of the cells of the theca interna, and there is also present a network of true reticulum stretching from the theca externa among the lutein cells and collected into a membrane next the tunica granulosa to form the membrana propria folliculi. When the follicle ruptures, this membrane is broken through by the growth of lutein cells and blood-vessels. As soon as the corpus luteum has reached its highest development, certain changes take place in the cells and the retrogression begins. Fatty degeneration in the lutein cells is followed by an increase in the connective tissue. The septa become thicker and all the connective tissue of the corpus luteum shrinks to form a firm, compact body, which is known as the *corpus albicans* or *c. fibrosum*. This becomes always more contracted, like scar tissue, and finally undergoes hyaline degeneration and is lost in the ovarian stroma.

We distinguish *corpora lutea vera* and *corpora lutea spuria* according to whether they arise from follicles whose eggs have become fertilized or not. There is no difference in the intimate

structure of these, but the corpora lutea vera, in consequence of the marked hyperæmia of the ovary during pregnancy, are larger. The corpora lutea vera as well as the corpora albicantia resulting from them remain longer in the ovary, because their retrogression is slower than in the corpora lutea spuria.

FIG. 186.



Part of a corpus luteum of a bitch. × 300.

It is to be noted that only a small proportion of the ova in the ovary become ripe. According to Henle, of about 72,000 ova in the ovaries of one individual, only 400 arrive at maturity. The rest undergo degenerative changes which represent an entirely physiological process, known as *follicular atresia*. This depends on a series of changes not only in the organ itself, but also in the follicular epithelium and the theca.

In the beginning a *chromatolysis* or *karyolysis* takes place in the nucleus. The chromatin becomes granular, and finally is dissolved and the nuclear membrane disappears. On the other hand, the nucleus may undergo simple atrophy. In the cell body, at the same time, fatty degeneration sets in, and the protoplasm becomes gradually liquefied. The zona pellucida swells, and finally is dissolved. These changes in the ovum are followed immediately by similar degenerations in the follicular cells. The absorption and disappearance of the dead cells are brought about mainly by phagocytic wandering cells.

This destruction of cells often leads to a new formation of tissue in the theca interna, consisting in the production of a fibrillar connective-tissue scar (Schottländer). Among the cells sometimes are found karyokinetic figures (Flemming).

The *blood-vessels* of the ovary arise on the arterial side from the ovarian and the uterine arteries. Branches of these enter the medulla through the hilum, and take a characteristic tortuous, corkscrew-shaped course. They divide many times, and the smaller branches diverge to the peripheral part of the medulla, where they form a rich plexus. From this, branches enter the cortex, and, spreading through the stroma, form capillary networks in the theca folliculi.

The lymph-vessels surround the Graafian follicle with a network and leave the ovary through numerous wide trunks in the hilum.

The nerves, partly medullated and partly non-medullated, enter the ovary through the hilum, following the course of the blood-vessels, in whose walls a great many fibres end. Other fibres reach the germinal epithelium and surround the follicles with dense networks. According to Retzius, and others, the nerve fibres do not enter the follicle, while Riese and v. Herff have found the nerve-endings between the follicular epithelial cells.

Among the rudimentary organs found in the neighborhood of the ovary and derived from the Wolffian body are the epoöphoron (parovarium, organ of Rosenmüller) and the paroöphoron. The first lies in the broad ligament at the hilum

of the ovary, and has the form of many coiled blind tubules lined with ciliated epithelium. The paroöphoron lies more medially, and consists of similar convoluted canals. The first is homologous with the epididymis, and the second with the paradidymis in the male.

Genito-urinary System of the Embryo.

The first part of the genito-urinary system to appear in the embryo is the Wolffian duct. The origin of this duct is doubtful. According to some authors (Hensen, v. Spee), it is derived from the ectoblast. Others believe it arises from the mesoblast; His and Kowalewsky, from the middle plate; and Remak, Kölliker, and Waldeyer, from the lateral plate of the mesoblast. Rensen, Dansky, and others derive it from the cœlomic epithelium. It is at first a solid rod of cells, which subsequently develops a lumen lined with epithelium-like cells. Tubules develop from this duct and form the Wolffian body. This embryonic organ was observed first, in 1759, by Wolff, who considered it the embryonic stage of the permanent kidney. Rathke (1825) first used the term Wolffian body in connection with this organ in birds, and called the corresponding organ in mammals, *Oken's body*. Jacobson, in 1824, termed it the primordial kidney, and recognized that it excreted uric acid, which was carried into the allantois.

The Wolffian body of mammalian embryos is a somewhat pyriform body symmetrically placed in the abdominal cavity. In early embryos it is, next to the liver, the largest abdominal organ. It consists of a tubular and a glomerular part. The glomeruli are situated medially, while the coiled tubules form the largest part of the organ. These come off from the Wolffian duct at right angles to it, and after a considerable coiling are connected with the glomeruli by means of end dilatations similar to the Bowman's capsules of the permanent kidney. In the human embryo the tubules have a somewhat S-shaped course. In the pig's embryo, on the contrary, the tubules are much convoluted. Their exact course has been determined (MacCallum) by means of injections into the Wolffian duct, and

by the construction of wax models after the method of Born. In general, there are two parts in the tubule, a secreting and a collecting segment. This was recognized first by Joh. Müller. In the pig the collecting tubule possesses two convoluted parts, while the secreting portion is a large loop in the central part of the organ. The epithelium is characteristic in these two parts, being low and cubical in the collecting segment, and columnar in the secreting portion.

The blood supply of the Wolffian body is derived directly from the aorta. This has been worked out in pigs' embryos (MacCallum). The arteries enter at the medial border of the gland and break up to form the glomeruli. From these many efferent arteries proceed in a radial manner toward the periphery. Around the tubules they form a fine capillary network, which empties into three series of veins. Two of these run on the periphery of the organ toward the medial border, over the dorsal and ventral surfaces, respectively. The other series of veins leaves the Wolffian body by the same path as that taken by the arteries in entering. A distinct blood vascular unit can be observed.

At a certain stage in the development of the embryo, which differs in different species, the Wolffian body begins to undergo retrogression. The tubules degenerate, and the glomeruli become occluded. The anterior tubules alone in the male remain connected with the Wolffian duct, and grow in size and complexity to form the head of the epididymis. The tail of the epididymis and the vas deferens are derived from the Wolffian duct. The posterior tubules of the Wolffian body form the paradidymis or organ of Giraldè.

In the female the Wolffian duct degenerates. The anterior part persists usually with the parovarium. When the whole duct persists, it is known as *Gartner's canal.* The Wolffian body in the female persists in its anterior (sexual) part as the parovarium (epoöphoron, organ of Rosenmüller). The tubules making this up increase considerably in size. The posterior tubules (renal part) disappear with the exception of a few tubules, known as the paroöphoron.

In both sexes a new tube is developed parallel with the Wolffian duct. This is the Müllerian duct. In the female it is connected with the peritoneal cavity, and persists as the Fallopian tube and uterus. In the male it disappears in large part. The persistence of the anterior part gives rise to the hydatid of Morgagni. The posterior part may remain as *Weber's organ*. In some cases the whole tube is found in the adult male, and then is known as *Rathke's duct*.

The way in which the head of the epididymis comes to be connected with the testis tubules has been determined in pigs' embryos and in man (MacCallum). It is well known that the seminiferous tubules in some of the lower vertebrates (fishes, etc.) carry the sexual products over into the Malpighian corpuscles of the urinary organ, and are taken to the outside through the urinary ducts. A somewhat similar condition has been observed in the embryos of pigs and man. The testis which develops from the peritoneal covering of the Wolffian body is at all times closely connected with this organ. Tubules develop in the testis, and at a certain period grow out through the tissue connecting the two organs, and break into the capsules of the Malpighian corpuscles of the Wolffian body. These tubules are very fine and form a dense network. Their lumina become continuous with that of Bowman's capsule, and in this way a communication is established between the tubules of the testis and the future epididymis and vas deferens.

The ovary develops on the medial surface of the Wolffian body in the same way as the testis.

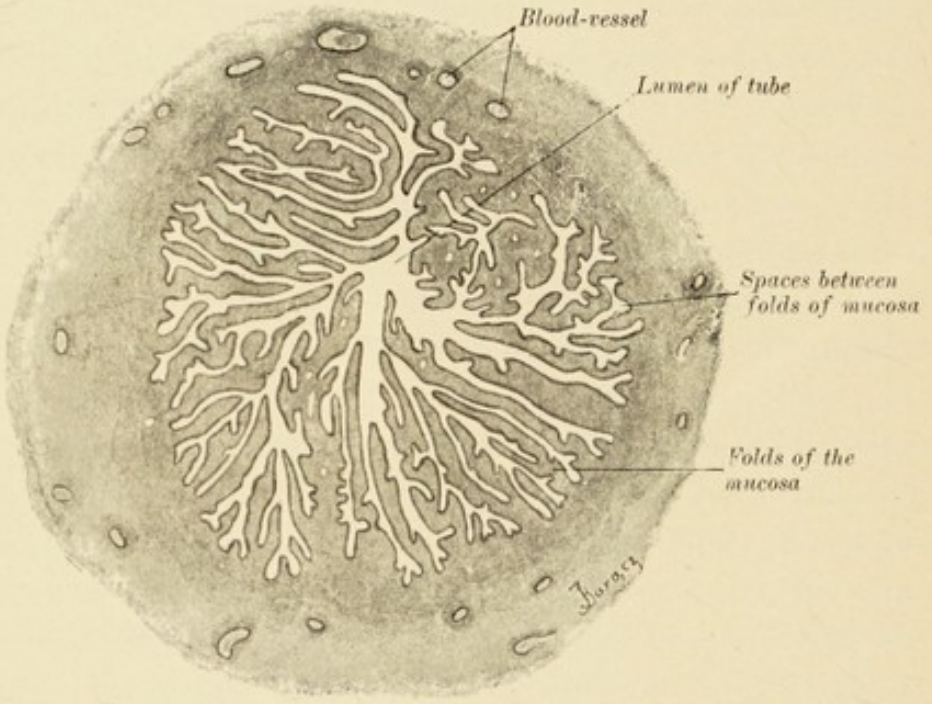
The permanent kidney develops as a knob-like growth at the end of the primitive ureter, posterior and dorsal to the Wolffian body. The exact course of the development of the kidney tubules has not been worked out satisfactorily. They arise in the beginning as long diverticula from the end of the ureter, which grow out to the periphery of the organ and divide into two branches, which arch backward toward the hilum to join, after many convolutions, with the Malpighian corpuscles. The exact origin of the kidney lobule and of the various segments of the uriniferous tubule is not known.

B. Fallopian Tube (Tuba Uterina Fallopii).

In the walls of this tube we can distinguish the following coats: mucosa, submucosa, muscularis, and serosa.

The *tunica mucosa* is thrown into many longitudinal folds, varying somewhat in different parts of the tube. In the ampulla they are highest and possess numerous branched accessory folds, so that the lumen seems filled with them (Fig. 187). There are, however, throughout the tube only four main folds, as can be seen more plainly in a tube taken

FIG. 187.

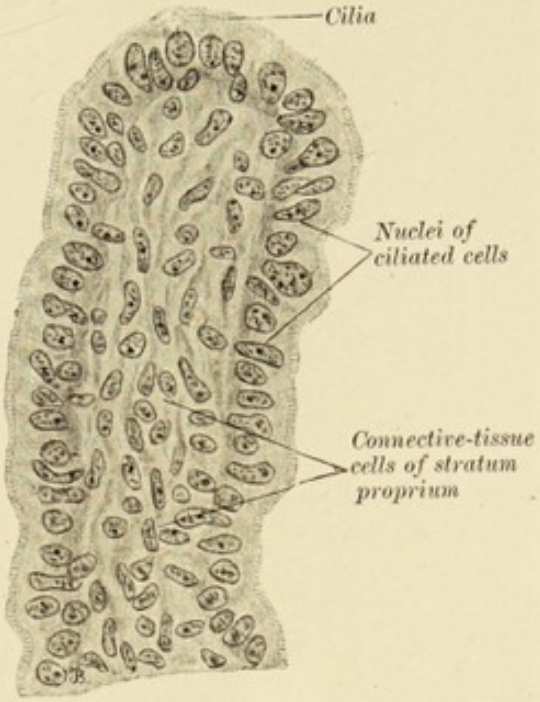


Transverse section through the ampulla of the Fallopian tube of a young woman. × 25.

from an embryo or newborn babe. The mucous membrane is covered on the surface with a single layer of columnar ciliated cells, the movement of whose cilia is toward the uterus (Fig. 188). The tunica propria is rich in cells and overlies a thin muscularis mucosæ composed of longitudinal smooth muscle fibres. The *tunica submucosa* consists of loose connective tissue, and is bounded on the outside by two layers of smooth muscle, making up the *tunica muscularis*. The fibres of the inner stronger layer run circularly, while the outer thin layer is longitudinal. The muscle layers are thicker near the uterus than at

the ampullar end. The *tunica serosa*, which has the same structure as the peritoneum, is joined to the muscularis by a loose connective tissue. The mucosa is supplied richly with blood-

FIG. 188.



From a section through a fold of the mucous membrane of a human Fallopian tube. × 480.

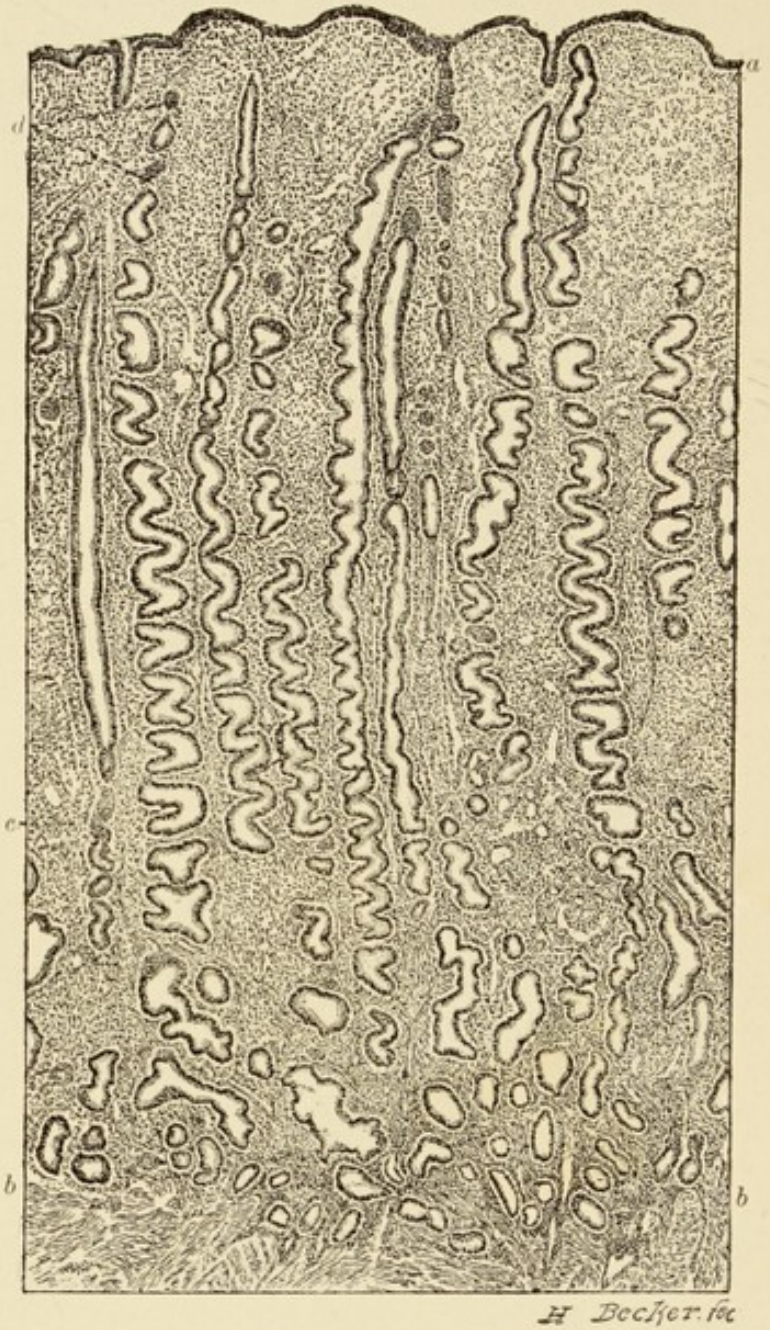
vessels. The nerves form in the tube wall a rich plexus, from which fine branches proceed to the mucosa to end in the neighborhood of the epithelial cells.

C. Uterus.

In the wall of the uterus there are three main coats: the mucosa (endometrium), the muscularis (myometrium), and the serosa (perimetrium).

The *mucosa* lining the whole uterine cavity is at the time of puberty about 1 mm. thick. It is covered on its surface by a single layer of cylindrical ciliated epithelial cells, whose cilia move toward the vagina. The tunica propria possesses many connective-tissue cells and leucocytes contained in a fairly dense connective tissue. Here there are found numerous simple or dichotomously branching tubular glands, which take on usually a coiled or corkscrew form in the deeper parts. They are lined with a single layer of ciliated cylindrical cells,

FIG. 189.



Normal endometrium in a patient twenty-six years of age. × 25.

The mucosa is slightly thickened, its surface is wavy, and its epithelial covering *a* is intact. In this section it is possible to trace the glands in their continuity almost from the surface to the muscle. A few of them are practically cylindrical throughout, but the majority have a wavy contour presenting a well-defined corkscrew arrangement. Quite a number, cut just along their margin, can be recognized as little masses of epithelial cells; *c*, is cut longitudinally; *d*, almost transversely. At first sight, one would think that there was a great excess of glands in the section, whereas in reality, at most, there are not more than twelve, the distances between any neighboring two being about the same. The gland epithelium is intact throughout. The stroma in the superficial portions is rather lax, in the deeper portions more compact. *b* indicates the line of junction between the muscle and mucosa. Its irregularity is especially noticeable. (T. S. Cullen, *Cancer of the Uterus:* New York, 1900.)

the ciliary current moving toward the mouth of the gland. A basal membrane (membrana propria) with a double contour limits this row of cells on the side toward the tunica propria, and is a continuation of the basal membrane of the surface epithelium. The glands probably possess no secretory function.

The mucosa of the cervix uteri shows some distinguishing features. The surface is thrown into folds, known as the *plicæ palmatæ*. The mucous membrane is thicker and firmer, and possesses much higher cylindrical cells than the corpus uteri. In the region of the external os it passes over into a stratified pavement epithelium with papillæ beneath. After repeated pregnancies this pavement epithelium covers also the lower part of the cervix. The mucosa of the cervix contains, besides the glands already described, numerous glands which secrete mucus (*glandulæ cervicales uteri*). Often the mouths of the glands become closed and there are formed retention cysts, containing a quantity of mucoid material and reaching the size of a pea. These were formerly known as *ovula Nabothi*.

A submucosa in the uterus cannot be made out. The mucosa lies directly on the *muscularis*, and the glands reach down so as to touch the muscle coats. The latter is the thickest layer of the uterus, and is made up of long, spindle-shaped, smooth muscle elements. In the non-pregnant uterus these are 40–60 μ long, while at the end of pregnancy they reach a length of 300–600 μ. They are arranged in bundles, mostly running concentrically around the blood-vessels. The whole muscle layer, however, can be divided roughly into layers, which in the adult are by no means distinctly separated from one another. The exact disposition of these layers has been the cause of much discussion, and there have been many ideas advanced with regard to this subject. In general, three layers can be made out: 1, a longitudinal inner layer (*stratum mucosum*); 2, a middle circular layer of bundles closely associated with the blood-vessels (*stratum vasculare*); and 3, an outer layer, in which the bundles run both longitudinally and circularly. The latter layer can be divided into two parts: an inner layer of mixed longitudinal and circular fibres (*stratum supravascu-*

lare), and an outer layer which consists exclusively of longitudinally disposed elements (*stratum subserosum*). The middle layer or stratum vasculare is by far the thickest of these coats.

The *serosa* is not different in structure from other parts of the peritoneum.

The *arteries* enter the muscularis and divide mainly in the stratum vasculare into numerous branches, of which the greater part run into the mucosa and break up there into capillary networks which surround the glands and reach up to the surface epithelium. The veins form a plexus in the deeper parts of the mucosa, and then pass into the stratum vasculare, where another larger plexus is formed.

The *lymph-vessels* form a network in the mucosa and another under the serosa. These are joined by anastomosing branches.

The *nerves* end partly in the muscularis (see Nerve-endings), and partly in the mucosa, where they form thick networks. From these, non-medullated fibres run, according to some authors, to the epithelium, where they end freely between the cells. Ganglion cells have been described in the course of these fibres.

In certain phases in the life of the uterus changes take place especially in the mucosa which must be spoken of here. These changes accompany menstruation and pregnancy.

In *menstruation* there is a certain amount of bleeding from the uterus occurring more or less regularly every twenty-eight days, and continuing throughout the life of the individual from the fourteenth to about the forty-fifth or fiftieth year. It is probable that the changes in the mucosa have to do with the reception and preservation of the ovum, since ovulation occurs at about the same time as menstruation. During the menstrual period, in the first place, there is a marked hyperæmia of the uterine walls five to ten days before the flow of blood. The blood-vessels are much dilated and the capillaries become large and well marked. According to Heape, there is also an increase in the number of blood-vessels. On account of the hyperæmia there are a swelling and a growth of the mucosa,

so that it attains a thickness of 6 mm. It then is called the *decidua menstrualis.* Changes occur also in the glands. They increase in length and become corkscrew-shaped. The increased size of the mucosa is due largely to a cellular multiplication. Karyokinetic figures in large numbers have been observed in the menstruating uterus by Mandl, not only in the epithelium, but in the interstitial tissue as well. After these changes have occurred there is an escape of blood in the subepithelial layers, which is due partly to a bursting of capillaries, and partly to a diapedesis of red corpuscles through the capillary walls. The epithelium covering these collections of blood is broken away and the blood escapes. The bleeding goes on for about four days, and then the regeneration of the mucosa begins. In the course of five to ten days the epithelium is quite restored and the glands regain their normal relations. Following this are a few days of rest before the next period begins. There has been considerable discussion as to the extent of the tissue destruction which takes place during menstruation. According to some, the whole mucosa is cast off at each period. Others hold that none at all is destroyed, and that pieces of the epithelium are lifted up merely to allow the blood to escape. It seems certain, however, that there is always some destruction of epithelium, and at the same time there is never a complete destruction. Parts of the gland tubules at least always remain uninjured, and from these and the surface cells that remain the whole epithelium regenerates.

During *pregnancy* the whole uterine mucosa suffers very marked changes in its structure. At the end of this time it is nearly all lost, and forms the so-called *decidua graviditatis*, of which there are three parts. The *decidua basalis s. serotina* is the part of the mucosa to which the ovum attaches itself, and in which later the placenta is developed; the *decidua capsularis s. reflexa* is that part which grows up to surround the ovum; while the *decidua vera* is the tissue which lines the rest of the uterine cavity.

In the part of the uterine mucosa where the decidua vera

developes, changes take place resembling those of menstruation. At the end of the fifth month the mucosa has become more than 1 cm. thick. This is due, in the first place, to the dilatation of the blood-vessels and the thickening of their walls, and also to the increase in length of the gland tubules. The latter become corkscrew-shaped or tortuous in their course. The tunica propria increases in its superficial part, so that there is a firm connective tissue between the necks of the glands. In consequence of this, the whole mucosa can be divided into two zones, a superficial *compact layer*, and a deep *spongy layer*. From these connective-tissue cells, the so-called *decidual cells*, arise. These are very large (30–100 μ), round or polygonal cells somewhat resembling epithelial elements. Each cell possesses usually only one nucleus, but some may contain as many as forty nuclei (giant cells) (Fig. 192). These will be spoken of later. The decidual cells are developed especially in the compact layer, where the glands have a straight course and are separated by much connective tissue. In the spongy layer the cells form narrow septa between the saccular ends of the glands.

The surface epithelium vanishes entirely, while the gland cells increase in number and become flattened to accommodate themselves to the widened gland lumina.

In the second half of pregnancy changes in the decidua vera occur, which are due mainly to pressure exerted by the growing fœtus and the increasing amniotic fluid. The decidua becomes gradually thinner, so that at the end of pregnancy it is only 2 mm. thick. The glandular epithelium degenerates, with the exception of that in the ends of the glands which rest on the muscle. This remains, and is the basis of the epithelial regeneration which takes place after pregnancy. The gland necks in the compact layer become obliterated and disappear about the middle of pregnancy. The gland lumina in the spongy layer, on the contrary, are converted into spaces which lie parallel to the surface of the uterine wall.

The decidua reflexa (capsularis) has originally the same structure as the decidua vera; but during the first months of

pregnancy a hyaline degeneration takes place (Minot), so that it cannot be recognized at the end of pregnancy. According to Leopold, however, it is fused with the decidua vera, and is always to be seen.

The decidua serotina (basalis) in the beginning has the same structure as the decidua vera, but becomes complicated in the course of pregnancy by the formation of the placenta.

Placenta.

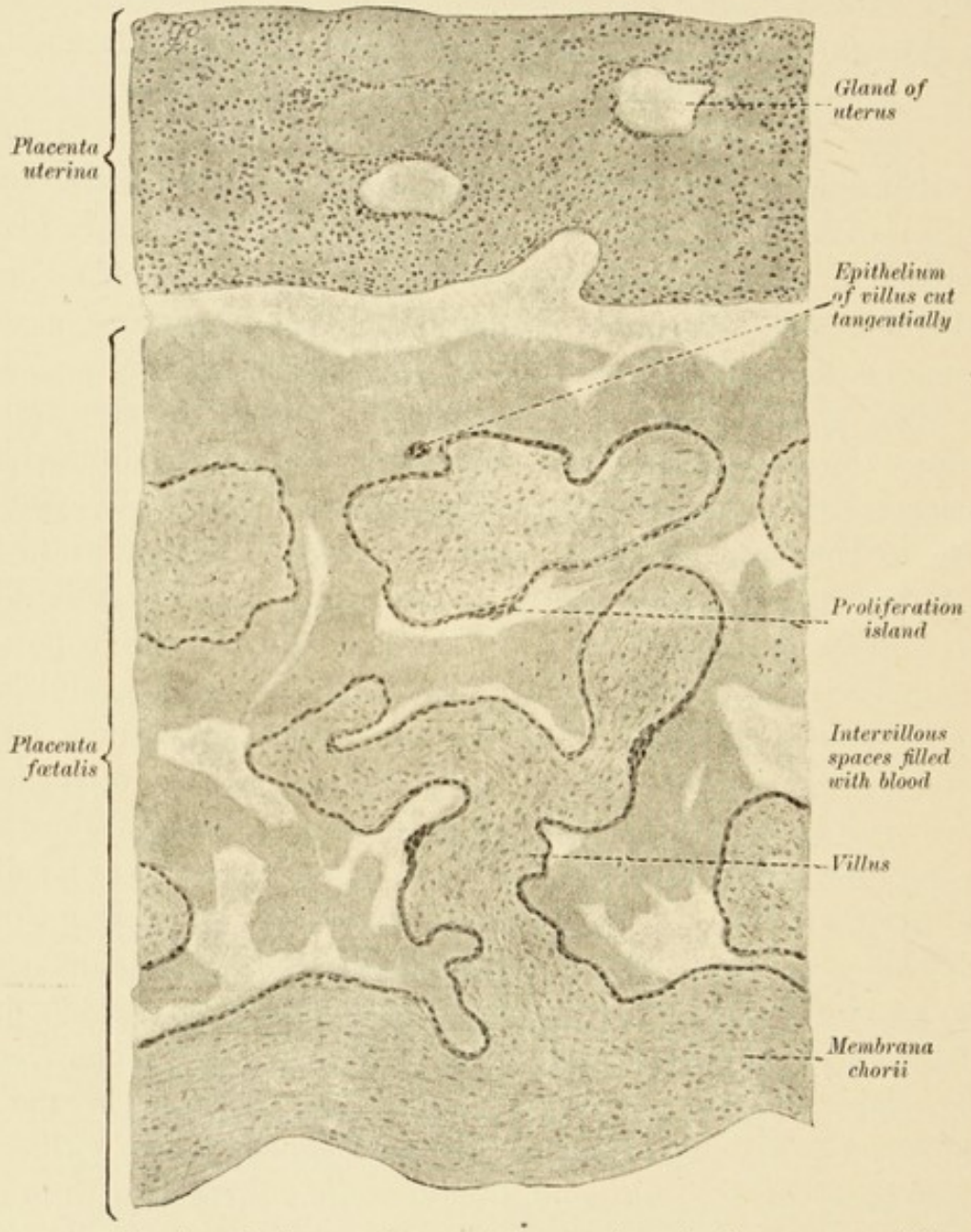
The placenta usually is discussed in detail in the text-books of embryology, but since it consists not only of an embryonic part (*placenta fœtalis*), but also a maternal part which is modified uterine mucosa (*placenta uterina s. materna*), a brief description must also be given here.

The placenta fœtalis consists of a connective-tissue membrane, the *membrana chorii*, which on the surface toward the uterine wall possesses many richly branched *villi*. These give rise to the name *chorion frondosum*, which is applied to the membrane. The chorionic villi are grouped in large bundles or *cotyledons*. After the third month the chorion comes in contact with the second fœtal membrane, the *amnion*, and later on is connected closely with it. The amnion is a thin membrane which consists of an epithelial and a connective-tissue layer. The epithelial coat covers its free surface and lines the whole amniotic cavity in the form of a single layer of flattened cells. The connective-tissue sheath fuses with that of the chorion. Through the umbilical cord there enter the membrana chorii two umbilical arteries, which carry the blood of the embryo to the placenta fœtalis, where they branch freely. To each cotyledon there runs one branch, which breaks up into many twigs and forms capillary networks in the villi.

A part of the villi end freely, while others pass into the placenta uterina and become firmly connected with it. The latter are called the *fastening villi* or Haftwurzeln. By means of these the two sides of the placenta are joined securely together, so that in the later months of pregnancy no separation occurs.

The chorion is a connective-tissue layer covered on the side toward the uterine wall with an epithelial layer. The connective-tissue part shows originally the structure of embryonic connective tissue—*i. e.*, stellate cells lying in a homogeneous

FIG. 190.

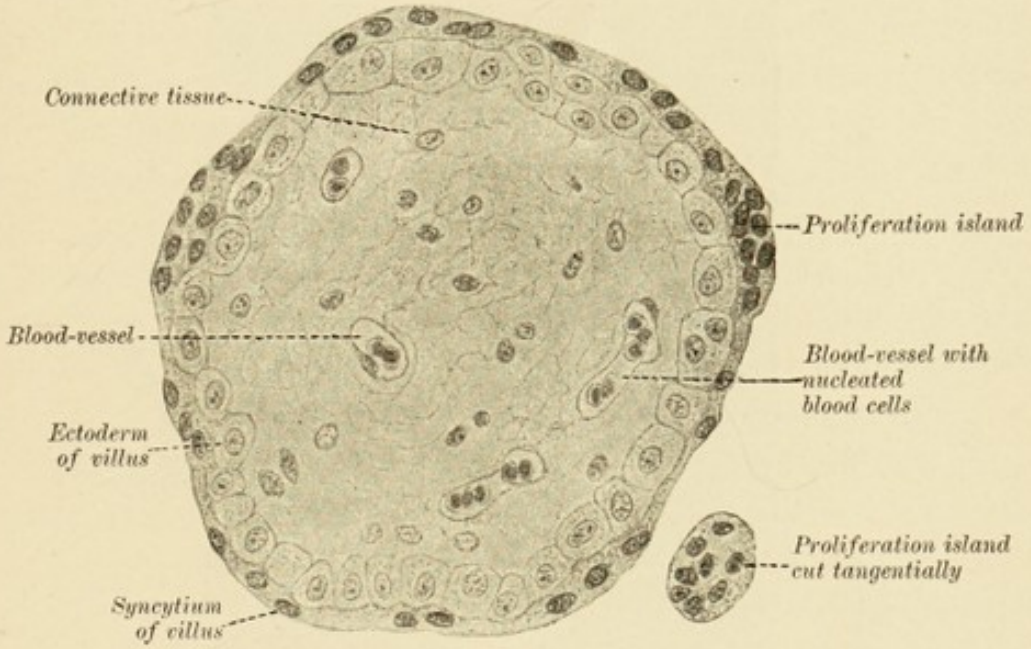


Transverse section through a human placenta at the second month of pregnancy. (After a preparation by Prof. Mars.) × 50.

ground substance. Later it assumes the character of fibrous connective tissue. The chorionic villi appear, during the first months of their development, in the form of short protuber-

ances consisting entirely of epithelium. Later they develop numerous branches which go on dividing dichotomously. They are made up of *gelatinous tissue*, which forms the axis, and a layer of epithelium, which covers not only the villi, but also the whole membrana chorii. In the larger stems of the villi we find, instead of the gelatinous tissue, a fibrillar connective tissue (Fig. 190). The epithelial coat is differentiated early into two distinct layers (Fig. 191). The layer touching the connective-tissue part consists of well-defined cells containing

FIG. 191.



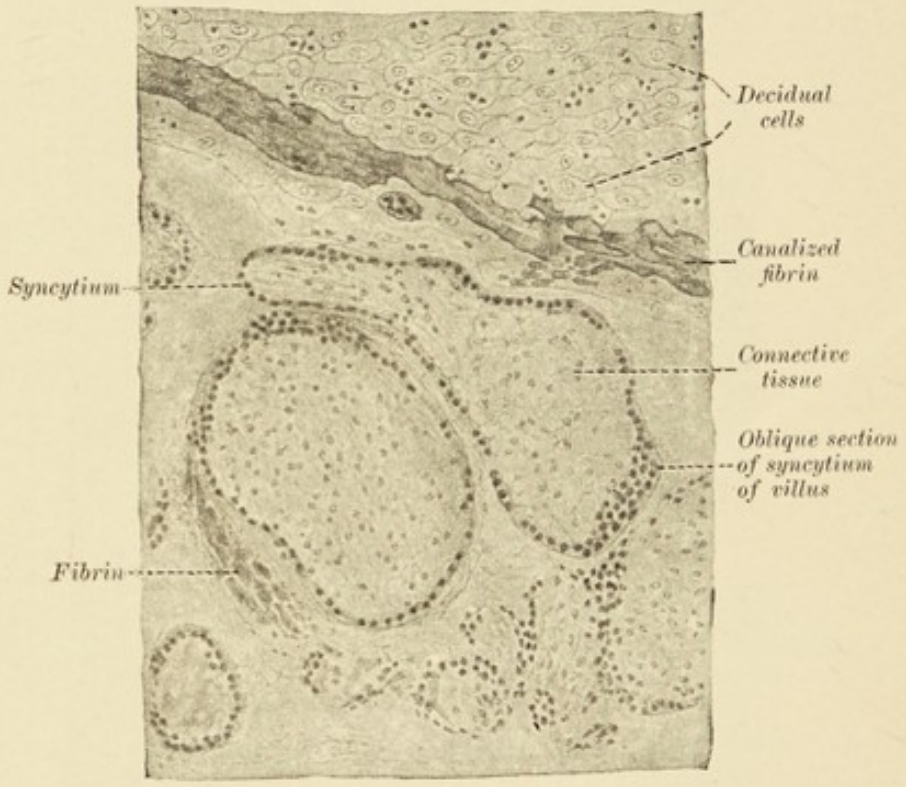
Transverse section of a human chorionic villus at the fifth month of pregnancy. × 300.

clear protoplasm, and is known as the *ectoderm layer* of the villus (Zellschicht of Langhans). The layer outside this consists of cells which are not sharply marked off from one another. It is made up of a continuous protoplasmic mass in which there are numerous nuclei. We have here to do with a syncytium, and we speak of this layer as the *syncytium* of the chorionic villus. These two layers are separated fairly sharply from one another, for the protoplasm of the syncytium has a special affinity for acid dyes and stains more deeply, while the nuclei are much smaller than in the ectoderm layer.

Toward the middle of pregnancy (fifth month) the ectoderm of the villi begins to degenerate, so that at the end of preg-

nancy it is almost entirely wanting and the villi are covered only by the syncytium. In certain places there are thickenings formed in the membrana chorii as well as in the villi. In the apices of the latter they are called *cell nodes*. Local thickenings in the syncytium are called *proliferation islands* (Fig. 191). Toward the end of pregnancy the syncytium also vanishes, and in its place there is a homogeneous, refractive, faintly staining substance containing numerous empty spaces, and known as *canalized fibrin* or *hyaline* (Fig. 192).

FIG. 192.



From a section through a human placenta at the fifth month of pregnancy. × 80.

This substance increases with the age of the placenta, but its origin and significance are by no means clear. Although there is no doubt that the villus ectoderm is of embryonic origin, there is still some question as to the derivation of the syncytium.

Between the villi we find so-called *intervillous spaces* which contain blood. The villi are thus surrounded by blood on all sides. The views held as to the origin and significance of these intervillous spaces are still much at variance. This problem is

associated closely with that concerning the villus ectoderm and syncytium, for the origin of the intervillous spaces is associated naturally with that of the syncytium. According to one theory, which seems to have the greatest number of supporters (Virchow, Ercolani, Leopold, Waldeyer, Keibel, and others), the intervillous spaces represent the widened capillaries from the uterine mucosa. It must be remembered that at an early stage the chorion and the decidua serotina lie with their surfaces closely applied to one another, and the epithelial layer of the decidua is cemented to a similar layer of the chorion. In this way villi grow into the decidual tissue, in which at the same time the capillaries become dilated to a system of spaces. These surround the villi, so that they become bathed in blood. Also flat endothelial cells lining the intervillous spaces have been observed by Turner, Leopold, Waldeyer, and Keibel, which represent the lining cells of the capillaries. Injections made by Waldeyer support this view. Many authors who share this theory claim that the syncytium and the ectoderm of the villus have different origins. The latter they describe as fœtal and the former as a part of the uterine epithelium.

According to other authorities (v. Kölliker, Langhans, Hofmeyer, Minot, and others), the intervillous spaces represent the original spaces between the placenta fœtalis and placenta uterina. The two parts of the placenta are joined together only by the villi. According to this theory, the intervillous spaces are interplacental cavities which originally contained no blood and became filled only when the maternal vessels opened into them. Almost all the adherents to this theory claim that both layers of cells covering the villi are of fœtal origin, and according to Minot's theory the syncytium is a differentiated product of the ectoderm layer beneath.

The maternal part, or placenta uterina, represents the decidua basalis, which has certain characteristics that distinguish it from other deciduæ. From the fifth month on, there develop in it large cells (giant cells) containing many nuclei. These cells are present in large numbers in the ripe placenta. From the side toward the placenta fœtalis more or less thick connective-

tissue bands arise, the so-called *septa placentæ*. These pass between the chorionic villi and separate them into groups or cotyledons. Only at the peripheral part of the placenta do the septa come into contact with the membrana chorii and fuse with it to form the so-called *subchorionic limiting ring*.

The *circulation* of blood in the maternal placenta takes place in the following way: numerous *arterial branches* enter through the muscular coats of the uterus to the outer layer of the placenta uterina. During their tortuous course these vessels lose their muscle cells and elastic elements, so that the thin walls that remain consist only of an endothelial and thin connective-tissue layer, and come to lie directly on the decidual cells. After branching, the arteries enter the septa placentæ, where they empty into the intervillous spaces through openings in the septa. The *veins* also open into these spaces, so that instead of a capillary system between the arteries and veins we find wide lacunæ, which, according to most authors, arise from the superficial blood capillaries of the uterine mucosa. The veins, whose walls, like those of the arteries, have been reduced in thickness, open into the intervillous spaces by comparatively wide orifices, which are more abundant near the middle of the cotyledons. The arteries, on the contrary, open in greatest numbers at the edges of the cotyledons, so that the blood in the intervillous spaces flows from the periphery to the centre of the cotyledons.

The intervillous spaces thus contain maternal blood, while in the chorionic villi the capillary vessels under the epithelial covering are all of fœtal origin. These two vascular systems never communicate directly with one another, and a mixture of fœtal and maternal blood never occurs. The diffusion of gases takes place through the walls of the capillaries and through two layers covering the villi.

D. Vagina and External Female Genitals.

The wall of the vagina is about 3 mm. thick, and consists of four layers: the mucosa, submucosa, muscularis, and fibrosa.

The *mucosa* is thrown into transverse folds, the so-called

rugæ. On their surface we find a stratified pavement epithelium, under which there is a thin connective-tissue tunica propria. At the external os of the uterus the flat epithelial layers, which cover the portio vaginalis uteri, pass over into the ciliated cylindrical epithelium of the cervix uteri. The tunica propria possesses papillæ which are rich in elastic fibres, and contain quite numerous masses of lymphoid tissue, often gathered into solitary follicles (noduli lymphatici vaginales). According to most authors, the vagina contains no glands, and the mucous secretion found there is derived from the glands of the cervix uteri.

The *submucosa* which joins the mucosa loosely with the muscularis consists of connective tissue characterized by its richness in elastic fibres.

The *muscularis* consists of an outer longitudinal and an inner circular layer of smooth muscle cells. The latter is usually not strongly developed.

The *fibrosa* which surrounds the muscle coat contains many elastic fibres and joins the vagina with the surrounding tissues.

The blood- and lymph-vessels form many plexuses parallel to the surface. The nerves enter the epithelial layer, where they end freely.

The *hymen* is a membranous reduplication of the vaginal mucosa. Its inner surface is covered with epithelium, which represents that of the vagina. The outer epithelial layer is like that of the skin. The whole vestibule possesses similar epithelium, with its outer cells non-nucleated. In the labia minora there are sebaceous glands.

The *labia majora* are covered with epithelium which is not at all different from that of the skin in other parts of the body. In the region of the clitoris and the urethral openings we find numerous mucous glands (*glandulæ vestibulares minores*). The larger glands of the vestibule (*glandulæ vestibulares majores s. glandulæ Bartholini*) correspond with Cowper's glands in the male, producing a similar mucous secretion.

The *clitoris* resembles somewhat in structure the penis.

There are in it considerable masses of erectile tissue and firm elastic strands like those of the penis. The glans clitoridis is supplied richly with nerves, and besides the Meissner's and Pacinian tactile bodies there are also special *genital corpuscles* (see Nerve-endings).

VI. LOCOMOTOR SYSTEM.

Here must be considered the skeleton, and the muscles, and their mode of development.

1. THE SKELETAL SYSTEM.

The bones form the essential part of the skeletal system, and in connection with these the cartilages play an important rôle. The structure of adult bone and cartilage as tissues has been described, but here they must be spoken of as organs.

A. Bones.

Bones considered as organs consist of bony tissue, periosteum, and bone-marrow, with blood-vessels and nerves supplying the different parts. Each bone (here the teeth are not considered) is surrounded by a connective-tissue sheath, the *periosteum*, with the exception of such places as are covered by cartilage. In this firm layer of connective tissue there are two layers: an outer fibrous layer, in which there are few cells, but numerous nerve plexuses and blood-vessels; and an inner delicate layer, poor in blood-vessels, but especially rich in elastic fibres and connective-tissue cells.

At the boundary between the periosteum and the bony tissue we find a layer of cubical cells (*osteoblasts*), which play an important part in the regeneration and development of the bone. A more or less intimate connection is established between bone and periosteum, partly by means of blood-vessels, and partly by bundles of connective-tissue fibres (Sharpey's fibres) which run from the periosteum almost at right angles to its surface and enter the bone.

(*a*) *Bone-marrow.*

In all bones of higher animals we find a *bone-marrow*. In the long bones this fills the axial cavity and enters the larger Haversian canals. In the flat bones, on the contrary, it fills up the meshes of the spongy substance. Two kinds of bone-marrow can be distinguished: *red* and *yellow marrow*. The first is found in all bones of embryos and young individuals. In the course of time it changes in some bones (*e. g.*, the diaphyses of the long and short bones of the extremities) into yellow marrow. Only in the epiphyses of these bones, in the bodies of vertebræ, and in the flat bones, is there found red marrow in the adult.

The red marrow is a lymphoid organ which is the main place of formation of the red blood-cells. The different elements contained in the red marrow are the following (Fig. 197):

1. *Myelocytes.*—These are somewhat similar to some kinds of leucocytes. In normal blood they are not found, while in leukæmia they are very abundant. Their nuclei are very large, sometimes lobed, and surrounded by a more or less finely granular protoplasm. The nuclei stain faintly, and the protoplasm is sometimes quite abundant.

2. *Nucleated Red Blood-corpuscles.*—The protoplasm is colored yellow on account of the hæmoglobin present. The nucleus usually is placed excentrically and stains very deeply. These cells are known also as erythroblasts or normoblasts, since they are the forerunners of the erythrocytes. They vary considerably in size, very large ones being known as megaloblasts, and small ones as microblasts. These unusual forms occur, however, more often in certain diseases.

3. *Non-nucleated Red Blood-corpuscles.*—These are derived from the nucleated red corpuscles.

4. *Giant Cells.*—These are probably modified leucocytes. They contain one or more nuclei, whose form may be round, lobed, or annular. The old theory that the multinucleated giant cells arise by a fusion of many cells is abandoned. They

are derived, on the contrary, from cells with a single nucleus which has divided to form many nuclei without a corresponding division of the protoplasm. This group of cells is made up of the so-called *osteoclasts*, which play an important part in the development of bone, and are spoken of in the discussion of this subject.

5. *Eosinophiles* are found often in bone-marrow; and also,

6. *Mast-cells* (γ-granulations), which are found exceptionally in the blood.

Some of these marrow cells contain pigment granules, which are the remains of disintegrated red blood-corpuscles. In the red marrow fat cells are not abundant, and the blood-vessels and nerves are found only in small number.

The *yellow* or *fatty marrow*, which owes its color to the large proportion of fat present in it, arises from the red marrow in the diaphyses of the long bones by a diminution of the marrow elements and an increase in fat. In old or emaciated individuals the yellow marrow becomes reddish and resembles mucus. Such a marrow is poor in fat, and is known as *gelatinous bone-marrow*. The connective tissue, which occurs only in small quantities in bone-marrow, is collected at the periphery of the marrow cavity, where it forms a firm fibrous membrane, lining the whole cavity. This represents a sort of inner periosteum, and is called the *endosteum*.

The bone, periosteum, and bone-marrow are supplied more or less richly with blood-vessels. These enter the periosteum, and from here they pass, by means of the Volkmann's and Haversian canals through the bone to form a network of vessels in the bone-marrow. All these vessels anastomose with one another. The so-called *nutrient arteries*, which supply the medulla with blood, break up into numerous branches, which form a rich capillary network in the medulla. Narrow capillaries broaden out, so that in joining together they pass into small veins with very delicate walls.

The veins of the bone-marrow as well as the bone possess no valves. The older idea, that the capillaries and small veins possessed no wall at all, or that they were in many places

broken through, so that the venous blood flowed freely in spaces of the marrow, has not been supported by recent investigations. The vein walls are exceedingly thin, but are always present.

The lymph-vessels form fine capillary networks in the periosteum. The nerves are partly medullated and partly non-medullated. They enter from the periosteum into the Volkmann's and Haversian canals and reach the bone-marrow. Some of these fibres end in Pacinian corpuscles in the periosteum.

(*b*) *Joining together of Bones.*

The bones are joined together either immovably (synarthrosis) or in such a way that they can move freely on one another by joints (diarthrosis).

The immovable combination is effected either by ligaments (syndesmosis) or by cartilage (synchondrosis). The ligaments may consist only of fibrous connective tissue and appear very like tendons, or they may contain numerous elastic fibres (ligamentum nuchæ, ligamentum flava, etc.). The synchondrosis is formed usually by fibrous cartilage, which at the border of the bone becomes hyaline. Special note must be made of the intervertebral ligaments. These contain in their interior a gelatinous mass (nucleus pulposus, gelatinous nucleus), which is the softened remains of the chorda dorsalis. Their periphery, however, consists of fibrous cartilage.

In *joints* we must consider the articular ends of the bones, the labra glenoidalia, the menisci interarticulares, and the joint capsules. The *articular ends* of the bone consist of hyaline cartilage, which is calcified on the side adjacent to the bone. Often they are made up of fibrous cartilage (*e. g.*, in the sterno-clavicular and maxillary joints). The *labra glenoidalia* and *menisci interarticulares* are fibrous cartilages. In the *joint capsules* we distinguish an outer part (*stratum fibrosum*, *capsula fibrosa*) and an inner part (*stratum synoviale*, *capsula synovialis*). The latter consists of loose connective tissue, which contains fat cells, vessels, and nerves, and is clothed on its inner surface

by a layer of flat epithelium. This is to be considered as a serous membrane. Often there extend from the synovial membrane into the joint cavity the so-called *synovial villi.* These are found abundantly on the borders of the joint-surfaces, and consist of a connective-tissue axis often containing blood capillaries and an epithelial covering. The *synovial fluid* (synovia) contains a few fat droplets and fragments of epithelium broken off from the joint-surfaces.

(*c*) *Development of Bones.*

Bony tissue develops later than any other tissue, and arises from some preformed tissue, such as hyaline cartilage or connective tissue. In young embryos the future skeleton exists as cartilage or connective tissue.

(*1*) *Development of Bone from Cartilage.*

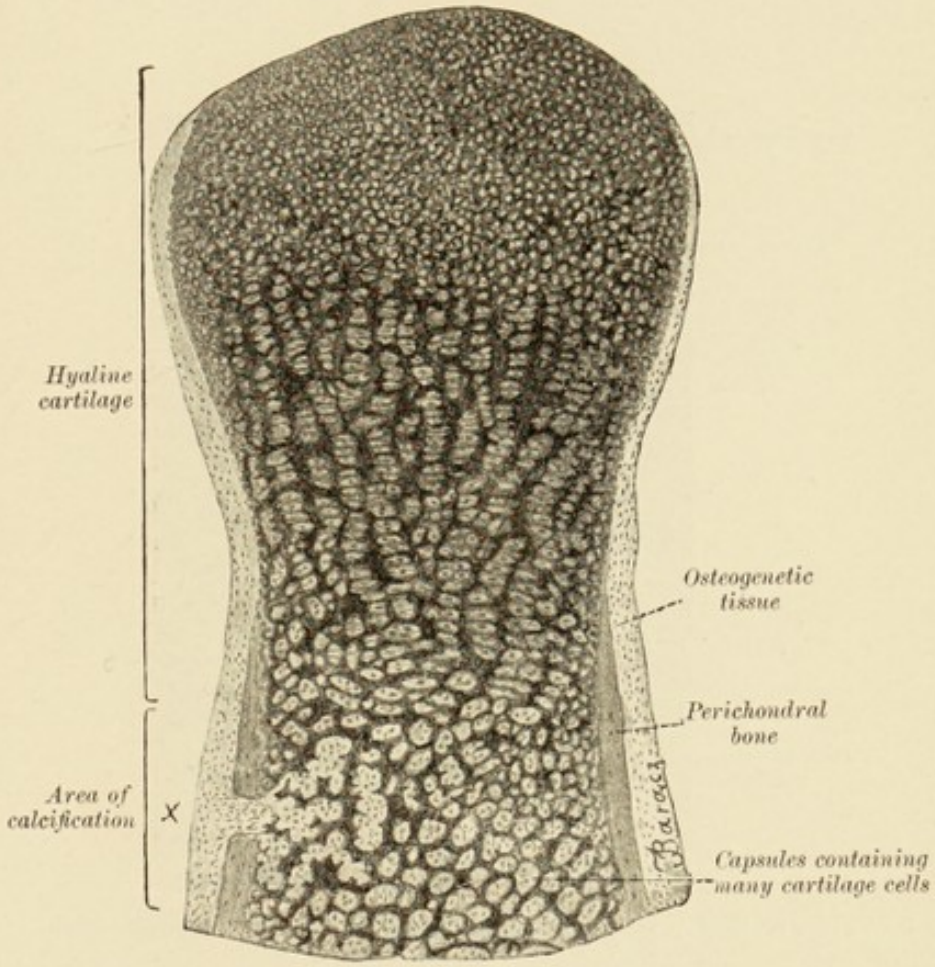
In bones which are developed from cartilage the bony tissue is laid down in two different places, either in the interior of the cartilaginous forerunner of the skeleton (*endochondral ossification*), or on the surface of the cartilage (*perichondral ossification*, wrongly called periosteal ossification).

The endochondral bone formation begins with the increase in size and number of cartilage cells through karyokinesis, so that many cells come to lie in each cartilage lacuna (Figs. 193 and 194). Certain changes then begin in the homogeneous ground substance of the cartilage. Calcium salts are laid down, so that the ground substance becomes opaque. The cartilage lacunæ become large and the cells shrink. Places where such changes have taken place may be quite numerous in a bone, and are known as *areas of ossification* or *calcification.* In the long bones such centres usually appear first in the diaphysis.

While this process is going on inside the cartilage certain changes take place on its outer surface. In the deeper cellular layers of the perichondrium an ossification (perichondral ossification) begins. These layers of perichondral cells, richly supplied with blood-vessels, are known as *osteogenous tissue.*

The ground substance becomes calcified and the cells become changed into bone cells. In this way there is formed at the border of the cartilage and perichondrium a bony layer, and the perichondrium becomes the periosteum. From the latter, buds grow in toward the areas of ossification, known as *periosteal buds* (Fig. 194). These penetrate the calcified ground

FIG. 193.

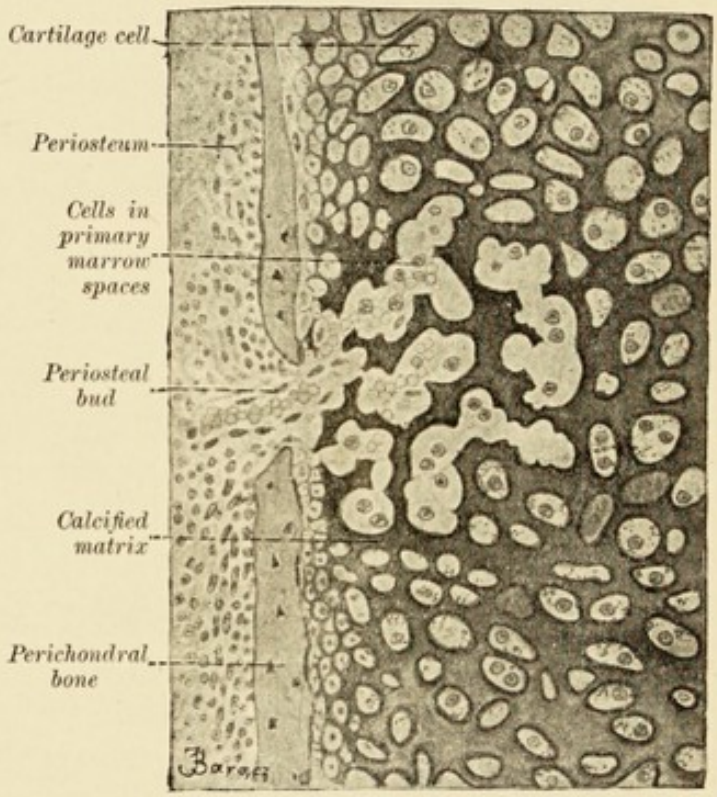


From a longitudinal section of a finger of a three and a half months' human embryo. Two-thirds of the second phalanx is represented. At × a periosteal bud is to be seen. × 85.

substance of the cartilage, whose cell capsules are broken down, allowing the cells to become free. In this way there gradually arises a cavity in the areas of ossification which forms a *primordial* or *primary medullary cavity*, and the first trace of the permanent marrow cavity. In this space are found blood-vessels and cellular elements, which are derived partly from cells brought in by the periosteal buds, and partly

from freed cartilage cells. Some of the cells form the elements of the future bone-marrow; a part, on the contrary, play the important rôle of bone-formers or *osteoblasts*. These are large, often-branched cells, which as a rule form a layer on the inner surface of the periosteum, and are carried into the marrow cavity along with the periosteal buds. Thus we find in the areas of ossification, first, proliferation of the cartilage cells and a calcification of the ground substance, and then a de-

Fig. 194.



The place marked × in the preceding figure with stronger magnification. × 185.

struction of this cartilage by the ingrowth of periosteal buds. In long bones the marrow cavity increases in size by a general breaking down of the calcified bone.

The cartilage lying at both ends of the diaphysis shows characteristic relations (Figs. 195 and 196). We may notice in this several zones which are well marked off from one another. The part most distant from the marrow cavity shows no changes, containing spindle-shaped cavities with small cells. The cells lying nearer the medullary cavity are larger and

PLATE XXIX.

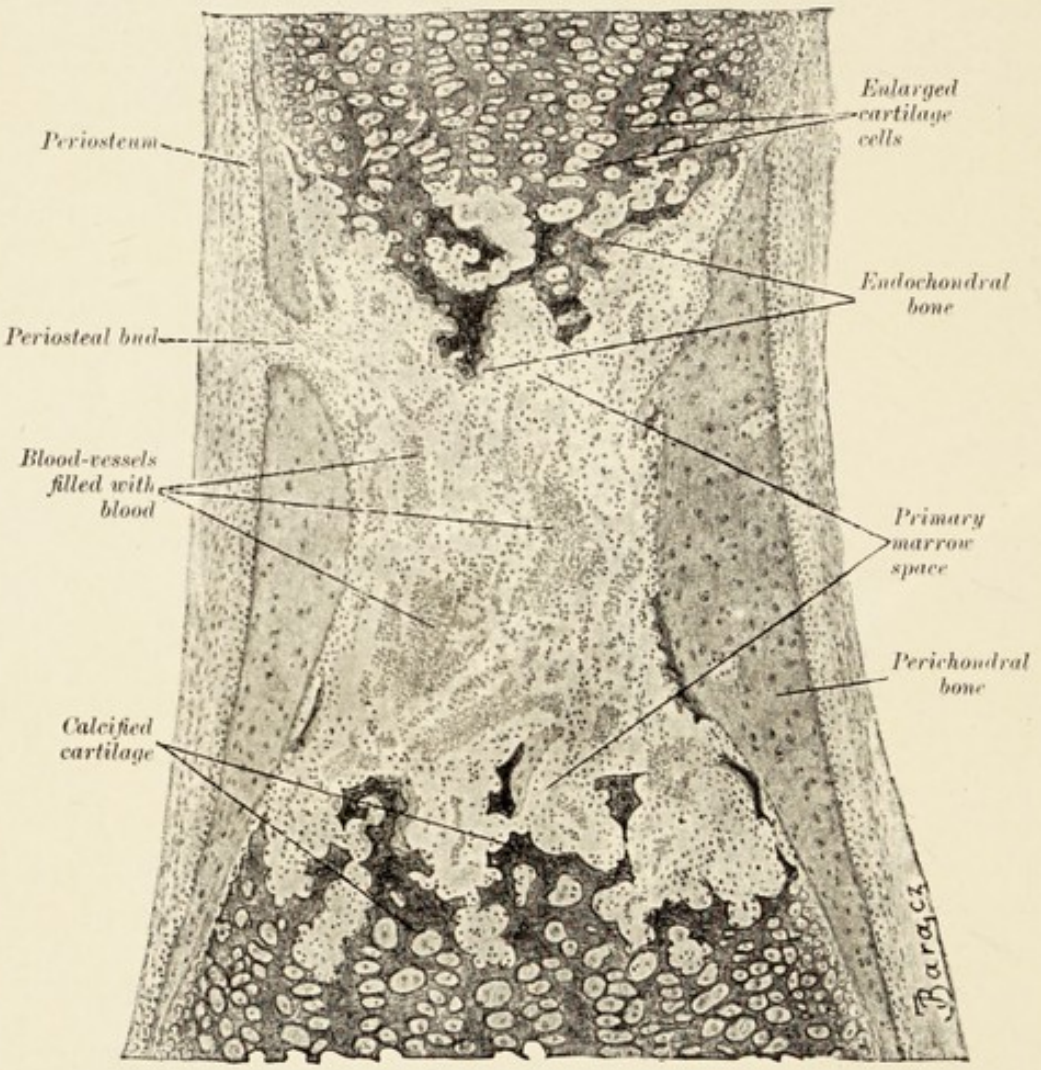


FIG. 195.—From a longitudinal section of a finger of a four months human embryo. Only the diaphysis of the second phalanx is represented. × 85.





J. Barącz ad nat. del.

Szymonowicz, Histology

Lith. Anst. v. Werner & Winter, Frankfurt a/M.

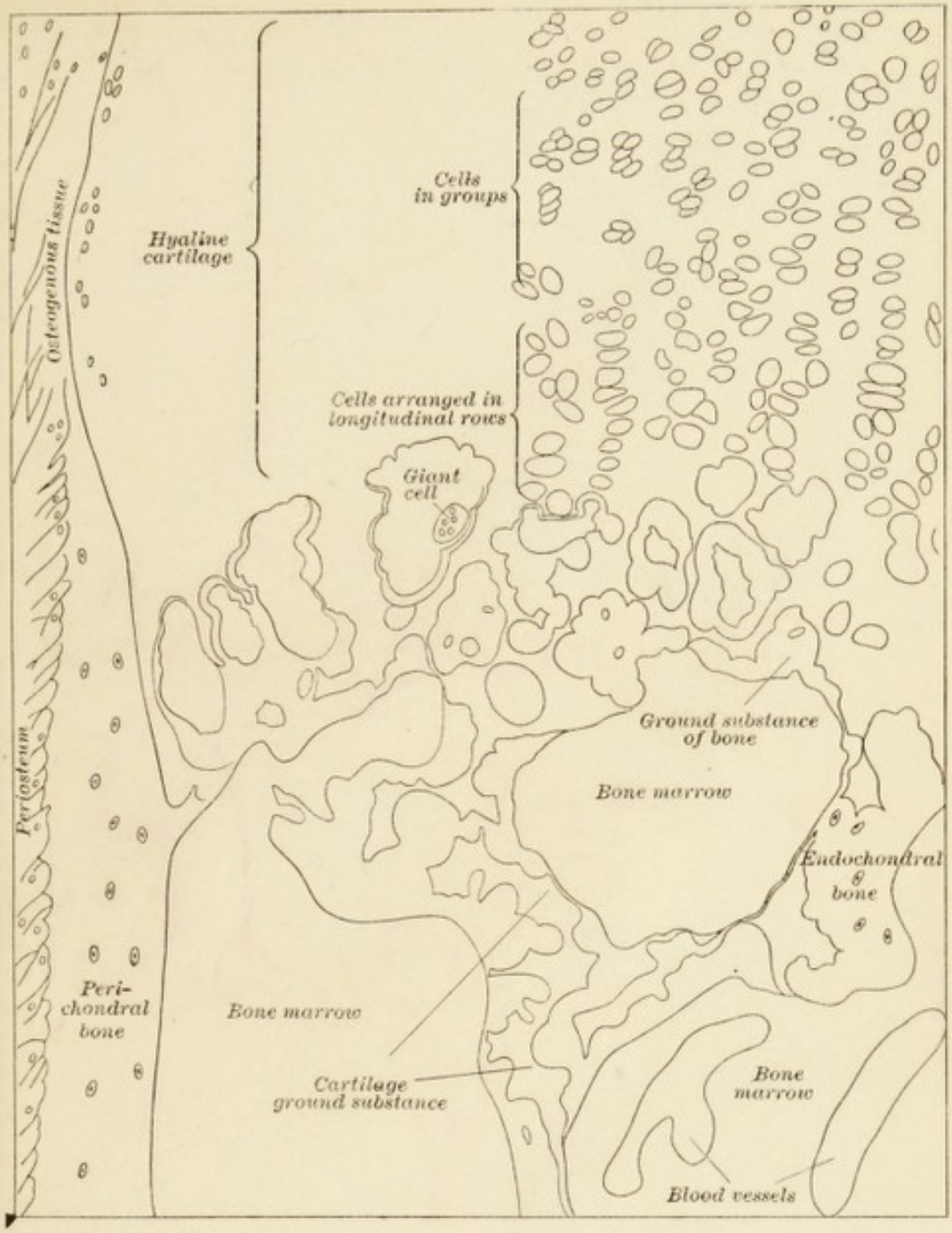


FIG. 196.—From a longitudinal section through the second phalanx of the finger of a seven months human embryo. Stained in hæmatoxylin and eosin. × 130.

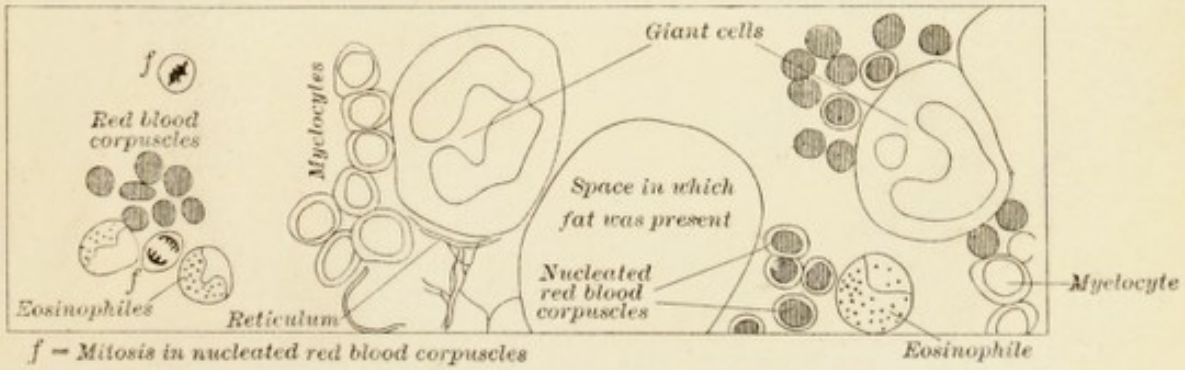


FIG. 197.—From a section through the red bone-marrow of a rabbit. Biondi's stain. × 800.

FIG. 196.—From a longitudinal section through the second phalanx of the finger of a seven months human embryo. Stained in hæmatoxylin and eosin. × 130.

f = Mitosis in nucleated red blood corpuscles

FIG. 197.—From a section through the red bone-marrow of a rabbit. Biondi's stain. × 800.

arranged in rows, or *cell columns*, between which there is a fibrous ground substance. The individual cells of the columns are separated by thin septa. Still nearer the medullary cavity the cell lacunæ are large and flattened against one another. The septa of ground substance become thinner, and finally vanish, and the lacunæ in many places coalesce to form larger cavities.

The ground substance is impregnated with calcium salts and becomes opaque. The spaces in the cartilage open into the marrow cavity, which in consequence seems to have many irregular cavities leading from it. Blood-vessels grow in from the marrow cavity together with marrow and osteoblasts, which on the inner surface of the increased medullary cavity begin the formation of a bony layer. The osteoblasts gradually become surrounded by ground substance which is converted into bone, the osteoblasts themselves becoming bone cells.

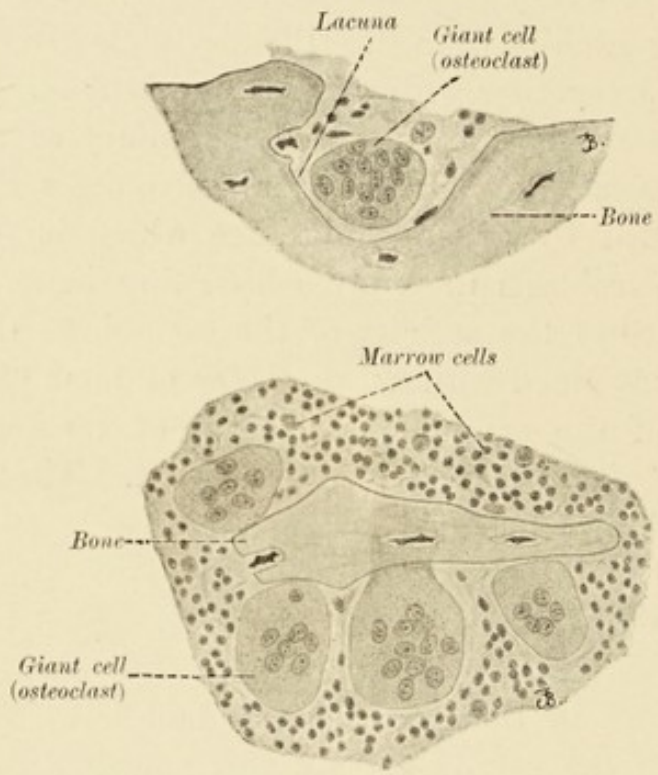
In consequence of the activity of the osteoblasts the whole medullary cavity is lined with a thin layer of bone (Figs. 195 and 196), and of the original solid mass of cartilage there remain only irregular pieces covered with bone. The cartilage is thus converted into a spongy bone. As already mentioned, the perichondral ossification goes on at the same time at the surface of the cartilage (Figs. 195 and 196). This is due to the activity of osteoblasts lying between the cartilage and perichondrium, and in this way bone is laid down in layers on the outside of the cartilage. By this so-called *apposition* the bone increases in thickness.

The vessels at the surface become enclosed in the developing bone in cavities which form afterward the Haversian canals. The osteoblasts contained in these form concentrically lying lamellæ in the ground substance of the bone. The epiphyses of the long bones become ossified later than the diaphyses; but the process in both cases takes place by an endochondral and a perichondral ossification. Areas of calcification are formed, into which blood-vessels grow from the surface of the cartilage or from the diaphysis. A medullary cavity is formed and the ossified borders of the diaphysis and epiphysis approach one

another. These are at first separated from one another by a thin layer of cartilage, the *epiphyseal line*. By means of this cartilage the bone is enabled to increase in length, and not until all growth in length has ceased does the epiphyseal line disappear.

In addition to this process of bone formation there is also a destruction of bone. In this process of absorption the so-called *osteoclasts* play an active part. These are giant cells (Fig. 198)

FIG. 198.



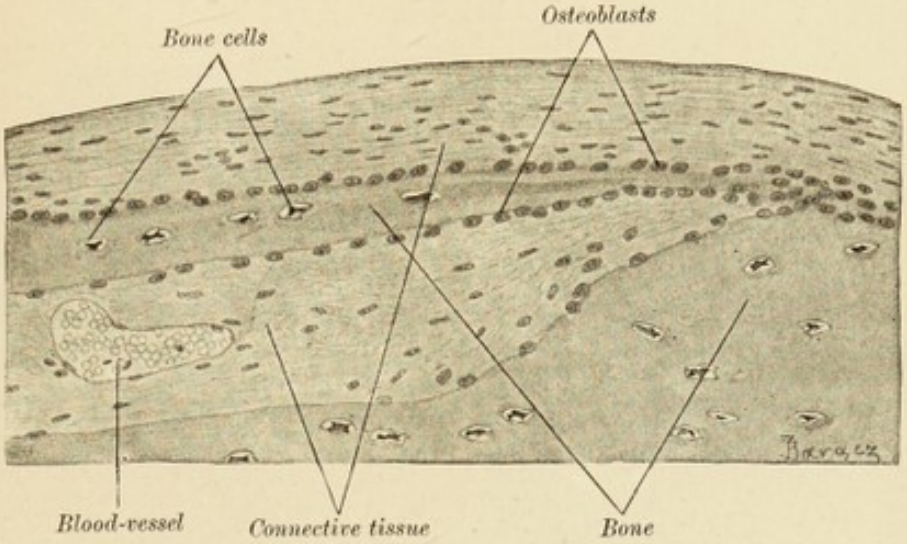
From a longitudinal section of the femur of a rabbit's embryo. × 335.

containing many nuclei and situated in small hollowed-out spaces in the bone known as *Howship's lacunæ*. It is believed generally that these osteoclasts in some way absorb or destroy the bone after it has been formed by the osteoblasts, and that in this way the medullary cavity is increased in size. They are to be observed not only in growing bones, but also in those that are fully developed. All the bones are formed from cartilage, with the exception of the bones of the roof of the skull, the lateral part of the skull, most of the face bones, and a small part of the base of the skull.

(2) Development of Connective-tissue Bones.

In those instances in which bones are developed in connective tissue certain bundles of connective tissue become calcified and form the ground substance of the bone. The connective-tissue cells arrange themselves in a layer on the surface of these bundles, and, becoming more rich in protoplasm, are converted into osteoblasts (Fig. 199). There is thus formed a bony plate by the addition of bone on the surface and at the borders of the calcified mass. This increases in thickness by

FIG. 199.



From a transverse section of the parietal bone of a human embryo. × 220.

the deposition of new bone on the two surfaces. The older bone between these two layers becomes a spongy bone substance (diploë). In this kind of bone production the osteoclasts are particularly active, for the bones that are so formed are constantly undergoing changes in form and relations. These are mainly the lateral bones of the skull, the facial bones, and the upper parts of the occipital bone.

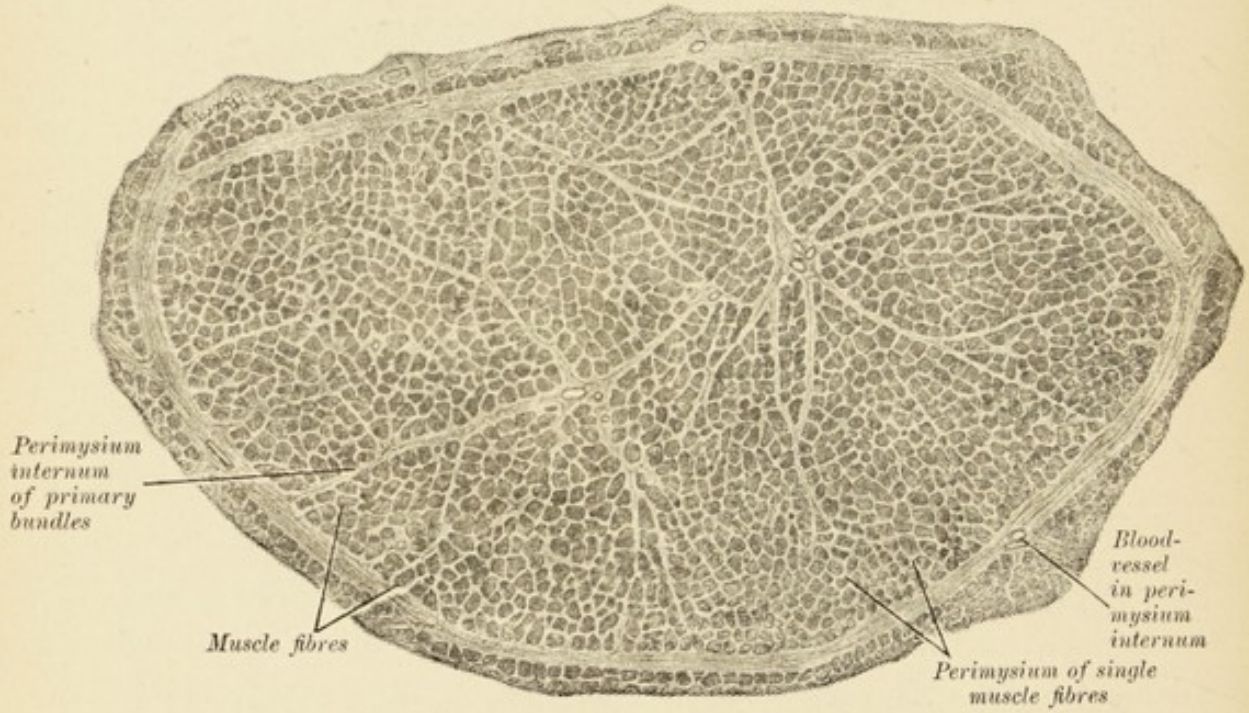
B. Cartilages.

The cartilages are covered with a perichondrium, with the exception of those covering the joint-surfaces and those joining together bones. In fully developed cartilages we find no blood-vessels. These, as well as the nerves, exist only in the perichondrium (see Cartilage tissue).

2. MUSCULAR SYSTEM.

Large aggregations of striated muscle fibres form organs which are called muscles. These taken collectively form the muscular system. The muscle fibres are grouped together in the muscles to form bundles (Fig. 200). Around each fibre there is always a certain amount of connective tissue containing blood capillaries, and bundles of these fibres are surrounded by thicker stands of connective tissue known as the *perimysium internum*. These *primary bundles* are grouped together by

FIG. 200.



From a transverse section of the human sterno-cleido-mastoid muscle. An entire secondary bundle, surrounded by the perimysium internum, is shown. × 45.

connective tissue to form *secondary bundles*, which in large muscles are enclosed still further to make up *tertiary bundles*. The whole muscle is surrounded by a thick connective-tissue capsule, the *perimysium externum*. This is in direct connection with all the strands of connective tissue that make up the perimysia interna. This can best be seen in a cross-section of a muscle stained to bring the connective tissue into prominence (*e. g.*, with acid fuchsin and picric acid). We see that the perimysium externum sends septa into the muscle between the

PLATE XXXI.

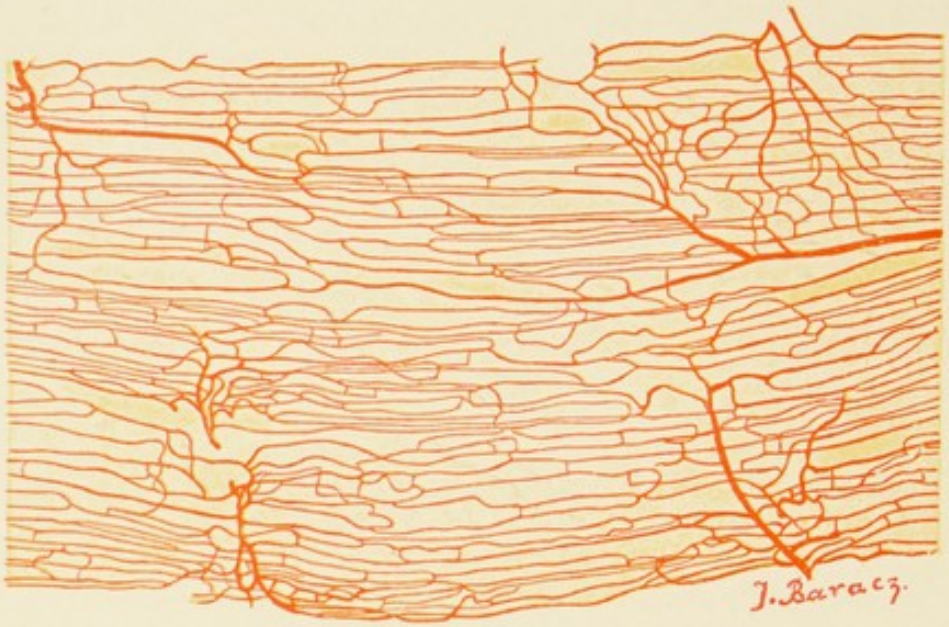


FIG. 201.—Piece of striated muscle from a rabbit; blood-vessels injected red. × 80.



FIG. 202.—From a transverse section of a striated muscle of a rabbit; blood-vessels injected red. × 100.

secondary bundles, to join finally with the perimysia interna to make up a continuous connective-tissue framework. The parts of this framework which enter the primary bundles to surround the individual muscle fibres usually contain very few elastic fibres and no fat cells; while the larger strands separating the primary and secondary bundles are rich in both these elements. Blood-vessels and nerves enter the muscle in the connective-tissue septa and surround the muscle fibres

The *blood supply* shows an exceptionally rich branching of capillaries around the muscle fibres. The blood-vessels enter the perimysium and run more or less parallel to the course of the muscle fibres (Fig. 201). In the perimysium between the primary bundles fine arterial branches proceed at right angles from the larger trunks between the muscle fibres. From these, there run again at right angles—*i. e.*, parallel to the course of the fibres—the capillaries, which form a fine network surrounding the individual fibres. They run in large part parallel with the fibres, and send off quite frequently fine anastomosing branches, so that the meshes of the network are for the most part rectangular or rhomboidal. Each fibre is surrounded on all sides by capillaries, as may be seen in a cross-section of an injected muscle (Fig. 202). The veins arising from the capillaries are characterized by the presence of valves, even in the finest branches. In the red muscles of the rabbit there are sinuses in many places between the arterial and venous ends of the network (Ranvier).

There is in all muscles a definite blood vascular unit, special attention to which was called by Spalteholz. Arteries can be seen entering the muscle bundles at regular intervals (Fig. 201), and sending out capillaries on all sides. The veins collecting the blood from these capillaries are placed quite regularly. The unit thus has the artery for its centre and the collecting veins at the periphery.

The nerves and their endings are spoken of in the section on Nerve-endings.

Development of Muscles.

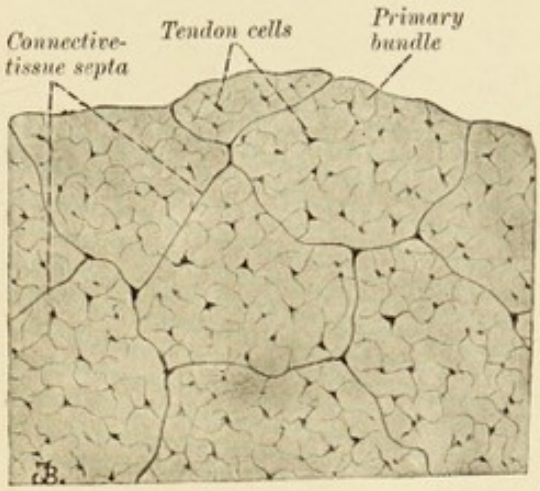
In the early study of the growth of muscles it was claimed by some investigators (Schwann, Valentine) that muscle fibres are built up by the fusion of many indifferent cells. Remak claimed that the muscle fibre is derived from a single cell, a view which since has gained general acceptance. The way in which such fibres are joined together in the embryo to form definite muscles is not satisfactorily understood. Certain facts, however, have been obtained as to the growth of embryonic muscles. The development of the human sartorius muscle has been worked over in recent years (MacCallum). At an early stage the cells making up the muscle are small and spindle-shaped, and are scattered in loose bundles. At first there are no fibril bundles, and the nucleus is placed centrally. Subsequently the fibril bundles appear around the periphery of the cell. The cells become more numerous and increase in size until the human embryo is between 130 mm. and 170 mm. in length from vertex to breech. At this stage the bundles of cells become more compact and the cells themselves are filled with fibril bundles as in the adult. The fibres now grow in length and thickness, but no longer increase in number. In embryos smaller than 170 mm. in length there is a progressive increase in the number of fibres found in a cross-section. After this, however, the number remains approximately constant. In other words, the fibres of the human sartorius do not increase in number after about the first half of embryonic life. After this period the increase in size of the muscle is due to growth of the individual fibres, and not to their multiplication.

Marpargo has observed that in the white rat the muscle cells continue to multiply for a short time after birth. According to Meek, hyperplasia of the muscle cells ceases at birth, and after this there are a reduction in the number of fibres and a hypertrophy of those remaining.

A vascular connective tissue separates the muscle bundles to form primary and secondary groups, which, according to Bardeen, are to be considered as units.

The muscles are connected with other parts of the body almost always by means of *tendons.* These consist, as has been stated, of connective-tissue fibrils, which are joined together by means of interfibrillar cement substance to form *primary bundles.* Many of these are combined by interfascicular cement substance to make up secondary tendon bundles (Fig. 203). The characteristic tendon cells lie between the primary bundles. The

FIG. 203.



Part of a cross-section of a human tendon (popliteal muscle). × 210.

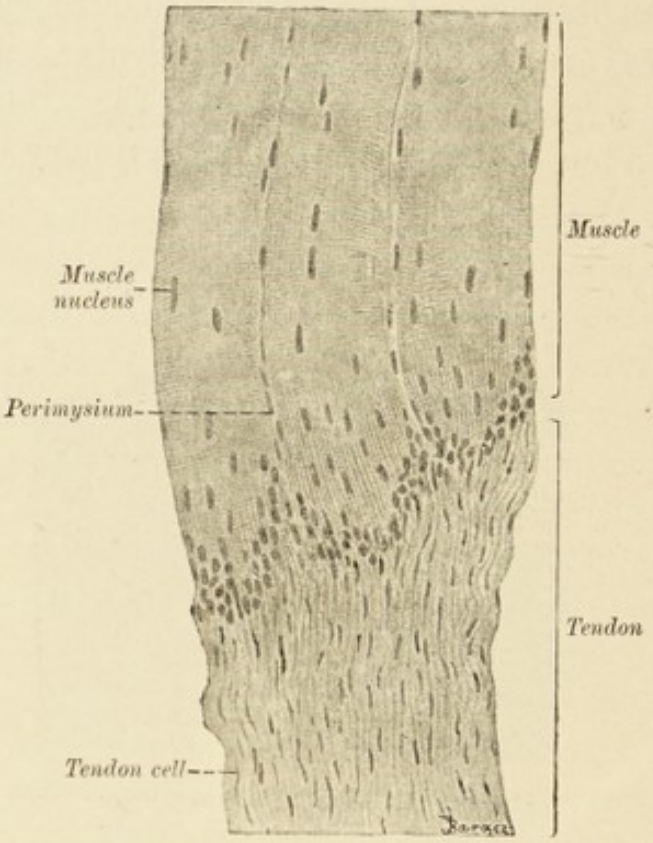
secondary bundles are surrounded by loose connective tissue containing elastic fibres and joined together to form tertiary bundles. The whole tendon is surrounded by a connective-tissue capsule, the so-called *peritenonium.* The tendon sheath consists of connective tissue lined on the inner surface with a layer of flat cells.

The intimate connection between muscle and tendon is brought about by the direct transition of the perimysium into the connective tissue of the tendon (Fig. 204). In cases in which the muscle is fastened to the periosteum or fasciæ, the perimysium alone effects the union by passing over directly into the periosteum or fascia.

The blood-vessels of tendons are not abundant. They run in the loose connective tissue between the tendon bundles. The lymph-vessels form a rich plexus on the surface of the tendon. The nerves end on the tendons partly by means of

arborizations, the so-called *Golgi's tendon spindles*, or by means of Vater-Pacinian corpuscles; some end in the vessels.

FIG. 204.



From a longitudinal section through the gastrocnemius muscle of a frog, showing the transition from muscle to tendon. × 200.

The *fasciæ* are connective-tissue membranes whose bundles of fibrils usually form interlacing layers. They contain as a rule a great many elastic fibres.

VII. NERVOUS SYSTEM.

1. CENTRAL NERVOUS SYSTEM.

A. Spinal Cord.

Even with the naked eye, the *gray* and *white matter* can be distinguished in a cross-section of the spinal cord. The former occupies a central position and is surrounded by white matter. The relative amount of gray matter varies in different regions of the cord. In the sacral region it is present in larger amount than is the white matter (Fig. 208). In all parts of the cord

PLATE XXXII.

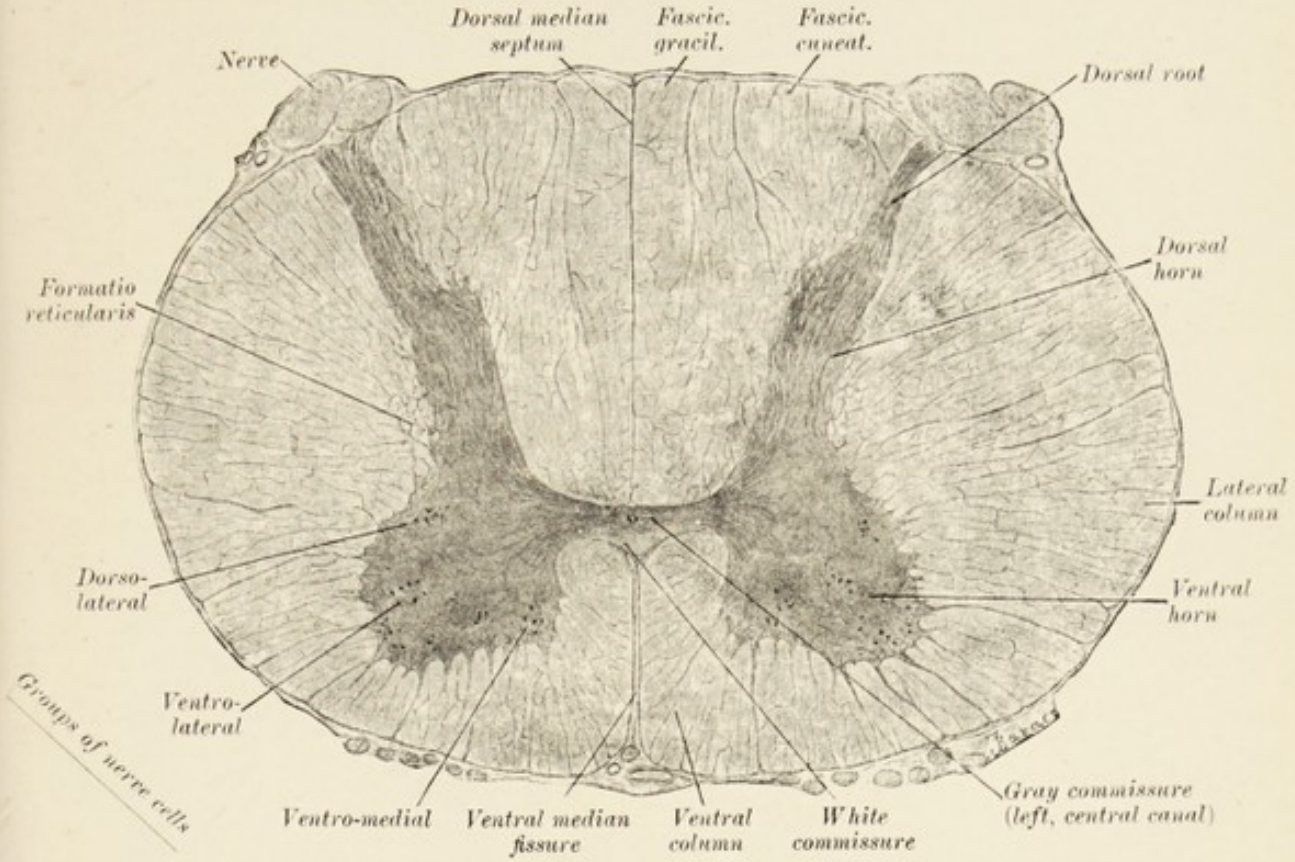


FIG. 205.—Transverse section of the cervical cord of man, at the level of the sixth spinal root. × 11.

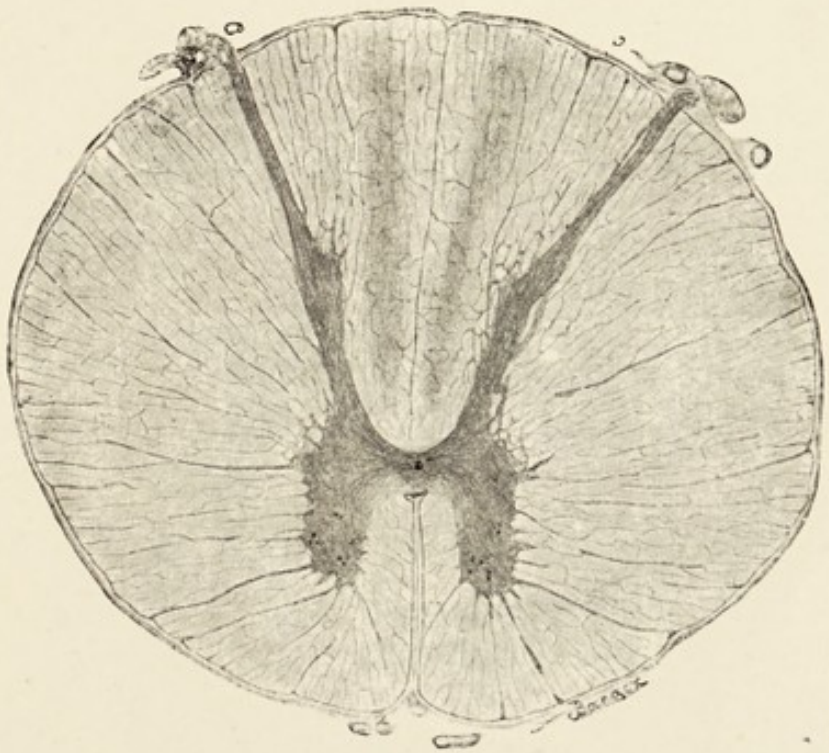


FIG. 206.—Transverse section of the dorsal cord of man, at the level of the eleventh spinal root. × 11.

PLATE XXXIII.

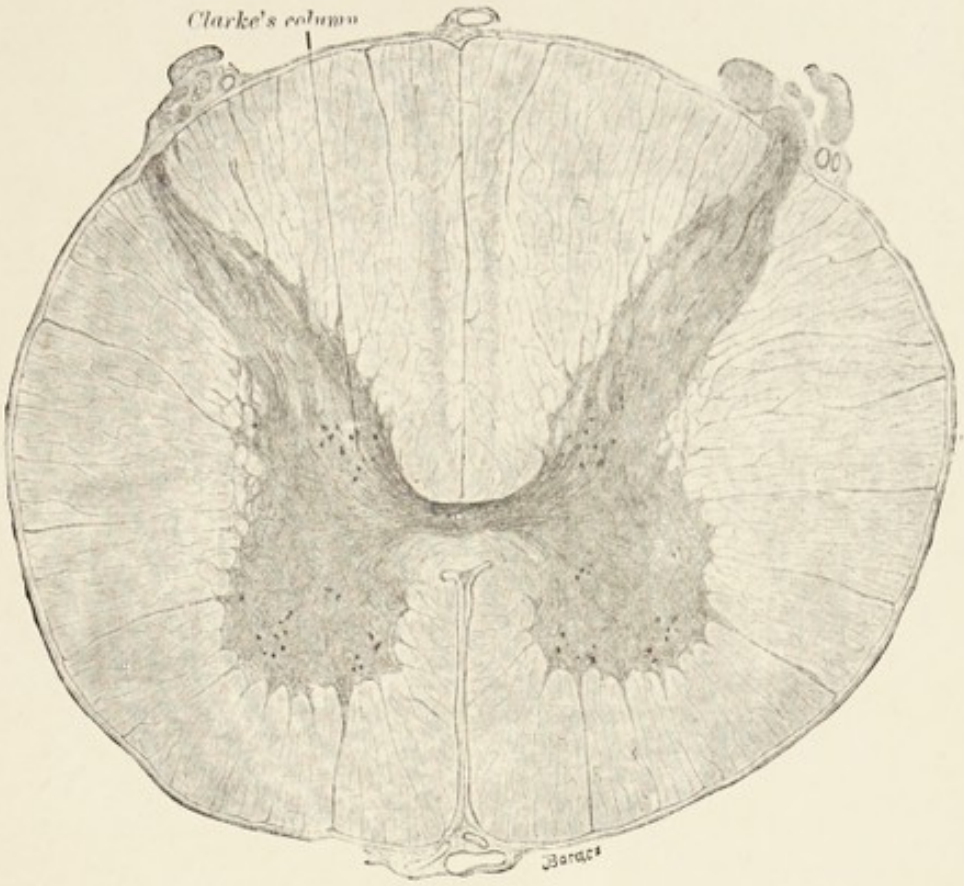


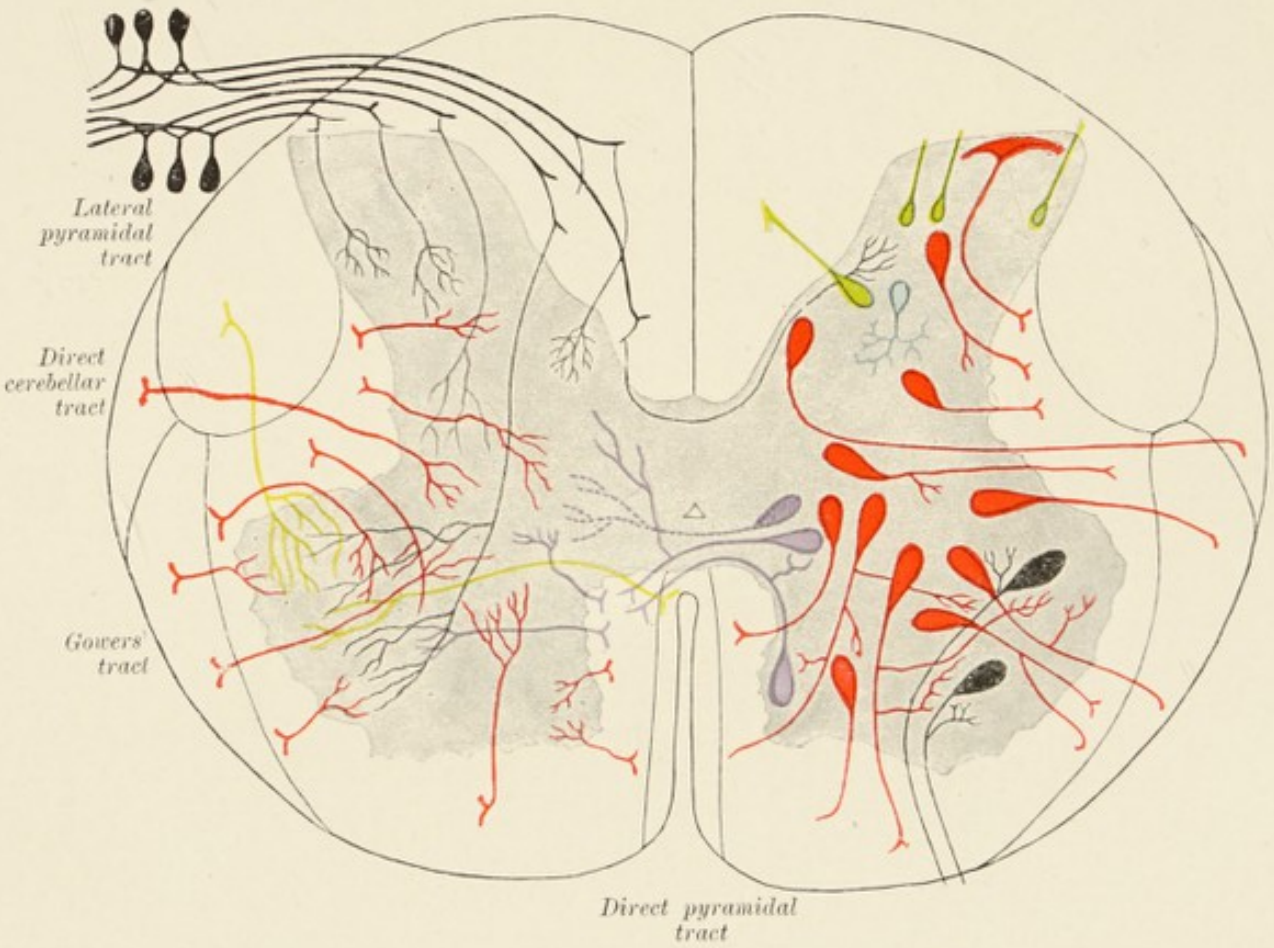
FIG. 207.—Transverse section of the lumbar cord of man in the region of the lumbar enlargement. × 11.



FIG. 208.—Transverse section of the sacral cord of man. × 11.

PLATE XXXIV.

Left: black, spinal ganglion cells, dorsal roots, their bifurcation and their collaterals, which end in different regions of the gray matter; in the dorsal horn, the middle zone of the gray matter; the ventral horn, the column of Clarke, and in the opposite dorsal horn; red, collaterals of the ventro-lateral columns; lilac, collaterals from the axones of commissural cells; yellow, endings of collaterals of the pyramidal tracts.



Right: black, motor cells; red, cells of ventrolateral columns, Clarke's column, the marginal zone of the substantia gelatinosa (Rolandi); lilac, commissural cells (short dotted cell, Golgi's commissural cell); blue, Golgi cell; green, dorsal column cells, the smaller of which are the cells of the substantia gelatinosa. (Rolandi.)

FIG. 209.—Diagram of spinal cord in transverse section. (After v. Lenhossék.) Left, collaterals; right, nerve cells.

the gray substance has in cross-section roughly the form of the letter H (Figs. 205–208), and, taken as a whole, consists of two long columns laid parallel to one another and joined together by the so-called *gray commissure*. Each of the columns is thicker on its ventral than on its dorsal side. There is therefore in cross-sections a wide *ventral horn* and a smaller *dorsal horn*. In the lower cervical and the upper thoracic regions of the cord there appears the *lateral horn* (*tractus intermediolateralis*). In the same regions processes of the gray substance extend into the white matter in such a way that a net-like structure is formed, containing in its meshes bundles of fibres from the white matter. This is known as the *formatio reticularis*, and appears at the junction of the ventral and dorsal horns (Fig. 205).

From the ventral surface of the ventral horn, bundles of nerve fibres run out through the white matter, forming the so-called *ventral root*. Similar nerve bundles are present on the dorsal side, making up the *dorsal root*.

With small magnification there can be distinguished in the thoracic region of the cord a well-defined group of cells known as the *column of Stilling-Clarke*, or the *nucleus dorsalis* (Fig. 207). It can be observed also in the upper part of the lumbar region. It occupies a position on the median side at the base of the dorsal horn opposite the formatio reticularis. Another conspicuous structure to be observed in the gray matter throughout the whole length of the cord is the *substantia gelatinosa* (Rolandi). This lies at the apex of the dorsal horn, and consists of small spindle-shaped cells with less neuroglia than other parts of the gray matter (Weigert). This is seen in preparations made by Weigert's method as a light band across the end of the dorsal horn (Fig. 212).

The *gray commissure* is a flat band of gray matter connecting the two lateral gray masses. In its centre is the *central canal*, which runs the whole length of the cord and is continuous with the cavities of the brain and medulla. The diameter of its lumen is usually about 1 mm. In embryos it is lined with ciliated epithelium and surrounded by the *substantia*

grisea centralis. In adults it is often partly obliterated on account of the growth of ependymal cells and neuroglia fibres. The gray commissure is divided by the central canal into a *dorsal* and a *ventral gray commissure.*

The white matter, as already mentioned, surrounds the gray matter, and is separated into right and left halves by the *fissura mediana ventralis* in front, and the *septum medianum dorsale* behind. The former is a longitudinal fissure which

FIG. 210.



The ventral half of the ventral horn from a calf's spinal cord. Section through the cervical enlargement. × 80.

extends the whole length of the cord, but never is quite deep enough to reach the gray matter. A thin strand of white matter intervenes, and is known as the *white commissure* (Figs. 205 and 212). Each of these halves of the white matter is divided by means of the ventral and dorsal nerve roots into *ventral*, *lateral*, and *dorsal columns* (Figs. 205 and 212). On the surface of the cord this division is marked by the sulci (*sulcus lateralis ventralis* and *dorsalis*).

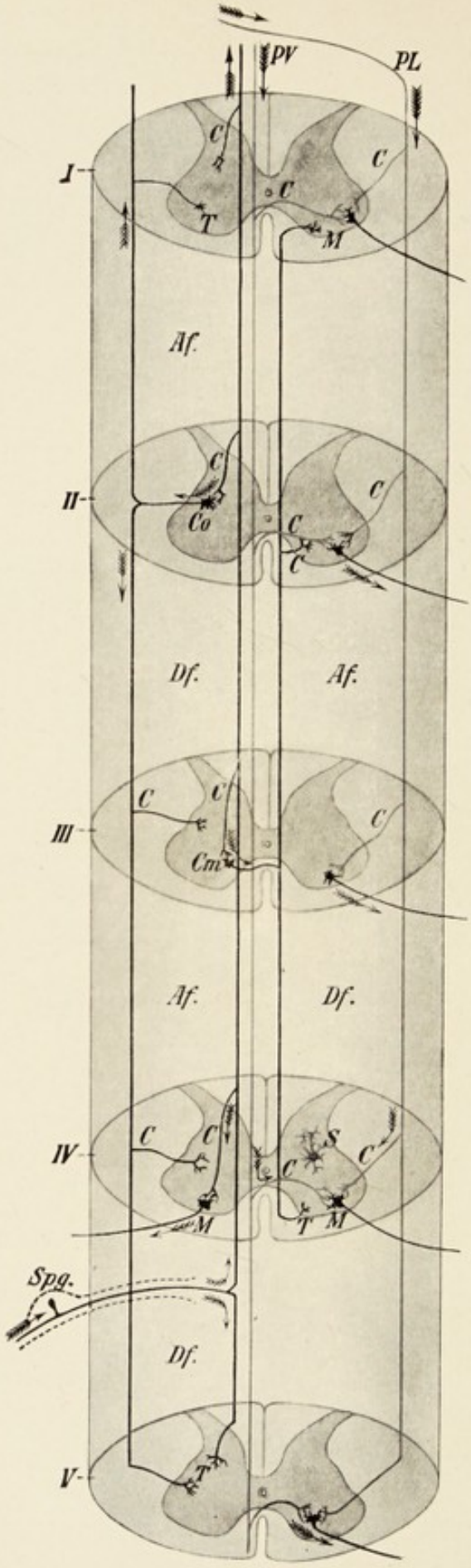


FIG. 211.—Diagram of the relations of neurones in the spinal cord.

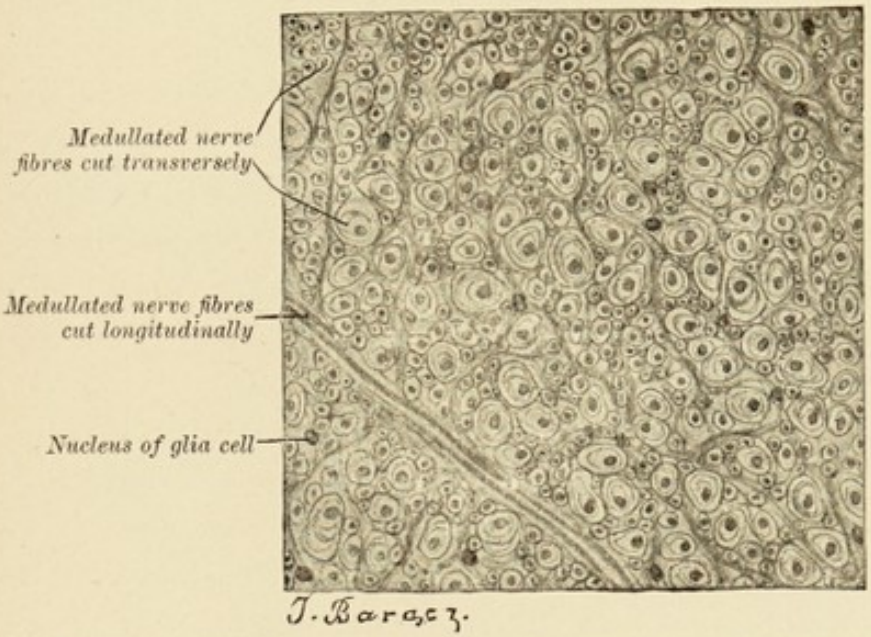
Spg, spinal ganglion cell; *Df*, descending fibres; *Af*, ascending fibres; *Co*, cells whose axones run in the lateral columns; *Cm*, commissural cells; *M*, motor cells; *S*, spider cells; *PV*, fibres of ventral pyramidal tract; *PL*, fibres of lateral pyramidal tract; *C*, collaterals; *T*, telodendria.

The dorsal column is marked off plainly in the cervical region into two parts, a median segment, the *funiculus gracilis* (*column of Goll*), and a lateral segment, the *funiculus cuneatus* (*column of Burdach*) (Fig. 205).

We may begin the study of the finer structure of the cord by a consideration of the *nerve cells*, which, as has been noted, are found almost exclusively in the gray matter. Of these, there are three main varieties:

1. *Motor cells* (Fig. 210) are situated in the ventral and lateral horns, and are arranged usually in groups. Especially in the cervical and lumbar regions are such groups to be observed,

FIG. 213.



Transverse section through the white matter of the spinal cord of an ox. × 260.

the more important being the dorso-lateral, ventro-lateral, and ventro-medial groups. Motor cells are unusually large cells, from each of which an axone extends into the ventral root of the same side to form the axis cylinder of a medullated nerve fibre. The dendrites are numerous, and extend back toward the dorsal horn.

2. *Cells of the columns* (Fig. 209) are cells which send out axones into the white substance to form the fibres of the white columns. They may be divided into (*a*) cells whose axones pass into the white matter of the same side (tautomeric), and

(*b*) cells whose axones pass over to the opposite side through the white commissure (*commissural* or *heteromeric cells*) (Figs. 209 and 212). These cells are present throughout the whole gray substance, and are smaller than the motor cells. Their axones usually give off numerous collaterals before entering the white matter, while those of the motor cells possess few collaterals. The axones of the cells of the columns usually pass into the ventral and lateral columns. Here they undergo fork-like divisions, one branch ascending and the other descending in the cord. Other axones do not divide, but pass either up or down in the cord. Still other cells divide in the gray matter, one branch remaining on the same side, and the other passing over in the white commissure to the opposite side (hecateromeric) (Fig. 214).

Some of the fibres of the columns run to the brain and cerebellum to form the *long paths*, while others have only a short course and make up the *short paths* in the white matter.

3. *Spider cells* (Binnenzellen) are cells whose much-branched axones do not leave the gray substance, but end by arborizations in its interior. They occur mainly in the dorsal horns.

The gray substance possesses nerve fibres as well as cells. These are in part processes of the cells, and in part originate elsewhere and end here, as, for example, collaterals from the axones of spinal ganglion cells. Neuroglia, to be spoken of later, is also abundant in the gray matter.

The white matter consists of medullated nerve fibres and neuroglia. The fibres may originate from three different sources, namely: from the column cells lying in the cord, from the cells of the cerebral cortex (centrifugal cells), and from spinal ganglion cells (centripetal).

By reason of histological, embryological, and experimental investigations we have a fairly exact knowledge of the course of some of these nerve bundles. In a cross-section of the cord we can map out certain fields in the white matter which contain fibres having a definite course. In the *ventral column* (funiculus ventralis) along the ventro-median fissure there is situated

FIG. 212.—Cross-section of spinal cord of calf in cervical region. Stained by Weigert's method. Only one-half of the grey matter, with the surrounding white matter, is given. × 25.

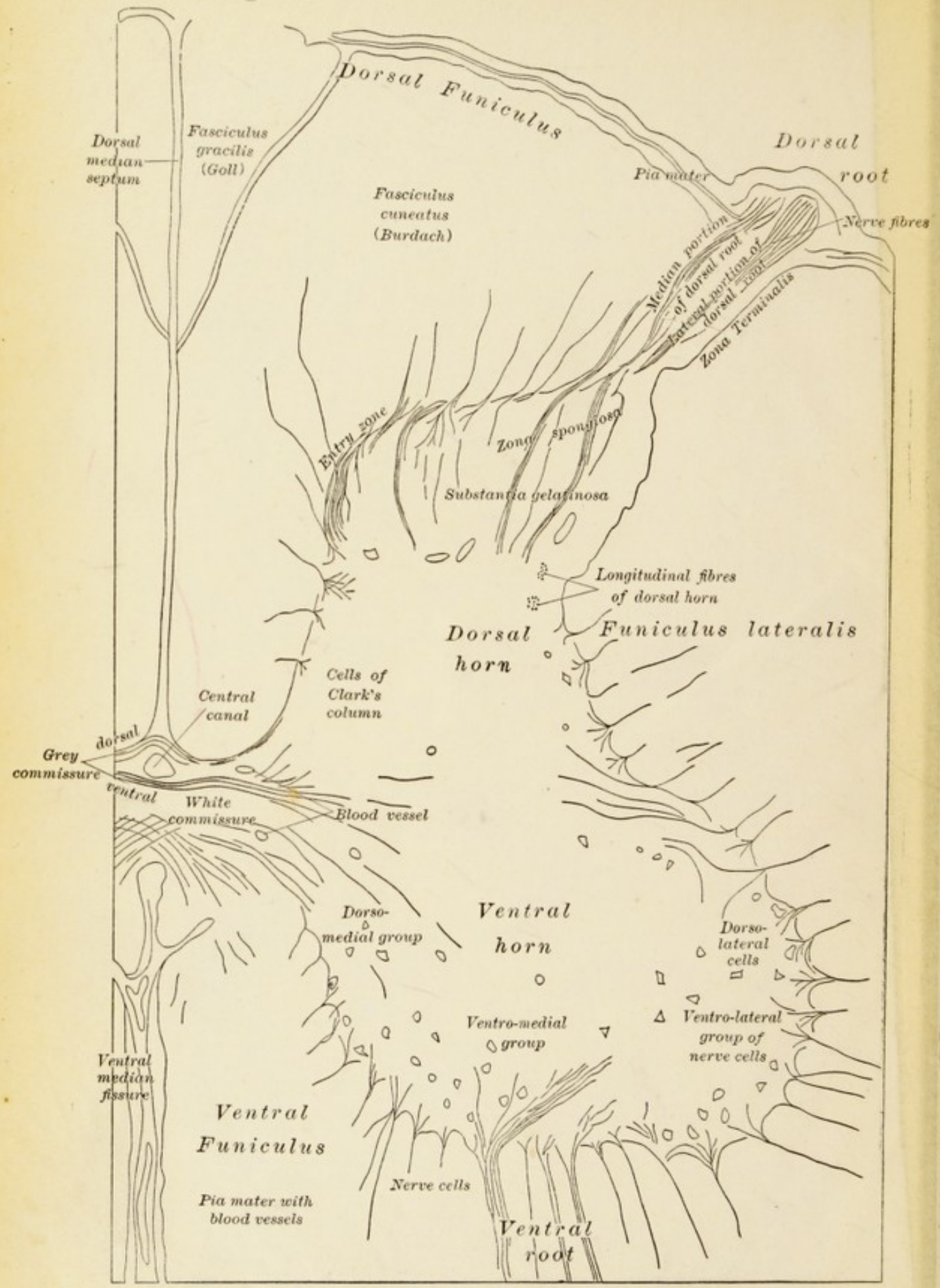


FIG. 212.—Cross-section of spinal cord of calf in cervical region. Stained by Weigert's method. Only one-half of the gray matter, with the surrounding white matter, is given. × 25.



J. Barącz ad nat. del.

Szymonowicz. Histology

Lith. Anst. v. Werner & Winter, Frankfurt a/M.

the *ventral pyramidal tract* (fasciculus cerebrospinalis ventralis) (Fig. 211). Its fibres run in the main from the cerebral cortex of the same side, and end by crossing over in the ventral commissure and forming end arborizations around the motor cells of the ventral horn. Lying lateral to this tract on each side is the *ground bundle* of the ventral column. It contains the axones of column cells.

In the *lateral column* (funiculus lateralis) we find the so-called *lateral* or *crossed pyramidal tract* (fasciculus cerebrospinalis lateralis). This tract contains centrifugal fibres arising in cells of the cerebral cortex of the opposite side. The crossing of the fibres takes place on the lower part of the medulla oblongata. They end by arborizations around the ventral horn cells of the same side. This column, together with the ventral pyramidal tract, forms a crossed tract, which carries practically all the motor fibres on the cord.

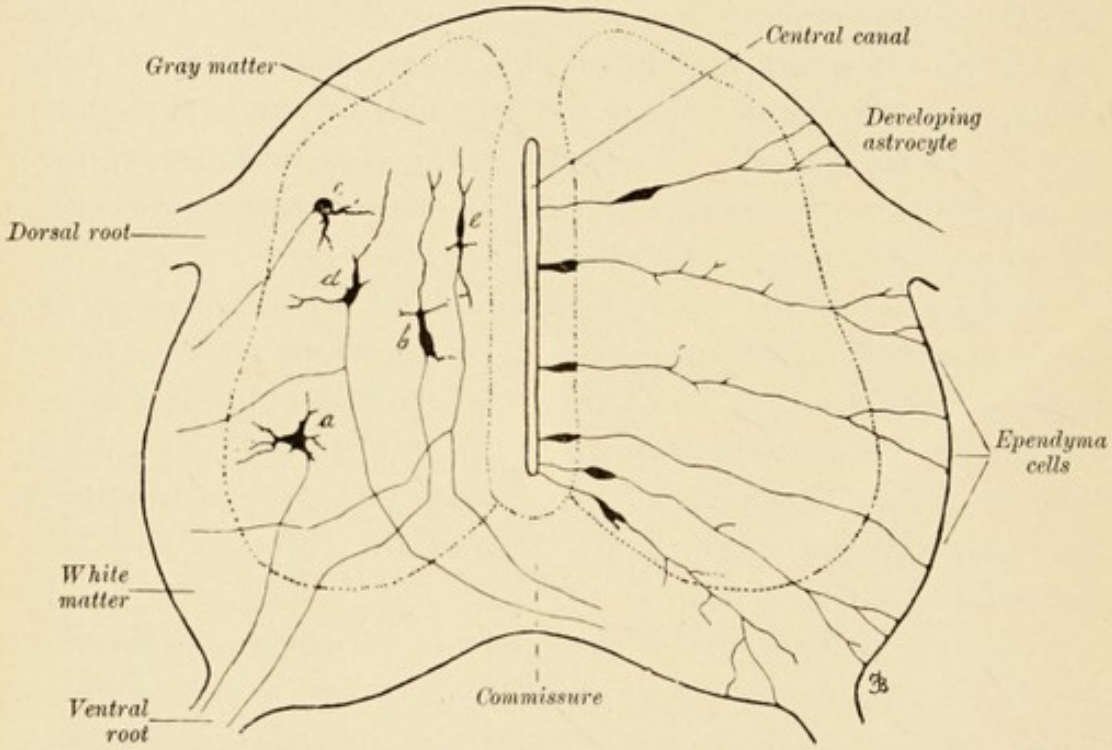
Peripheral to the crossed pyramidal tract lies the *cerebellar tract* (fasciculus cerebellospinalis dorsalis), which contains fibres derived from the axones of cells in Clarke's column (nucleus dorsalis). These fibres run up to the cerebellum. Ventral to this we find the *column of Gowers* (fasciculus ventrolateralis Gowersi). It has its origin in cells of the columns and runs upward to the cerebellum.

The rest of the lateral column, the so-called *ground bundles*, consist of axones having their origin in cells of the columns. These axones divide into ascending and descending branches, which run only a short distance (short paths). The function of these bundles is to join together neighboring segments of the cord.

The *dorsal column* (funiculus dorsalis) is formed from the fibres of the dorsal root, through which the axones from spinal ganglion cells enter the cord. On entering the dorsal column each axone divides into an ascending and a descending branch. Each of these gives off many side branches (*collaterals*), which enter the gray matter to end in fine arborizations. We find such end arborizations from the dorsal column in the nucleus dorsalis, in the substantia gelatinosa Rolandi, and in the ventral

horns in the region of the motor cell groups (reflex collaterals). Only very few of these collaterals pass through the dorsal commissure to the opposite side. The descending branches of the dorsal column fibres run only for a short distance, while the ascending branches reach usually as far up as the medulla, where they end in the nuclei of the columns of Goll and Burdach. The fibres in their course upward tend to approach the median side of the dorsal column, while the newly entering fibres of the dorsal root are always lateral to those arising in ganglia

FIG. 214.



Transverse section through the spinal cord of an eight-day chick. Left, nerve cells; right, neuroglia cells; *a* and *b*, motor cells; *c*, cells of lateral columns; *d* and *e*, hecateromeric cells. × 80.

lower down. Thus in cross-sections of the cord the fibres entering low down (*e, g.*, those supplying the lower extremities with sensory nerves) are situated always near the septum dorsale in the fasciculus gracilis; while similar fibres for the upper extremities are placed quite laterally in the fasciculus cuneatus. A slight addition to the fibres contained in the dorsal column is afforded by axones from small cells on the dorsal horn. These fibres after running for a short distance in the fasciculus cuneatus sink into the gray substance.

The fibres making up the white matter are medullated. They all lack the sheath of Schwann, and in consequence of this show no nodes of Ranvier or segmentation. Not until we reach the roots do the fibres show a neurilemma and nodes of Ranvier. In observing a cross-section of the cord (Fig. 213), we notice a difference in thickness in the fibres. In the fasciculus cuneatus and the funiculus ventralis are to be found the largest fibres; while those of the smallest diameter are seen in the fasciculus gracilis and the funiculus lateralis. In such a section it is to be noted that the great majority of the fibres are cut transversely—*i. e.*, they run parallel to the long axis of the cord. Diagonal and transverse fibres are relatively rare.

The supporting framework of the cord, as well as of the whole central nervous system, consists of *neuroglia*. This is of ectodermal origin, and arises in a way quite similar to the rest of the nervous system. In the study of neuroglia there are to be considered the neuroglia cells and neuroglia fibres (*glia cells* and *glia fibres*). In the medulla of adults we find glia cells of two kinds, the so-called *ependyma cells* and the *astrocytes* (Deiters' cells).

Ependyma cells are cylindrical cells bordering on the central canal. They form either a single layer or are arranged in two or three rows. In embryonic life these cells are ciliated on the surface toward the central canal, but these cilia disappear later on. Toward the surface of the cord each cell sends out a long, filiform process (*ependyma fibre*), which enters the gray substance, and in the embryo reaches the surface. In post-embryonal life the ependyma fibres reach the periphery of the cord only in the region of the septum dorsale. The ependyma cells are phylogenetically and ontogenetically the oldest neuroglia cells, from which the astrocytes take their origin. A part of the cells, which arise by division of the ependyma cells, leave the region of the central canal, and, moving peripheralward in the gray and white matter, become astrocytes.

The *astrocytes* are small nucleated cells containing little protoplasm. They are more or less stellate in outline, and owe their name to this peculiarity. According to the length

of the processes, we speak of astrocytes with long rays or short rays.

The *glia fibres*, which formerly were believed to be cell processes, are to be considered as entirely independent elements. They react to certain coloring reagents quite differently from the cell protoplasm or its processes, and pass through the cell body, so that their course can be followed uninterruptedly. They usually run through the outer layers of the cell body or lie on the cells. They are probably products of the cells which have become so much emancipated from the cell body that some of them seem to have no definite connection with the cell. These fibres are of different thicknesses and form a dense network. A considerable aggregation of neuroglia is found around the larger nerve cells, in the region of larger vessels, and especially around the central canal (*central glia-mass, substantia grisea centralis*). It also occurs on the periphery of the cord (*superficial glia capsule*).

Concerning the significance and function of the neuroglia, many theories have been advanced. According to Golgi, the neuroglia serves as a source of nourishment for the nerve cells. Ramón y Cajal claims that it has an insulating function in connection with the neurones. Weigert considers that it serves only as a supporting tissue to fill up the spaces between the neurones. According to R. Krause, the cells and fibres form paths for the circulation of lymph.

For a detailed description of the medulla, pons, midbrain, and the higher centres, the reader must be referred to special text-books on the subject.[1] In the space at our disposal only a brief account can be given.

[1] Barker, L. F.: Nervous System, Appleton, New York, 1899.
Edinger: Bau der nervösen Centralorgane, Leipsic, 1893.
v. Kölliker: Handbuch d. Gewebelehre, Bd. II., Leipsic, 1896.
van Gehuchten: Anatomie du systeme nerveux de l'homme, Louvain, 1897.
Sabin, F. R.: Atlas of Medulla and Midbrain, Baltimore, 1901.

PLATE XXXVII.

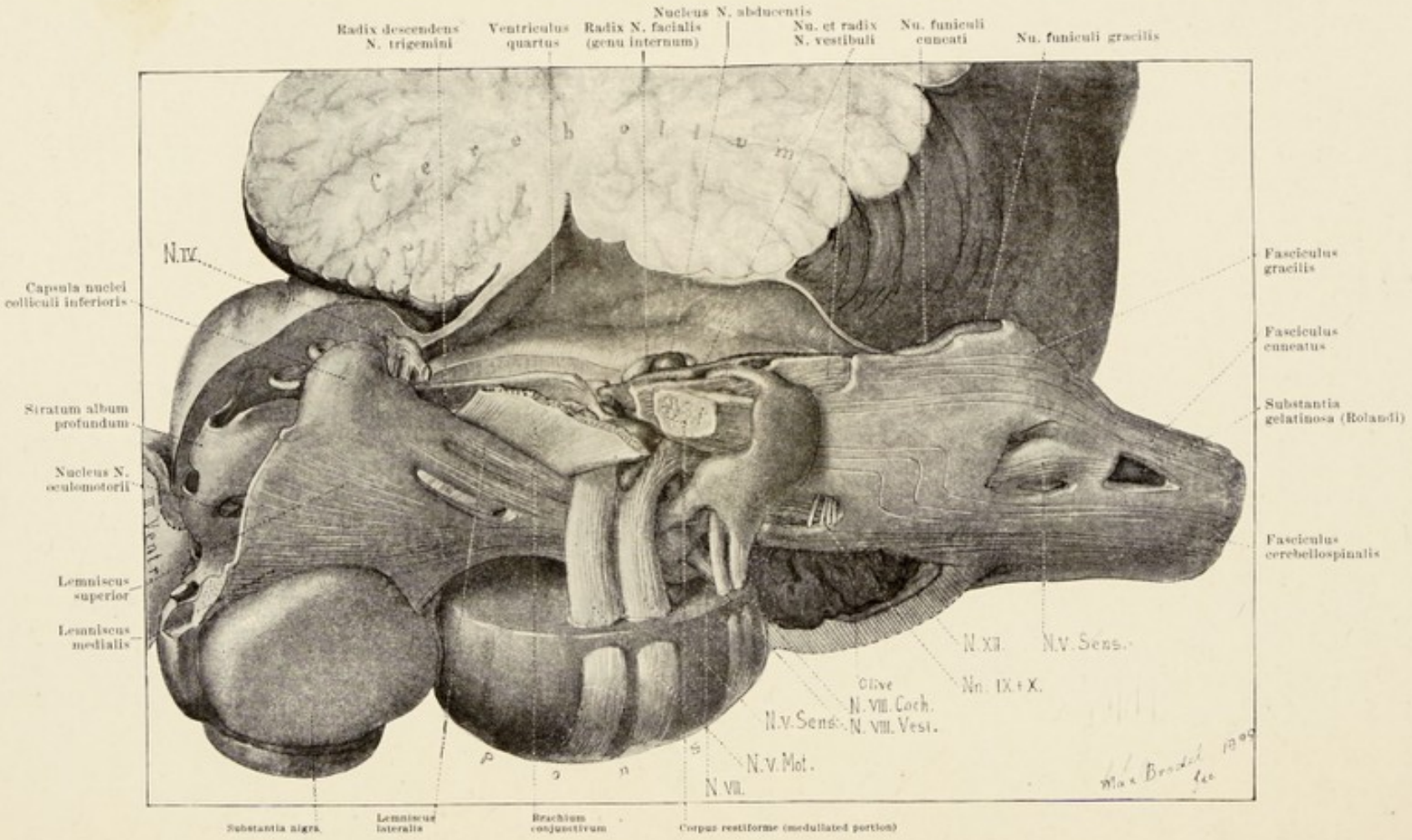


FIG. 215.—Model of medulla, pons, and midbrain from lateral surface. (F. Sabin.)

B. The Medulla, Pons, and Midbrain.

The brain-stem, comprising the medulla, pons, and midbrain, is the pasasge-way between the cord, the cerebellum, and the cerebrum; and, at the same time, a great reflex centre with its own nerves, both motor and sensory. It will be considered under four heads: (1) the tracts that connect the cord with the cerebrum; (2) the tracts that connect the cerebellum with the cord and the brain; (3) its reflex centres; and (4) its nerves.

Group 1.—Two tracts connect the cord with the brain, a sensory and a motor. The latter is called the *pyramidal tract.* The sensory path contains a part of the ventral and lateral columns of the cord and almost all of the dorsal columns. In entering the medulla, some of the fibres of the lateral and ventro-lateral columns of the cord curve a little dorsalward and inward, to make two bands of fibres that pass upward in the medulla on either side of the raphe. These two bands are the sensory path, here called the *interolivary bundle.* At the same time the central canal of the cord curves dorsalward and opens into the fourth ventricle. The roof of the fourth ventricle is at first a thin veil of tissue, but opposite the pons it becomes the cerebellum (Fig. 215). By this thinning out of the dorsal wall the dorsal columns of the cord are pushed outward to end in the two nuclei that make the prominences on the surface of the medulla just above the clava. From these nuclei, which represent the spinal nerves, as well as from all the sensory nuclei of the medulla and the pons, fibres curve across the brain-stem, decussate in the raphe, and enter the sensory tract. These fibres are called the *internal arcuate fibres.*

Throughout the medulla the two bands or sheets of fibres forming the sensory path are parallel. In passing into the pons, however, the ventral fibres spread out like a fan into a horizontal sheet, which divides the pons into two parts, a dorsal and a ventral. Here the bundle is called the *medial lemniscus.* In entering the midbrain the sheet curves outward

and rotates partially, so that it becomes oblique. In the midbrain the pyramidal tract lies external and ventral to the medial lemniscus, but in passing upward the sensory tract passes in front of the pyramidal tract, and the two bundles together make the internal capsule which lies just external to the thalamus and is connected with the region of the cortex around the fissure of Rolando. The form of the sensory tract is emphasized, because all the other structures are related to it. In the medulla it is the medial, vertical sheet; opposite the ventral part of it is the olive; opposite the dorsal part of it is the area of the formatio reticularis, which contains all the nerves of the region. In the pons the sensory tract forms a horizontal sheet. Ventral to it lie the pontal nuclei; while dorsal to it lie the formatio reticularis and the nerves.

In the midbrain the sensory tract is an oblique sheet. It lies between the red nucleus and the formatio reticularis on the inside, and the pyramidal tract on the outside.

The pyramidal tracts start from the cerebral cortex around the fissure of Rolando, and pass downward in the posterior part of the internal capsule into the peduncle or midbrain. Here the tract is a compact band of fibres external to the medial lemniscus. It passes into the ventral part of the pons, where it is broken into small bundles by the cells of the pontal nuclei. In entering the medulla, these bundles collect into a tract that passes to the cord just ventral to the interolivary bundle. At the lower end of the medulla these fibres decussate in the raphe. Part of them enter the ventral columns of the cord, part cut through the ventral horn and enter the lateral columns. In the brain-stem, fibres leave the pyramidal tract, decussate in small bundles or as single fibres, and enter the motor nuclei.

Group 2.—The cerebellum has three peduncles—inferior, middle, and superior. The inferior receives fibres from the cord and the medulla. The direct cerebellar tract, which is a narrow band on the surface of the cord, becomes a compact bundle in entering the medulla, and receives a group of fibres from the dorsal columns of the cord (Fig. 215). These fibres,

PLATE XXXVIII.

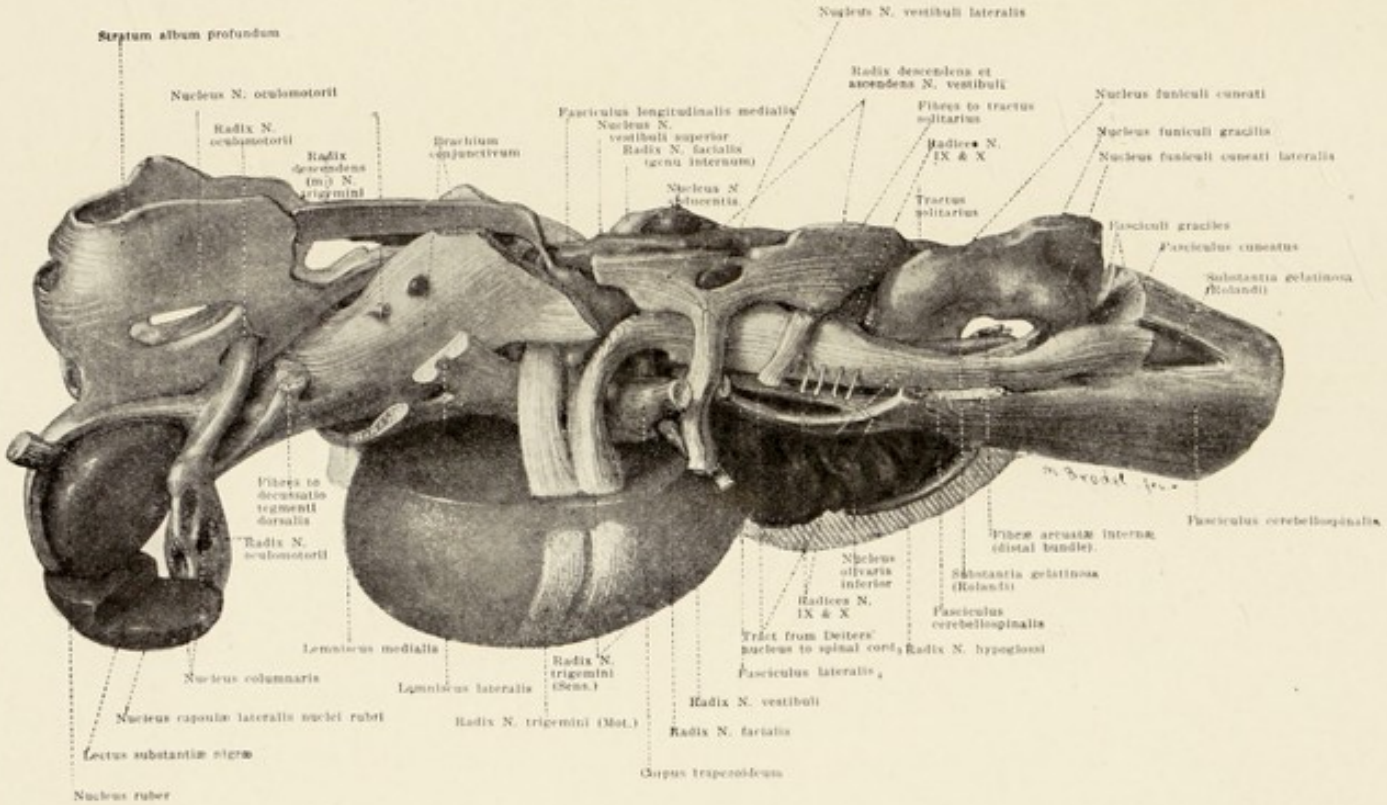


FIG. 216.—Model of medulla, pons, and midbrain from lateral surface, showing mainly the sensory nerves and their nuclei. (F. Sabin.)

PLATE XXXIX.

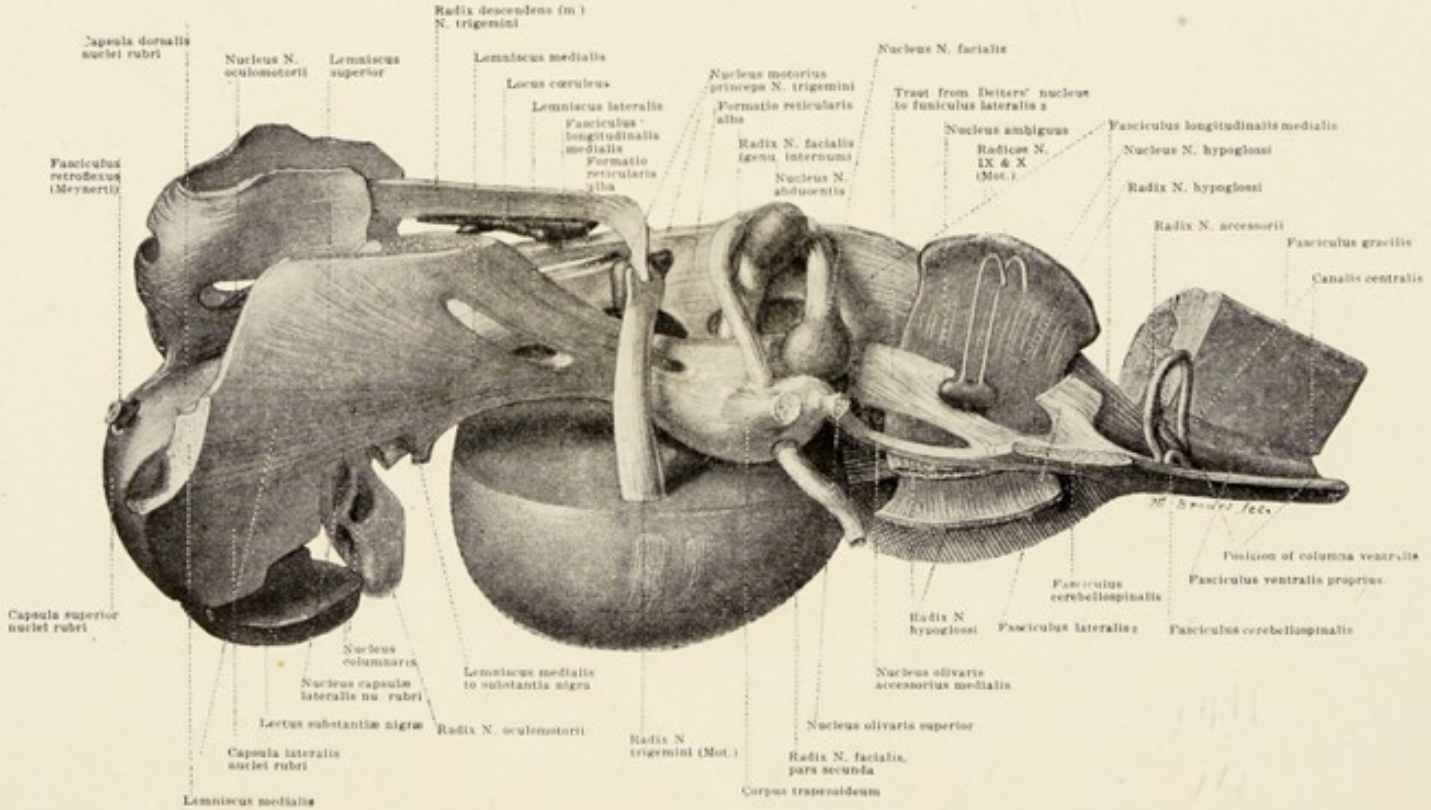


FIG. 217.—Model of medulla, pons, and midbrain from lateral surface, showing mainly the motor nerves and their nuclei. (F. Sabin.)

together with bundles from the olive and the vestibular nuclei, make the inferior peduncle. It passes upward on the surface of the medulla, between the cochlear and vestibular nuclei, to the lower end of the pons, where it turns dorsalward, enters the cerebellum, and decussates in the roof of the fourth ventricle. In passing dorsalward it lies just outside the dentate nucleus, which receives the superior peduncle. The superior peduncle starts in the red nucleus. Its fibres decussate in the dorsal part of the pons, and enter the cerebellum just internal to the inferior peduncle. The fibres of the middle peduncle come from the pontal nuclei. They decussate in the pons and enter the cerebellum external to the inferior peduncle.

Group 3.—In the cord the gray matter between the two horns is much broken by fibres, and is called the *formatio reticularis.* It is a reflex centre. In the brain-stem it is greatly developed. It occupies the dorsal half of each region. It contains countless cells and fibres. The fibres are either scattered or in more or less definite bundles. One short path in the brain-stem is very distinct, the posterior longitudinal bundle. It receives fibres from the ventral column of the cord and lies just ventral to the central canal throughout the brain-stem. It receives descending fibres from the midbrain.

Group 4.—The nuclei of the motor cerebral nerves are derived from the ventral horn; of the sensory, in part from the dorsal horn. Of the motor nuclei (Fig. 217), four lie near the raphe just ventral to the central canal. They are the hypoglossal in the medulla, the abducens in the pons, and the trochlear and oculomotor in the midbrain. The fibres of all these nerves, except the trochlear, pass ventralward and emerge near the median line. The fibres of the trochlear nerve pass dorsalward, decussate in the velum, and pass out near the median line. The other four motor nerves, the spinal accessory, the glossopharyngeal and vagus together, in the medulla, the facial and the trigeminal in the pons, lie farther lateral and ventral. The fibres of all these nerves, except the trigeminal, pass inward toward the central canal, there turn outward and ventralward to emerge on the ventral surface in a lateral line.

The fibres of the trigeminal pass directly to a surface origin in the lateral line.

The sensory nuclei (Fig. 216) represent the dorsal horn, and lie for the most part in the dorsal part of the medulla and pons. The type of a sensory nerve in this region is to divide into a long descending and a short ascending tract, each of which is accompanied by a nucleus. The long descending tract of the glossopharyngeal and vagus is the tractus solitarius, which lies in the border of the central gray matter of the lower half of the medulla. It has its own nucleus. Parallel and just internal to it is another long nucleus, the ala cinerea, belonging to the same nerves.

The tracts of the vestibular and trigeminal nerves are parallel, the former lying just dorsal to the latter (Fig. 216). The descending tract of the vestibular nerve is in the medulla, while the ascending tract enters the pons. The cells which accompany these two tracts have received three names: those opposite the descending fibres are called the *median nucleus;* those opposite the ascending fibres, the *superior nucleus;* while a small group of cells in the angle of the two tracts makes the *lateral nucleus.* The lateral nucleus places the nerve in communication with the cerebellum. The trigeminal tract is long, covering half of the pons and all of the medulla. The descending tract joins with Lissauer's zone in the cord, and its nucleus joins the posterior horn. Lissauer's zone is external to the substantia gelatinosa of Rolando. The ascending fibres end in the main sensory nucleus.

The cochlear nerve has no descending tract, but a long and complex ascending one. Its fibres end in a nucleus on the lateral surface of the medulla (Fig. 215). Part of the fibres pass inward, dorsal to the inferior peduncle, and decussate in the floor of the fourth ventricle as the striæ acusticæ; others pass ventral to the peduncle as a compact bundle, which, as it decussates, forms the trapezoid body. The fibres of the trapezoid body and the striæ acusticæ make the lateral lemniscus, which passes upward and dorsalward through the pons to the inferior colliculus. Here many fibres end; others pass to the

PLATE XL.

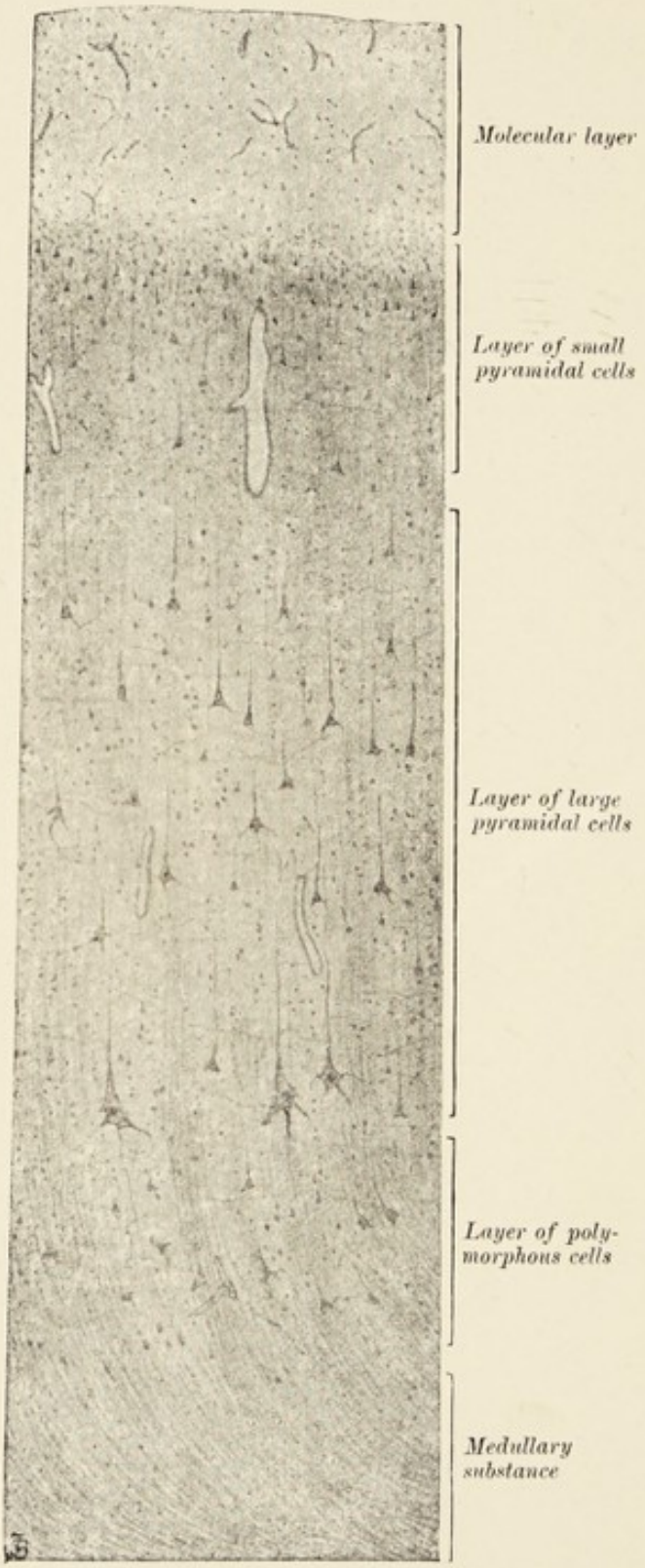


FIG. 218.—Part of a perpendicular section through the cerebral cortex of man × 70.

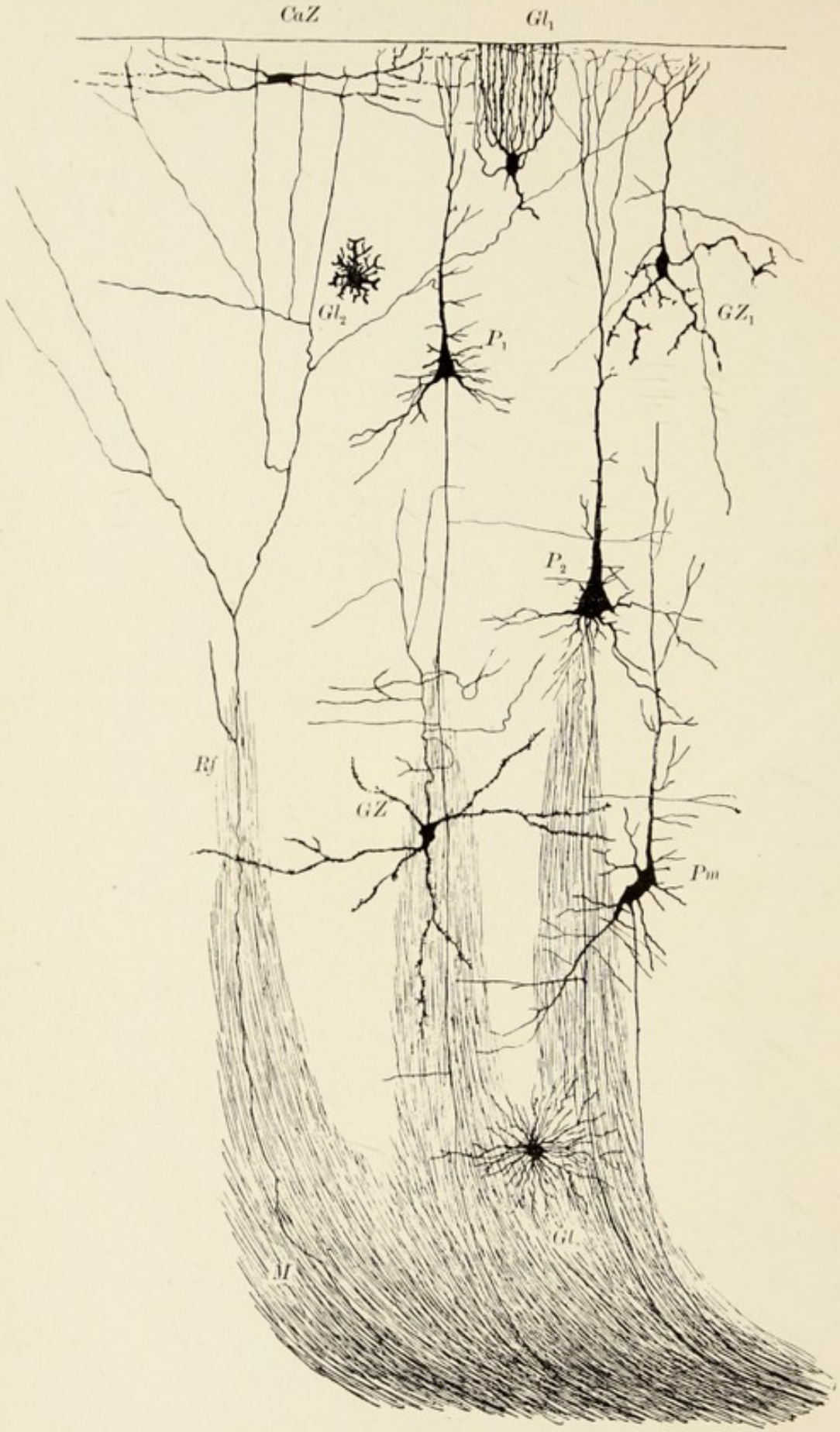


FIG. 219.—Diagram of the structure of the cerebral cortex. (Prepared by Golgi's method; partly after Stöhr.)

CaZ, Cajal's cells; *GZ*, Golgi cells; P_1, small pyramidal cell; P_2, large pyramidal cell; *Pm*, polymorphous cell; *Rf*, Ramon's fibre; Gl_1, Glia cell of the superficial glia layer (cell of Retzius); Gl_2, short-rayed cell; Gl_3, long-rayed cell; *M*, medulla.

cortex of the temporal lobe through the medial geniculate body and the internal capsule.

The sensory path of the facial nerve—that is, the pars intermedius—is not known.

The fibres of the optic nerve enter the brain in the region of the thalamus. A part of the fibres pass downward into the border of the superior colliculus; the rest enter the internal capsule just posterior to the pyramidal tract fibres and pass out to the occipital lobe. The fibres of the olfactory nerve have no direct connection with the brain-stem. They enter the olfactory bulb, beneath the frontal lobe, and pass to the cortex of the frontal and temporal lobes.

Only a small part of the cortex of the brain represents the nerves of the body. In general, the area around the fissure of Rolando receives sensory impressions from the entire body and sends out the fibres of voluntary control. The special senses are represented as follows: sight, in a small part of the occipital lobe; hearing, in a part of the temporal lobe; and smell, in a part of the temporal and frontal lobes. All the rest of the cortex is the "great silent area," or the association centres of the brain. These areas are connected richly by fibres both with the same side and with the opposite side of the brain. These are the association paths which make the brain the organ of thought.

C. Cerebral Cortex.

The cerebral cortex shows certain differences in structure in different regions, into the details of which we cannot here enter. All regions have a structure which conforms to one type, which will be described. The cortex consists of gray substance in which four layers can be recognized. These pass over into one another without sharp boundaries (Figs. 218 and 219). Beginning at the outside, we meet with the following structures:

1. *The Molecular Layer* (*Stratum Zonale*).—This is a layer which is poor in cells, but shows a finely granular and reticular structure. This is due partly to the interlacing dendrites and axones of nerve cells whose bodies are situated more deeply, but

mainly to nerve fibres lying parallel to the surface, the so-called *tangential fibres.* In this layer we find the *cells of Cajal*, which are spindle-shaped, pyramidal, or stellate cells, whose processes run horizontally in every direction, giving off fibres to the surface of the cortex. These are considered generally as nerve cells.

2. *Small Pyramidal Cell Layer.*—This zone owes its name to the fact that it is made up of comparatively small cells of a pyramidal form, so arranged that the apices are directed toward the surface of the cortex, and the bases in the opposite direction. Fig. 69 represents such a cell and illustrates the relation of the axone and dendrites to the cell body. From the apex of the cell the main dendrite proceeds toward the surface of the cortex, passing through almost the entire thickness of the molecular layer. Throughout its course it gives off numerous side branches, and ends freely after many arborizations in the outer part of the molecular layer. Other smaller dendrites proceed from the lateral and basal parts of the cell. The axone usually emerges from the middle of the basal surface, and runs toward the medullary substance. It gives off many collaterals on the way which run parallel to the surface.

3. *Large Pyramidal Cell Layer.*—This is made up of cells quite similar in general form to those of the layer just described. They are, however, much larger, especially in the motor area of the cortex. The axones of these cells in part enter the pyramidal tracts of the cord.

4. *Layer of Polymorphous Cells.*—In this layer we find polygonal cells, which give off dendrites, and send axones into the white matter. There are found also spindle-shaped cells in this region. These cells, which are typical for individual layers, and send their axones far beyond the cortex, are known as *Golgi cells type I.* In addition there are numerous cells whose axones never reach outside the limits of the cortex, and end not far from the cell body. These are known as *Golgi cells type II.* Some of these cells send their axones toward the molecular layer, instead of toward the white matter, and are known then as *cells of Martinotti.*

The various layers are made up not only of cells, but contain

also networks of medullated nerve fibres. A part of these fibres run at right angles, while others lie parallel to the surface. Among the former are the axones derived from the pyramidal cells, as well as those fibres proceeding to the cortex from lower down in the central nervous system. These fibres run in bundles through the third and fourth layers up to the layer of small pyramidal cells. They form the so-called *radial bundles.* The strands of fibres running parallel to the surface are derived from many sources. The outermost forming the tangential fibres, and those contained in the small pyramidal cell layer, as well as those belonging to the so-called *supraradial network*, represent largely the side branches of fibres running from below up to the brain surface.

The deeper fibres cross the radial bundles and form the so-called *interradial bundles.* Some of these run in the large pyramidal cell layers, and form there the horizontal fibre tracts of Gennari or Baillarger. The fibres of the interradial network are formed from collaterals of axones of the pyramidal cells.

The neuroglia distributed unequally in the different layers of the brain consists of two elements, the glia cells and glia fibres. By means of the Golgi method the following forms of glia cells have been made out: *short-rayed cells* (Fig. 219, Gl_2), which lie in the gray matter and possess much-branched processes; *long-rayed cells* (Gl_3), which lie mainly in the white matter and possess fine processes branched only slightly; and *arborescent cells* (Gl_1), which lie at the surface of the cortex and send their processes outward.

Weigert's method which gives a special differentiation to the glia fibres, shows in the outer layer of the cortex a thick *cortical sheath*, composed of a rich tangentically placed plexus of glia fibres In the deeper layers of the cortex the glia fibres are not so abundant, while in the medullary substance they form again a dense network.

D. Cerebellum.

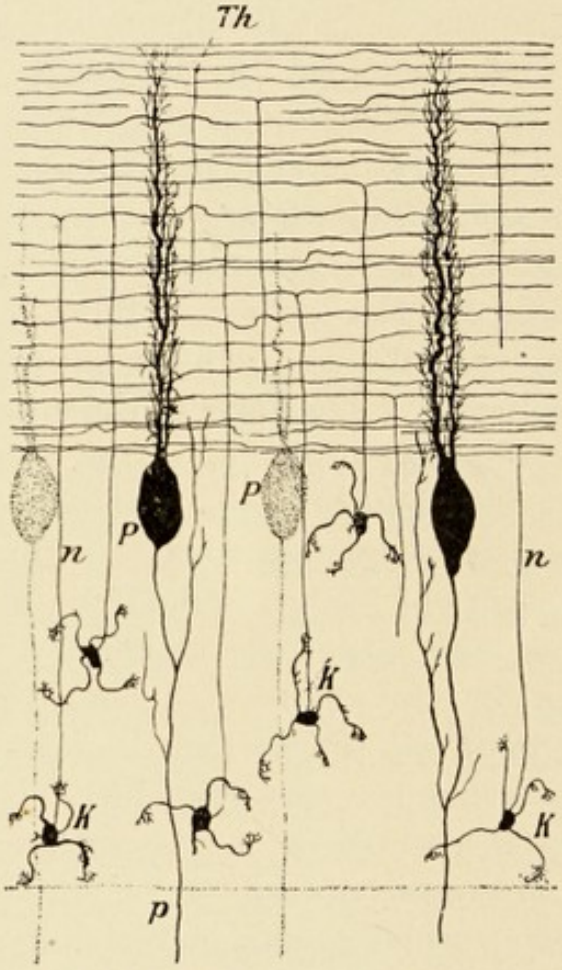
The layers of the cerebellum are marked off much more sharply from one another than those of the cerebrum (Figs.

220 and 221). Three main layers can be distinguished, namely, the granular, ganglionic, and molecular.

1. The *granular layer* lies immediately on the medullary substance. In it there are to be seen two kinds of cells: (*a*) small granular cells and (*b*) large granular cells.

(*a*) The *small granular cells* form the greater proportion of this layer. They are very small multipolar nerve cells, which

FIG. 222.



Diagrammatic representation of a longitudinal section through a convolution of the cerebellar cortex. (After v. Kölliker.) *P*, Purkinje's cells; *p*, axone of cell of Purkinje; *K*, granular cell; *n*, axone of a granular cell; *Th*, place of division of axone of granular cell.

give off an axone and a few dendrites ending in claw-like arborizations. The axone runs outward at right angles to the surface and divides in the outer layer of gray matter like the letter T. The two branches run parallel to the surface of the cortex and to the long axis of the convolution, and end freely. This is shown in Figs. 221 and 222.

PLATE XLII.

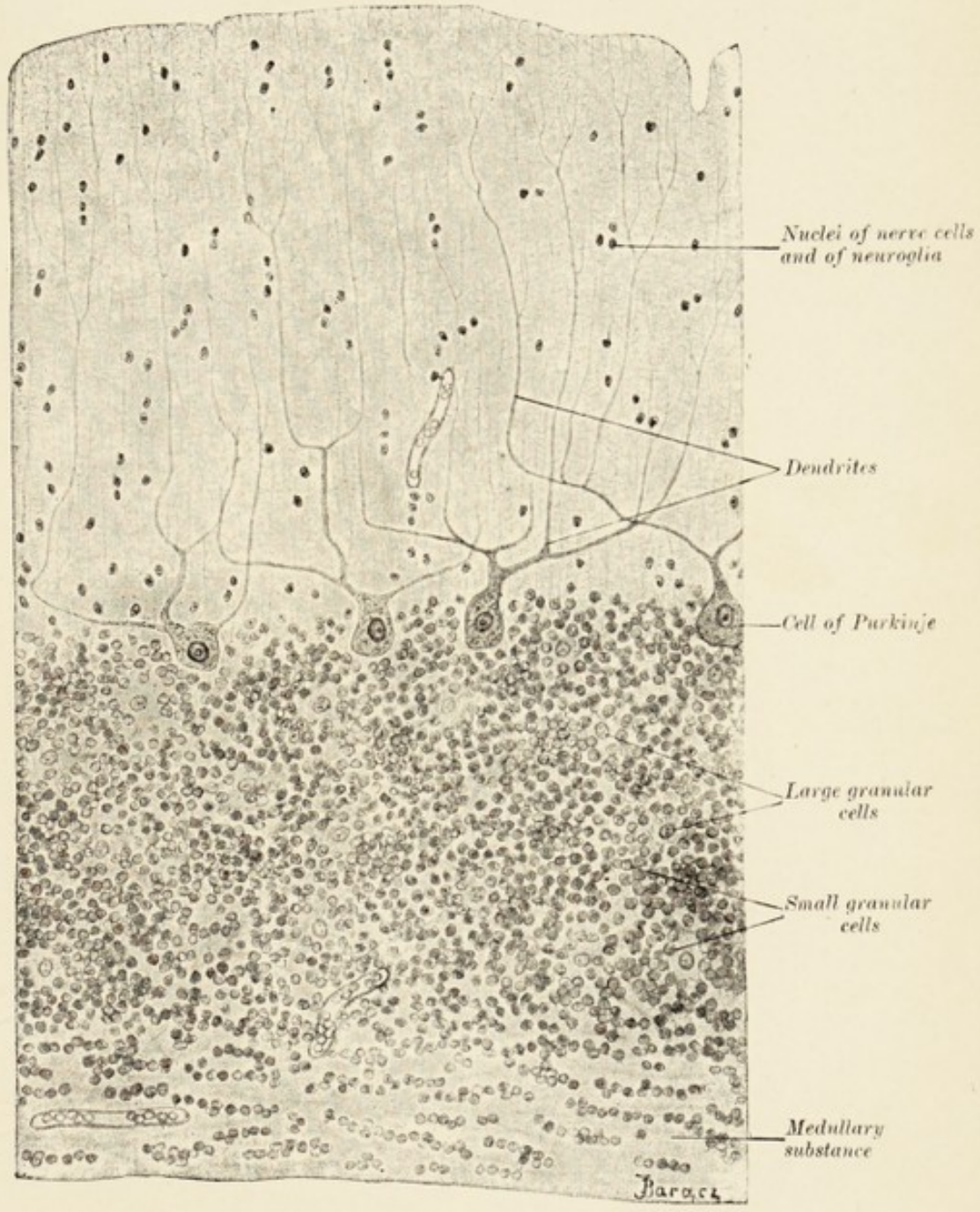


FIG. 220.—Part of a perpendicular section through the adult human cerebellar cortex. × 158.

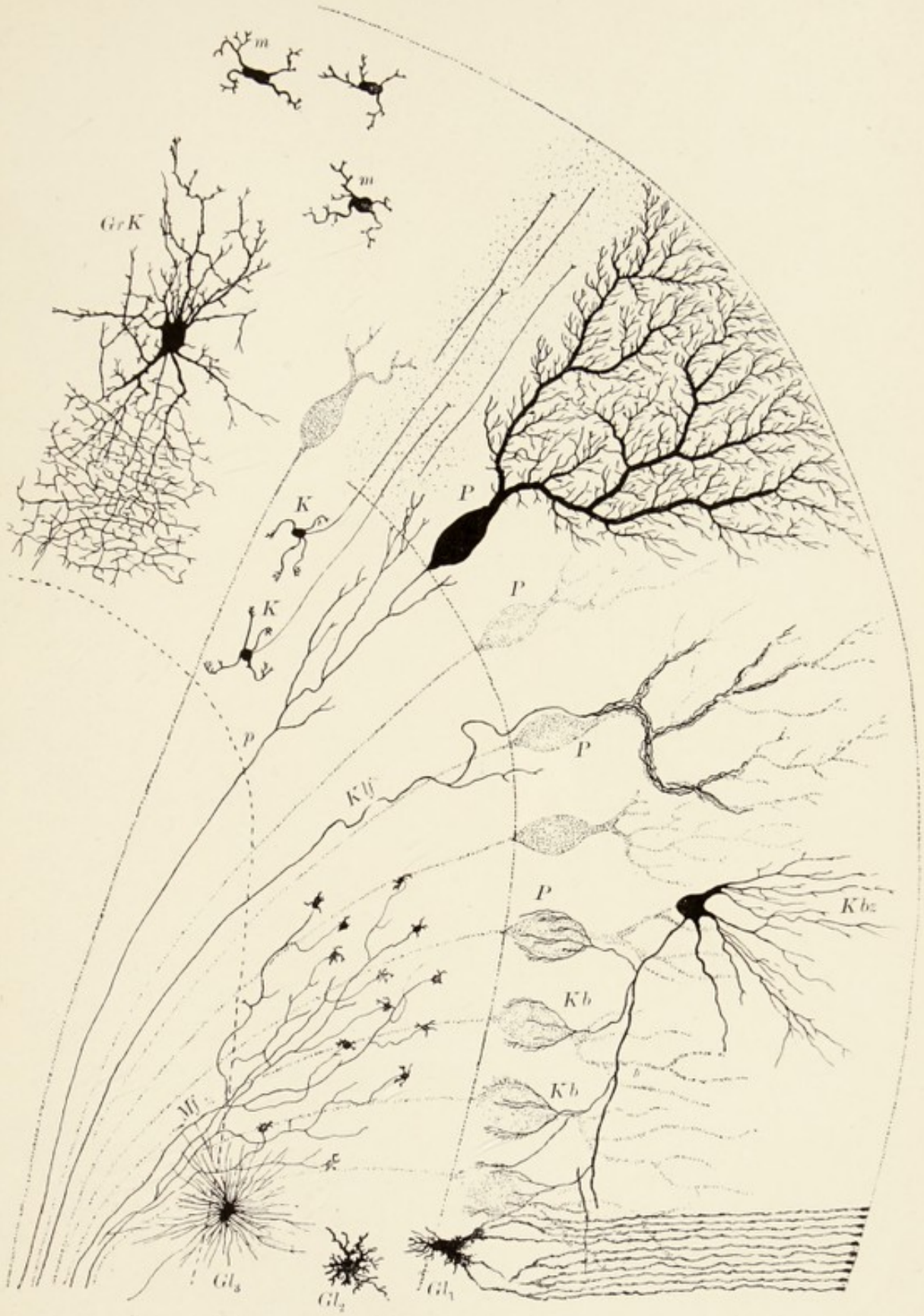


FIG. 221.—Diagram of the structure of the cerebellar cortex. (Prepared by Golgi's method; in large part after v. Kölliker.)

P, Purkinje's cells; *p*, axones of Purkinje's cells with returning collaterals; *Kbz*, basket cells; *Kb*, baskets which surround the bodies of the Purkinje's cells; *K*, small granular cells, whose axones penetrate the molecular layer and then appear in cross-section as fine dots; *GrK*, large granular cells; *m*, small cells of the molecular layer; *Mf*, mossy fibres; Gl_1, glia cells of the molecular layer; Gl_2, short-rayed cells; Gl_3, long-rayed cells.

(*b*) The *large granular cells* are large multipolar cells whose dendrites and axones run in quite the opposite direction to that taken by the processes of the small granular cells. The axone extends in the granular layer toward the medullary substance, giving off numerous collaterals which end around the small granular cells. The dendrites run, on the contrary, into the molecular layer (Figs. 220 and 221).

In the granular layer we find between the cells described a network of medulated fibres which pass through the layer, partly from the white substance outward, and partly from the cells of the ganglionic layer to the medulla.

2. The *middle or ganglionic layer* is made up of the so-called *cells of Purkinje*. These are arranged in a single layer. Each cell consists of a large pyriform cell body giving off one or two dendrites in the direction of the molecular layer. These dendrites break up into numerous branches which reach almost to the surface of the cortex. They resemble a very richly branched tree, whose branches spread out in a single plane at right angles to the long axis of the cerebellar convolutions. Thus in a cross-section of the convolution the whole extent of the arborization may be seen, while in a longitudinal section this is not the case (cf. Figs. 221 and 222). The profuse branching and general relations of these cells can be made out especially well in Golgi preparations.

The axone which emerges from the opposite side of the cell runs in the medullary substance, and sends out collaterals in its course through the granular layers, which branch and run back in part to the molecular layer (Fig. 221).

3. The outermost, so-called *molecular layer*, shows two kinds of nerve cells: large cells lying in the deeper layers, and small cells more superficially situated. The former are multipolar cells with many dendrites directed mainly toward the periphery, and an axone running transversely to the long axis of the convolution. The axone lies parallel to the border between the granular and the molecular layers, and gives off at intervals many branches which surround the bodies of the Purkinje cells in a sort of basket-work. One axone thus joins together

several cells of Purkinje. The smaller cells are multipolar, and lie in the outer part of the molecular layer.

Besides these nerve-cells which we have described, there are in the cortex of the cerebellum nerve fibres which are for the most part medullated and extend into the white substance.

The *white substance* or *medulla* of the cerebellum consists of medullated nerve fibres. The bundles are made up of axones from the Purkinje cells, as well as fibres which arise from cells in other parts of the nervous system, and enter the cerebellum through one of the three peduncles. Certain special fibres have been described by Ramón y Cajal as *mossy fibres.* These seem, however, to represent only a stage in the life of other cells in the granular layer. At their ends and where division takes place there are mossy swellings.

The *neuroglia* is studied best in Golgi preparations. The elements are quite similar to those of the cerebrum. The arborescent cells are situated with the cell body between the granular and molecular layers. The cells with long rays are found especially in the white matter (Fig. 221); while those with short rays occur in the gray substance.

By Weigert's method we learn that the glia fibres do not form a dense network in the outer layers, as in the spinal cord and cerebrum. On the contrary, we find in the molecular layer radial fibres running from the surface into the deeper parts. Only a few transverse fibres occur, which often in the region of Purkinje's cells form a somewhat thick plexus. In the granular layers the glia fibres are very scarce, while in the medullary substance they form a rich neuroglia network.

E. Membranes Covering the Central Nervous System (Meninges).

Enclosing the brain and spinal cord there are three membranes: the outermost, known as the *dura mater;* the middle, the *arachnoidea;* and the innermost, the *pia mater.*

The *dura mater spinalis* is a membrane made up of connective-tissue bundles containing fine elastic fibres. Both surfaces are covered with a layer of endothelial cells.

The *dura mater cerebralis* is made up of two layers, an inner

one which in all respects resembles the dura mater spinalis, and an outer one which lines the inner surface of the skull like a periosteum. In the latter layer there are two sheaths of fibres crossing one another. According to Luschka, the inner surface of the dura mater cerebralis is covered with a double layer of flattened epithelium. The dura mater is poor in blood-vessels, with the exception of the outer layer of the dura mater cerebralis, which contains numerous vessels and sends off many to the bones of the skull. According to some authors, the spaces which can be injected in the dura are to be considered as lymph-channels in communication with the subdural space, and lined partly with endothelium.

The dura mater cerebralis contains many nerves which end partly in the dura itself and partly in the vessels. Those ending in the dura (*nervi proprii*) break up into numerous branches, which terminate between the endothelial cells on the inner surface of the dura by means of bulbar thickenings.

The *arachnoidea* is a thin membrane made up of connective-tissue bundles joined together in a net-like structure. It contains numerous elastic fibres, and is clothed on both sides by a layer of endothelial cells. From its inner surface it sends off many connective-tissue strands, which pass through the sub-arachnoidal space to join with the pia mater. These also are covered by endothelium. There are to be found in the arachnoidea neither vessels nor nerves. In certain places (*e. g.*, on both sides of the sinus sagittalis superior) there are on the outer surface of the arachnoidea non-vascular villus-like outgrowths, which bulge out the thin inner lamella of the dura and project into the venous sinuses. These are the so-called *Pacchionian bodies* or granulationes arachnoidales (Pacchioni).

The *pia mater* is a very thin membrane made up of fine connective tissue. It covers the whole brain and spinal cord, and follows all the sulci and down-dippings of the surface. In the cord it forms the septum longitudinale ventrale. There are to be distinguished in the pia mater of the spinal cord two layers: the outer one resembling the arachnoidea in structure, and joining with the connective-tissue strands passing across the sub-

arachnoidal space. The inner layer (intima pia) is a thin membrane made up of connective-tissue bundles running circularly.

The pia mater of the brain resembles the intima pia of the spinal cord.

The pia mater contains many vessels, partly belonging to itself (*plexus chorioideus*) and partly derived from those which enter the brain and cord. The vessels of the pia mater spinalis run between the two layers.

Numerous fine nerve branches, partly from the sympathetic system and partly from cerebro-spinal nerves, enter the pia mater, to supply the vessel walls. They pass into the cord and brain together with the vessels.

The *telæ chorioideæ* and *plexus chorioidei* are structures which are formed from the pia mater and ventricular epithelium. They consist of a connective-tissue membrane which contains many blood-vessels, and is covered by a layer of cubical epithelium. The layer represents the much-thinned brain wall, and in the embryo consists of ciliated cells. The plexuses contain no nerves.

F. Blood-vessels of the Central Nervous System.

The blood-vessels of the spinal cord have the following relation, according to the work of H. Kadyi: The arterial stems running along the nerve roots (arteries of the ventral and dorsal roots) branch many times in the pia mater and join with one another by numerous anastomoses. There can be distinguished nine longitudinally disposed lines of anastomosis, of which the ventral unpaired one is the greatest and is in connection with the arteria spinalis ventralis. From this a series of arterial branches proceed with the pia into the fissura mediana ventralis, giving off side branches right and left into the column of gray matter (*central arteries*). From other parts of the arterial network of the pia mater numerous fine branches enter the white matter (*peripheral arteries*), and extend as far as the gray matter. The central and peripheral arteries do not anastomose with one another, but are what Cohnheim termed end-

PLATE XLIV.

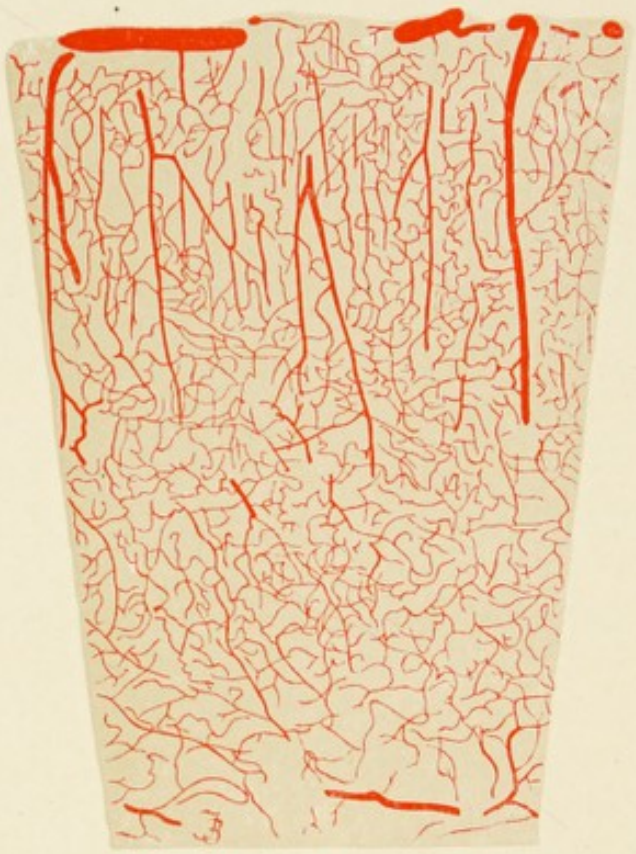


FIG. 223.—Section through the cerebral cortex of a rabbit; blood-vessels injected red. × 40.



FIG. 224.—Section through the cerebellar cortex of a guinea-pig; blood-vessels injected red. × 44.

arteries. The capillaries of the cord everywhere form networks with meshes somewhat lengthened in the direction of the long axis of the cord. In the white matter the capillary network is much less abundant than in the gray matter, where it is richest in the region of the cell groups.

The *veins* of the spinal cord follow the course taken by the arteries. The central veins are relatively small in relation to the central arteries, and are connected with the peripheral veins by various well-developed anastomoses. On the dorsal surface of the cord there are found much larger venous networks than on the ventral side. From the venous plexuses of the pia mater the blood reaches the outside through the veins of the ventral and dorsal roots.

In the *cerebrum* and *cerebellum* we meet with a dense capillary network around the cell groups of the cortex (Figs. 223 and 224). In the cortex the arteries break up into a fine capillary network, which in the medullary substance becomes coarser. The meshes of the network run in the direction of the nerve fibres.

The subdural and subarachnoidal spaces must be considered as lymph spaces. It is believed also that they are in communication with the lymph-vessels of the nasal mucous membrane, and those of the peripheral nerves. All the blood-vessels of the central nervous system are surrounded by a *perivascular* space which is to be regarded as a lymph space.

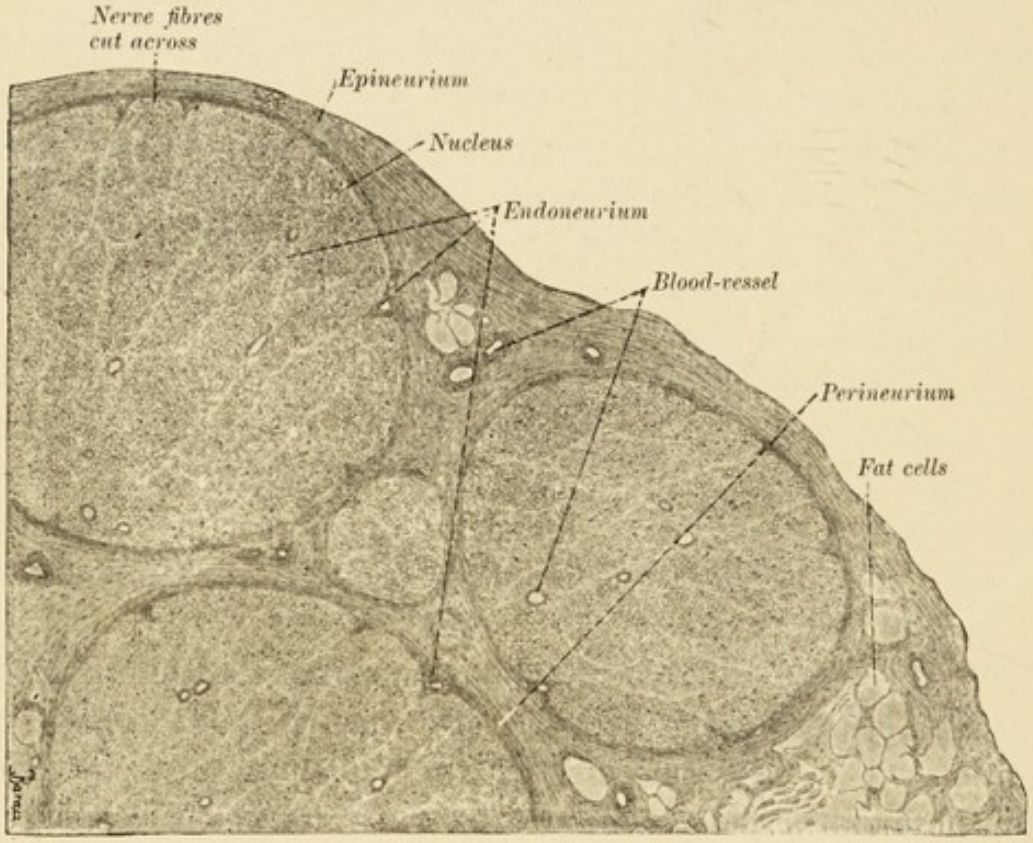
2. PERIPHERAL NERVOUS SYSTEM.

A. Nerves.

The cerebro-spinal nerves consist almost entirely of medullated nerve fibres, which always are joined together into bundles by a loose connective tissue. In this connective tissue there can be distinguished a layer which surrounds the whole nerve. This is known as the *epineurium* (Fig. 225). From this there run into the interior of the nerves connective-tissue strands between the so-called secondary bundles of nerve-fibres. These strands are arranged around the secondary bundles in concentric lamellæ, which vary in thickness with the size of the

bundle, and are lined on the inner surface with a layer of flat cells, whose outlines can be well made out in silver nitrate preparations. This connective tissue separating the individual bundles is known as the *perineurium* (Fig. 225). From it

FIG. 225.



Part of a transverse section of the human nervus tibialis anticus. × 76.

connective-tissue septa run into the interior of the bundles of nerve fibres, forming the so-called *endoneurium*. This tissue surrounds small bundles of fibres (primary bundles), and gives origin to the *endoneural sheath* (Henle's sheath) of the individual fibres. The epineurium and perineurium contain, as opposed to the endoneurium, fat cells and elastic fibres.

As the nerve approaches its termination, it breaks up into fine branches. Those made up of a simple bundle are surrounded by a lamellated sheath. Fibres which are not joined to form bundles possess only Henle's sheath.

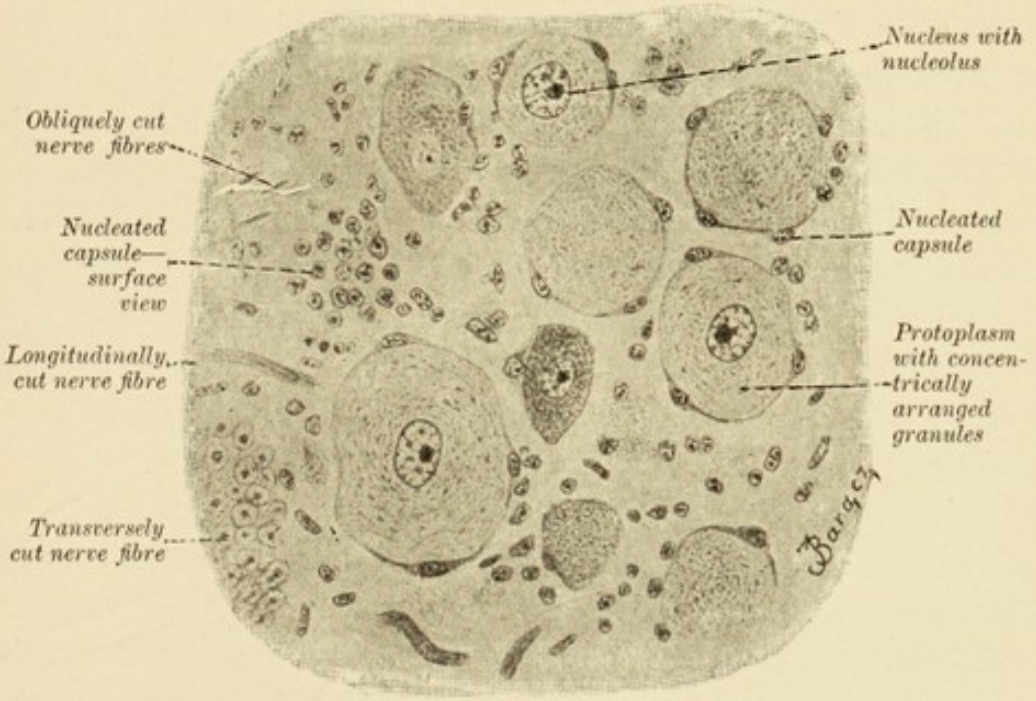
The *sympathetic nerves* consist for the most part of non-medullated fibres, although a certain number of medullated fibres may also be present. They are grouped together in

bundles, separated by connective tissue. The latter brings with it the blood-vessels, which break up into capillary networks in the perineurium and endoneurium. We find in the bundles of nerve fibres no true lymph-vessels. The lymph passes between the individual nerve fibres and in spaces between the lamellæ of the perineurium. *Nervi nervorum* are present in the nerve stems, and end partly in the vessels and partly in the connective tissue.

B. Ganglia.

By a *ganglion*, we mean a larger or smaller collection of nerve cells (*ganglion cells*) lying outside the central nervous system in the course of a peripheral nerve. It contains groups of ganglion cells and bundles of nerve fibres which run both to and from the ganglion. The connective-tissue perineurium

FIG. 226.



From a transverse section of a spinal ganglion of a rabbit. × 400.

of the nerve bundles passes over into the ganglion, carrying blood-vessels between the ganglion cells. Numerous capillaries, formed from the breaking up of the arteries, surround the individual cells.

We recognize two types of ganglia: the *spinal ganglion type* and the *sympathetic ganglion type.*

The *spinal ganglia* contain in the lower vertebrates (fishes) and in the embryos of higher vertebrates bipolar cells; while in the adult of the latter class the cells are almost all unipolar. The cell body is usually large (40–70 μ in diameter), and contains a vesicular nucleus with a distinct nucleolus (Fig. 226). Yellowish-brown pigment granules are also often found. There is always present a nucleated capsule around the cells, which is probably only a continuation of Schwann's sheath. It is made up of a single layer of flat connective-tissue cells (Fig. 226).

The relations of the processes of these cells and their branches have been investigated in recent years by Ramón y Cajal, Dogiel, and others. According to the results of this work, we can distinguish in the spinal ganglion two kinds of ganglion cells: one in which the cell process divides like the letter T or Y into two or three branches, which run in opposite directions. These branches are medullated, and run for some distance outside the ganglion. This cell belongs to type I. The cell of type II., whose process breaks up into numerous branches, is confined to the ganglion. None of the branches extends beyond its limits. They break up, on the contrary, into a plexus which surrounds the nucleated capsule of the cells of type I. From this plexus fine branches break through the capsule and surround the cell itself (*pericellular plexus*).

One cell of type II. is related usually to many cells of type I.; and many cells of type II. take part in the formation of the plexus around each cell of type I.

Besides these nerve elements already described, there are present in the spinal ganglia, endings of nerve fibres arising in sympathetic ganglia. These fibres break up into fine branches, which surround the cells, penetrate the capsule, and give rise to a pericellular network. These sympathetic fibres are related especially to cells of type II., and by means of them to cells of type I.

A similar structure as that described is found in the ganglion Gasseri, ganglion jugulare, plexus nodosus n. vagi, ganglion petrosum n. glosso-pharyngei, and the ganglion geniculi n. facialis.

The ganglion spirale cochleæ and ganglion vestibulare are distinguished from the spinal ganglia by the fact that the cells are bipolar.

The *sympathetic ganglia* contain multipolar ganglion cells which are smaller than those of the spinal ganglia (13–40 μ in diameter). They contain pigment granules and often two nuclei, and are surrounded, like the spinal ganglion cells, by a nucleated capsule. These cells give off an axone which possesses no medullary sheath and becomes a fibre of Remak; or may, on the other hand, become medullated and run peripheralward. All these fibres originating in sympathetic cells are to be regarded as cellulifugal. They end either in the smooth muscle of the intestinal walls, the vessels, the arrectores filorum, the iris, the corpus ciliare, etc., or in the mucous membranes, and the glands (liver, kidney, etc.), where they influence the secretory function.

The dendrites, of which the sympathetic cells possess many, are short. They branch many times and form at their ends fine networks which surround other cells. Besides the cells, we find in the sympathetic ganglia nerve fibres partly medullated and partly non-medullated. The latter arise from the cells of the ganglion itself, while the former are medullated cerebro-spinal fibres which have passed over to the sympathetic system through the rami communicantes. These are partly sensory and partly motor fibres. The sensory ones run to the periphery and end there; the motor end, on the contrary, in the sympathetic ganglion, where they form pericellular networks around the ganglion cells. In this way the sympathetic cells are influenced by the motor fibres of the cerebro-spinal system. The sympathetic nerve cells themselves, however, send their axones to the periphery, where they end freely, so that the cerebro-spinal fibres may be considered as motor

fibres of the first order, while the sympathetic axones are motor fibres of the second order.

It must be noted that in the sympathetic ganglia of amphibians there are unipolar cells without dendrites. The one process is to be regarded as an axone. It is surrounded by a spiral fibre which branches and forms an end plexus around the ganglion cells. These spiral fibres are derived from cells lying at a distance, and represent motor fibres of the first order. Among sympathetic ganglia are to be considered, the ganglion ciliare, splenopalatinum, oticum, and submaxillare.

C. Nerve-endings.

The nerve-endings are the final terminations of individual neurones. By means of these the nervous system is put into communication with other organs and tissues, and in the nervous system itself individual neurones or segments are joined together. It is through their agency that sensory impulses are sent to the central nervous system, and motor impulses transmitted from the nervous system to peripheral organs. We distinguish *free nerve-endings* in which the much-branched nerve filament receives or gives out impulses without the intervention of other tissues; and nerve-endings connected with some specialized *end apparatus*. In the latter the nerve-ending is combined with other tissues to form a special structure. We can classify nerve-endings according to the tissue in which they have been formed. Thus we find nerve-endings in: 1, epithelium; 2, connective tissue; 3, muscle; and 4, nervous tissue.

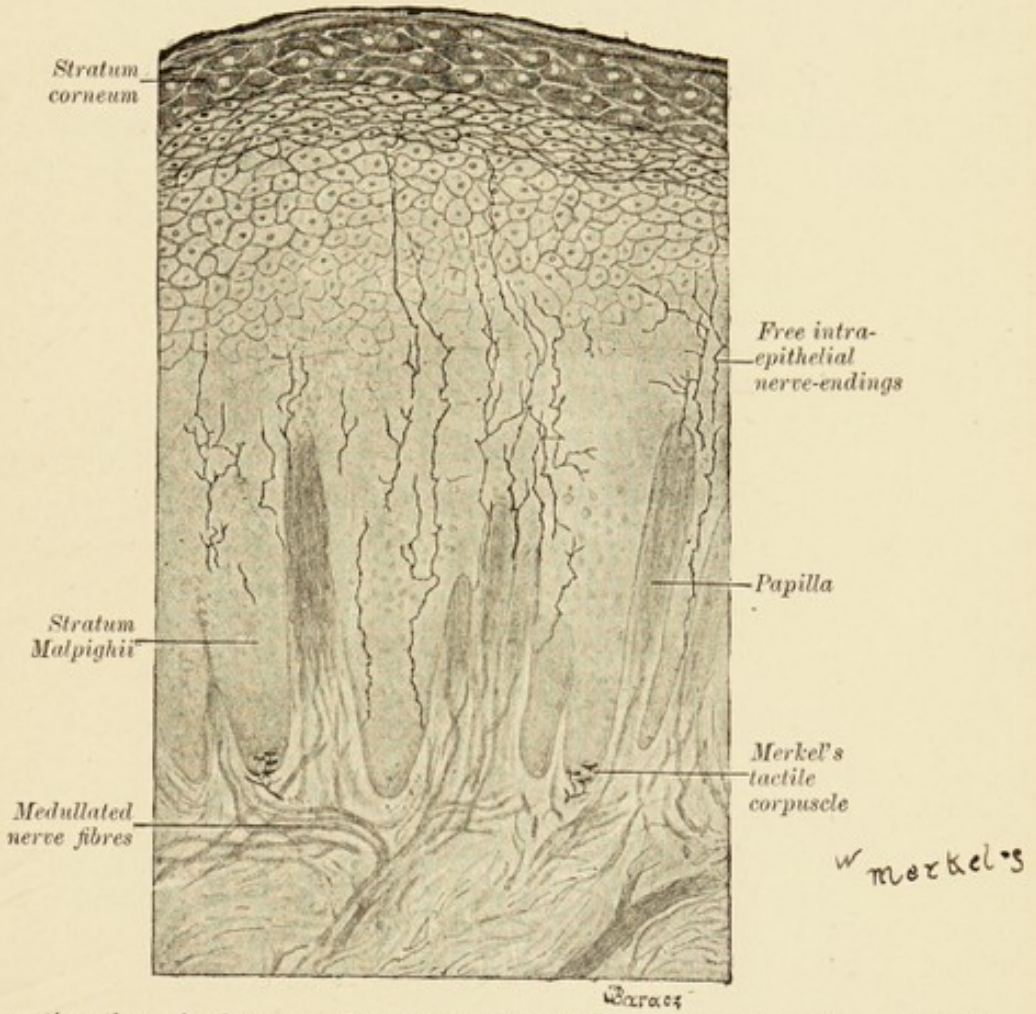
Finally, one may also consider nerve-endings from a physiological standpoint; but here unusual difficulties present themselves. A classification of nerve-endings according to their functions is not practicable as long as we are ignorant of the anatomical difference between centripetal and centrifugal nerve fibres. For example, in glands we do not know which endings are secretory and which are sensory. Also the division of sensory endings according to their powers of transmitting special sense impressions (temperature, pressure, pain, etc.) is

not of great value. In the following description the nerve-endings will be taken up according to the tissues in which they occur.

(*1*) *Intra-epithelial Nerve-endings.*

We can, in the first place, distinguish *free nerve-endings* (Fig. 227), which innervate especially the epithelium of the mucous membranes and epidermis. The nerve fibres run in bundles in the underlying connective tissue up to the margin of the

FIG. 227.



Vertical section through the skin of a pig's snout, which contains free intra-epithelial nerve-endings and Merkel's tactile corpuscles. Stained with gold chloride. × 300.

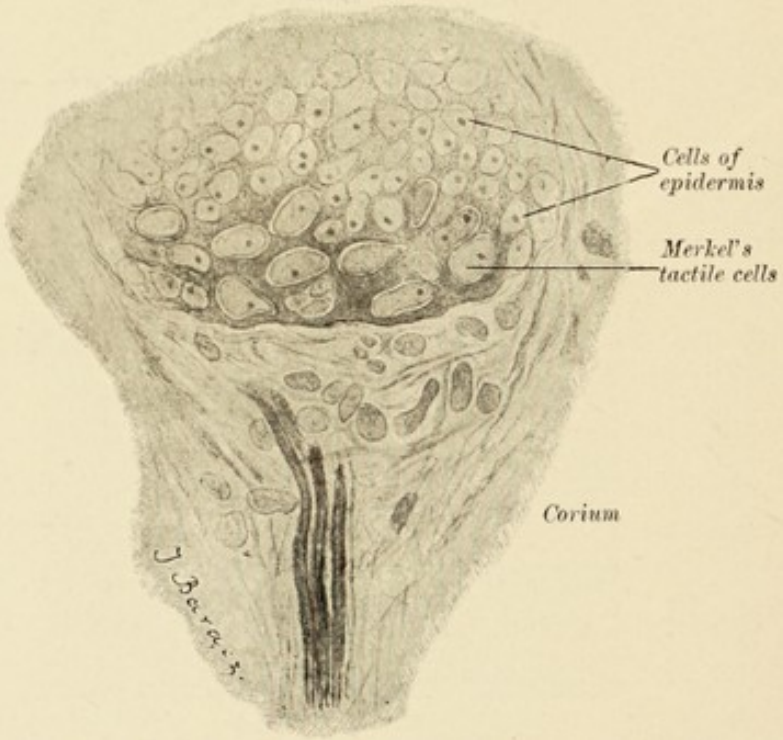
epithelium. Here they lose their various sheaths and the naked axis cylinders pass over into the epithelium and break up into fine branches. Such fibres reach often up to the outer layers of the epithelium (*e. g.*, in the epidermis to the stratum granulosum); in some cases (urinary bladder) they run back

to the deeper layers, where they end freely (Retzius). The ends of the fibres often show knob-like thickenings. Variations in thickness in the course of the fibre, the so-called *varicosities*, are, on the contrary, due to methods of preparation or to post-mortem changes.

Among the intra-epithelial nerve-endings must also be considered those of the glands. As investigations of late years have shown, the nerve fibres end on the surface of the gland cell, and never enter into it, as formerly was supposed. Often the terminations of fibres on the cell surface are thickened and flattened.

Also we find in the epithelium nerve-endings in the form of end corpuscles, the so-called *Merkel's corpuscles* (Figs. 227, 228, 229). These are found most numerously in the pig's

FIG. 228.



From a vertical section through the skin of a pig's snout. In the corium three medullated nerve cells run upward; on the epidermis lie many tactile corpuscles of Merkel. × 450.

snout and in the outer root sheath of tactile hairs. In the deepest layer of the epidermis we find cells which are distinguished from other epithelial cells by their greater size and clearness, and by their large vesicular nuclei. By means of

PLATE XLV.

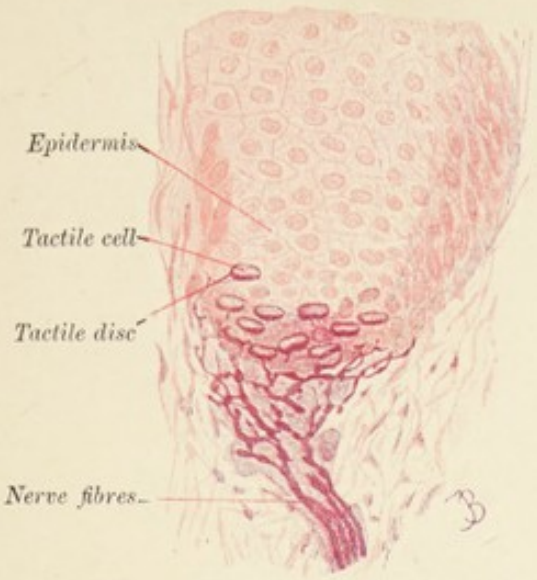


FIG. 229.—From a vertical section through the skin of a pig's snout. Gold chloride. × 300.

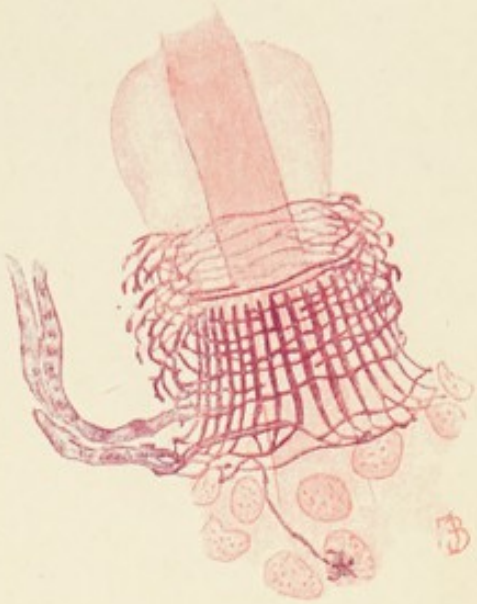


FIG. 231.—Nerve-ending on an ordinary hair of a white mouse. In the centre the hair is seen. Gold chloride. × 900.



FIG. 230.—Motor nerve-endings in a frog's muscle fibres. One nerve fibre supplies two muscle fibres. Gold chloride. × 300.



FIG. 232.—Nerve-ending on an ordinary hair of a white mouse. In the centre lies the hair. Gold chloride. × 1250.

special methods, such as the gold chloride method, and the methylene-blue stain, it can be demonstrated that the nerve fibres which lose their sheaths at the margin of the epithelium form at their ends shell-like thickenings, the so-called *tactile menisci*. Each meniscus lies closely applied to one of the large clear cells spoken of (*Merkel's tactile cells*) in such a way that its concave side is adjacent to the lower surface of the cell. The tactile cells are to be considered as modified epithelial cells, whose differentiation is initiated by the entrance of the nerve fibre into the epithelium (Szymonowicz).

As a transition form between the free intra-epithelial nerve-endings and Merkel's corpuscles may be mentioned the nerve-endings found in the frog's tongue. According to the work of Bethe, the nerve fibres are connected by flattened end plates with specialized epithelial cells. To this class belong also the nerve-endings in the mole's snout (*Eimer's organ*). The nerve fibres in this organ enter into combination with modified epithelial cells by means of lateral knob-like branches. Here must also be classified the nerve-ending in the organs of taste, hearing, and sight; for in these the branched and thickened ends of the nerves come into contact with the so-called *sense cells* or *neuro-epithelial cells*. In the olfactory organ the relation is otherwise (see later).

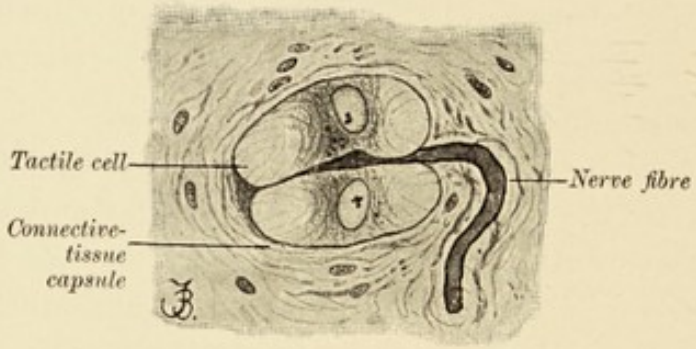
(2) *Nerve-endings in Connective Tissue.*

Here also there are free nerve-endings found in many parts of the body. The nerve fibre loses its sheaths in the connective tissue, and the naked axis cylinder breaks up into more or less numerous fine branches. Such endings are established in the tendons (Golgi, Cattaneo, and others), where the much-branched axis cylinder enters between the tendon bundles and ends freely. They are also found in the skin under the basal membrane and at the boundary between the epidermis and the true skin (Ranvier, Szymonowicz); in the endocardium (v. Smyrnow); in the hyaline membrane of the hair follicle (Figs. 231, 232); in the ciliary body; in the lungs, and in other

places. These free endings appear in the form of irregularly outlined end plates.

Other nerve-endings in the connective tissue have the form of corpuscles. The so-called *Grandry's corpuscles* have a certain similarity to Merkel's tactile bodies (Fig. 233). They are

FIG. 233.



Grandry's tactile corpuscle, composed of two tactile cells and a tactile sheath. From a vertical section through the cere of a duck's bill. × 400.

about 50 μ in diameter, and are surrounded by a connective-tissue capsule. Inside the capsule there are present one or more *tactile cells* and a *tactile disc* representing the final termination of the nerve fibre. The fibre loses its sheaths at the point where it passes through the connective-tissue capsule, and the naked axis cylinder spreads out at the end to form the tactile disc. It may undergo no division, or may give rise to two or more branches, each of which becomes flattened and forms a tactile disc. These axis cylinders are bounded on both sides by tactile cells. In a corpuscle that contains only one disc we find two tactile cells which are somewhat kidney-shaped. When two discs are present, three tactile cells are found; with three discs, four cells, etc. The largest corpuscles are found in the duck's bill, and contain four discs and five tactile cells. The tactile discs are thinner at their periphery than in the centre. In these discs primitive fibrils can be made out by special methods. These run into the disc from the place where the axis cylinder enters, like the rays of a fan. The discs and tactile cells lie parallel to the outer surface of the skin. The cells show in the central part of their

protoplasm curved fibrils, so situated that the convex sides are always toward the centrally placed nucleus. Grandry's corpuscles are found especially on the cutis of the cere of the bill of aquatic birds, such as the goose and duck. They occur also in the tongue. The tactile cells of Grandry's corpuscles are of connective-tissue origin, as shown by Szymonowicz. Thus their origin is entirely different from that of Merkel's tactile bodies.

The other kinds of nerve-endings in connective tissue may be grouped under what are known as *end bulbs*. In all terminations of this sort we can distinguish three constituents, namely, the axis cylinder, a thickened structure surrounding this, and a capsule enclosing the whole. The axis cylinder usually ends in a small swelling. The capsule is composed of connective tissue, and contains a small number of connective-tissue cells. These end bulbs are usually long, and often spirally coiled. In some cases the axis cylinder breaks up into many branches, each of which terminates in a thickening, and is surrounded by connective-tissue sheaths. End bulbs of this sort are found in the skin of the pig's snout (Szymonowicz) and in the conjunctiva (Krause).

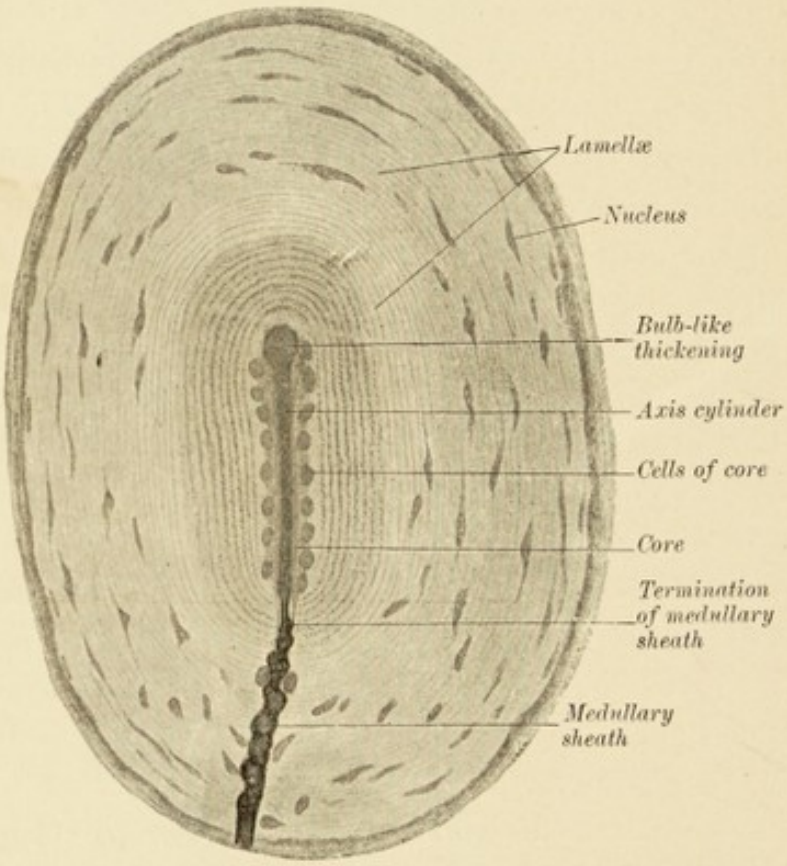
End bulbs of a more complex character are found in the genitalia, especially in the glans penis and the clitoris. In these so-called *genital nerve corpuscles* the axis cylinder breaks up into many branches which, according to some authors (Retzius), end freely, and according to others (Dogiel), form a dense network.

The so-called *Meissner's tactile corpuscles* (Fig. 244), which occur especially in the papillæ of the skin, may be considered as end bulbs. They are ellipsoidal corpuscles, often more than 100 μ long and 50 μ wide. They are surrounded by a thin nucleated connective-tissue capsule which contains a gelatinous inner sheath. At the lower pole of the corpuscle, one to four nerve fibres are usually present. They lose their medullary sheath immediately after entering the connective-tissue capsule. The naked axis cylinder takes a spiral course and breaks up into many branches in the inner sheath. There can usually

be seen numerous varicosities, which give the inner sheath the appearance of containing nuclei.

Ruffini's corpuscles are in some respects similar to Meissner's tactile bodies. They are found at the border of the cutis and subcutis, and also in the subcutis itself. They are about 1.35 mm. in length. The nerve fibres, after losing their sheaths, divide into numerous varicose branches which end freely by small knob-like thickenings. The entire corpuscle is surrounded by a thin connective-tissue capsule.

FIG. 234.



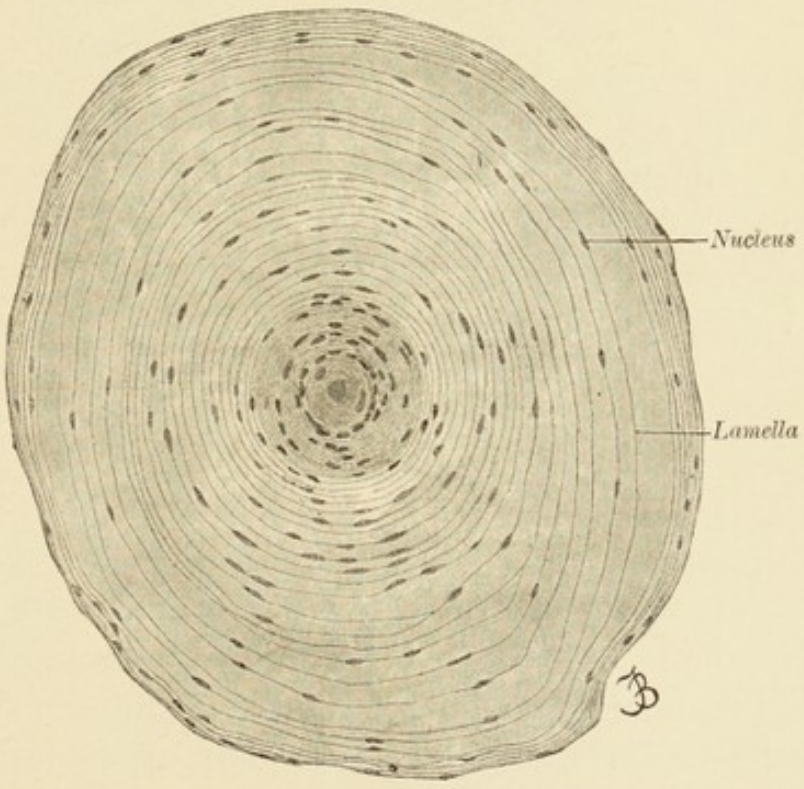
Herbst's corpuscle from the cere of a duck's bill. × 450.

Other end bulbs described as *Golgi-Mazzoni corpuscles* are quite similar to these. They possess, however, more strongly developed connective-tissue capsules.

Two closely related forms, the *Herbst corpuscle*, and the *Vater-Pacini corpuscle*, are end bulbs in which the axis cylinder is not at all or only slightly branched, and the connective-tissue capsules are strongly developed in the form of concentric lamellæ.

Herbst's corpuscles (Fig. 234) are found, like Grandry's corpuscles, usually in the skin of aquatic birds. They are ovoid bodies, about 140 μ long and 80 μ wide. The inner part contains an axis cyclinder thickened at the end, and surrounded by the inner sheath. The latter possesses a series of cells on its outer surface, which seem to have the same function as the tactile cells in Merkel's corpuscles. The outer lamellated part consists of numerous concentrically arranged connective-tissue lamellæ, of which the outer contain a few flat cells. The nerve fibre enters at the end of the corpuscle, and passes together with the Schwann's sheath and medullary sheath through the outer lamellated part. Both layers end at the boundary between the inner sheath and the lamellæ.

FIG. 235.



Transverse section of a Vater-Pacinian corpuscle from a cat. In the centre lies the axis cylinder cut across. × 200.

The Vater-Pacinian corpuscles (Fig. 235) are slightly different from those of Herbst. Instead of the large tactile cells surrounding the core, we find a series of flat cells. The lamellated part is developed more strongly, and in a large

corpuscle there may be as many as sixty lamellæ. Between the lamellæ there is a clear serous fluid. Each lamella is lined on its inner surface with flat epithelioid cells lying near one another. The outlines of these can be demonstrated by treatment with silver nitrate. Blood capillaries have been found in the lamellated part. These corpuscles are over 2 mm. long and are easily visible to the naked eye. They are found in the connective tissue under the skin of the palms of the hands and soles of the feet, especially in the fingers and toes. They occur also in the joints, the periosteum, in the mesentery and pancreas of the cat, etc.

(3) *Nerve-endings in Muscle.*

(a) *Motor Nerve-endings.*

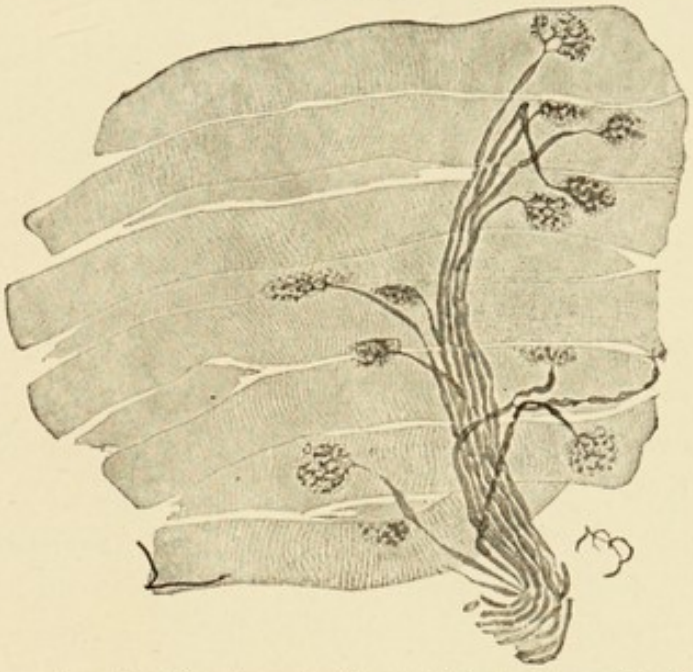
In *smooth muscle* the nerve-endings have the following arrangement: The nerve fibre enters between the muscle bundles, and, dividing there, passes between the individual muscle cells. The whole fibre shows varicosities throughout its course, and ends freely on the surface of the cell by means of end thickenings. The latter are in direct connection with the cell, although the termination of the fibre never reaches the inside of the cell. It therefore has no connection with the nucleus of the muscle cells, as was claimed formerly.

In *heart muscle* the motor nerves end on the surface of the cell in small swellings. In most cases it is probable that each muscle cell possesses a different nerve fibre. By an anastomosis of the nerve fibres a terminal network is formed, from which the final end fibres proceed to the muscle cells.

In *striated skeletal muscle* bundles of medullated nerve fibres form networks in the perimysium. Terminal fibres proceed from these networks to the individual muscle fibres, on whose surface they end (Fig. 236). The sheath of Schwann, as well as that of Henle, ceases before it reaches the muscle fibre. According to some authors, however, these two sheaths fuse with the sarcolemma. The medullary sheath ends where

the nerve fibre enters the muscle fibre. The axis cylinder breaks up into an end arborization. The relation of this to the protoplasm of the muscle fibre is described variously by different authors. According to some, it lies on the sarcolemma. Other authors who believe that the sarcolemma and the sheath of Schwann fuse together, hold that the end arborization of the axis cylinder lies under the sarcolemma in immediate contact with the sarcoplasm. There can often be observed at the place where the nerve fibre enters the

FIG. 236.



Motor nerve-endings in striated muscle fibres (abdominal muscle) of a rat. × 170.

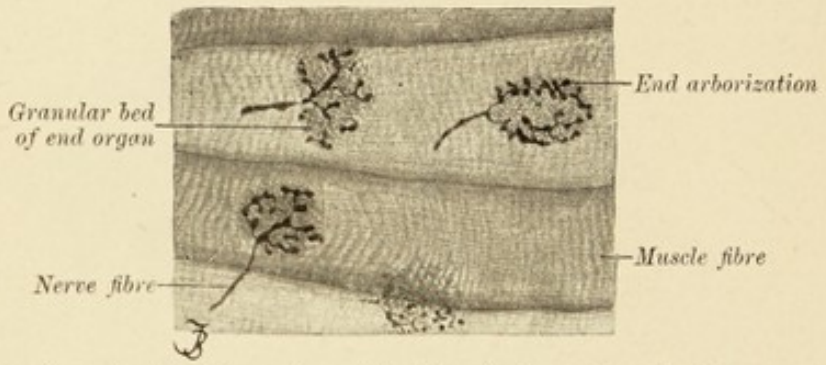
muscle fibre an elevation, which in optical section has the form of a hillock. This was observed first by Doyère in the muscles of insects, and hence is known as *Doyère's hillock*.

The end arborization of the axis cylinder varies in form according to the animal in which it is observed. In amphibians the branches are more or less straight and simple (Fig. 230); in reptiles, birds, and mammals, on the contrary, they are S-shaped (Fig. 231).

Around the end arborization there is a larger or smaller quantity of a finely granular substance, which is called the *granulosa* or *granular bed*. Authors differ as to the significance of

this substance. Those who claim that the end arborization is under the sarcolemma, consider the granulosa to be a collection of sarcoplasm. Others, on the contrary, who believe that the axis cylinder ends on the sarcolemma, regard the granulosa as a product of the neuroplasm. Nuclei are present in this substance, and are said by some to belong to the muscle, and by others to the sheath of Schwann. Each muscle fibre possesses usually only one motor nerve-ending. Where, however, more

FIG. 237.



Motor nerve-endings in the fibres of a rat's abdominal muscle. In the upper fibre two end plates are to be seen.

than one nerve fibre approaches a muscle fibre, there are present in the latter two or more nerve-endings (Figs. 235 and 236). Often, on the contrary, one nerve fibre innervates two muscle fibres (Fig. 229).

(*b*) *Sensory Nerve-endings.*

Muscle Spindles.—These structures were described first by v. Kölliker as bundles of small muscle fibres closely related with nerve fibres. They were called by him *muscle buds* (Muskelknospen). Later on, Kühne observed them, and proposed the name now in use. Since this time they have been frequently found and regarded variously as growth centres, as pathological structures, and as sensory nerve-endings. At the present time they are regarded usually as sensory end organs, as proven by the investigations of Kerschner, Ruffini, and Sherrington. It has been suggested that their function is connected with the muscle sense. The following account is based on a description given by Huber.

The muscle spindle consists of the following structures: capsule, periaxial space, axial sheath, intrafusal muscle fibres, and spindle nerves (Fig. 238).

The *capsule* (perimysial sheath) consists of white fibrous connective tissue arranged in six to eight consecutive layers. Practically no elastic fibres are present. In mammals the capsule is usually thicker than in lower vertebrates. The capsule is continuous with a connective-tissue sheath surrounding the

FIG. 238.



Cross-section of muscle spindle from plantar muscle of cat. (After Huber.) *c*, capsule; *a. s.*, axial sheath; *i. f.*, intrafusal fibre; *p. a. s.*, periaxial space; *s. n.*, medullated spindle nerve; *s. m.*, ordinary muscle fibres.

muscle fibres which enter the muscle spindle at its proximal end. The long axis of the spindle lies parallel to that of the muscle fibre. The distal end is continuous with the perimysium internum.

The *periaxial space* is a lymph space described by Golgi and Sherrington lying immediately under the capsule. It is widest at the centre of the spindle.

The *axial sheath* consists of a layer of fine white fibrous connective tissue enclosing the *intrafusal muscle fibres*. The latter vary in number (one to twenty), and are smaller than ordinary muscle fibres. They are rich in protoplasm, and are formed by the division of ordinary muscle fibres entering the spindle. They run more or less parallel to the long axis of the spindle. A sarcolemma is not always present (Sherrington). At the periphery of the fibre there is, according to Sherrington, a series of muscle nuclei. These are regarded by Huber as be-

longing to the connective-tissue sheath of the fibre. Fibril bundles are often absent in the centre of the fibre. Here there is a core of sarcoplasm containing a number of nuclei. This is more noticeable in the equatorial region of the spindle than at either pole. In comparing this structure with that of developing muscle fibres, as described in a previous section, it will be noted that there are many points of resemblance.

Spindle Nerves.—These are large medullated nerve fibres which break up in the muscle spindle. They are spinal ganglion fibres which do not degenerate on the destruction of motor fibres supplying the muscle (Sherrington). Two to eight nerve fibres enter each spindle near the proximal end. The capsule of the spindle becomes continuous with Henle's sheath or with the connective tissue covering a bundle of fibres. Medullated fibres pass through the axial sheath with which the remains of the connective-tissue sheath become continuous. Within the axial sheath the fibres may become non-medullated. The ultimate nerve-endings are non-medullated branches which occur between the sarcolemma and the connective-tissue sheath surrounding the intrafusal fibres. According to Ruffini, the terminations of these branches may be spiral, annular, or flower-like. In the first kind the nerve fibre flattens out and winds spirally around the intrafusal fibre. This is the most characteristic ending, and that described as annular is only a modification of this. The flower-like endings are formed by a branching of the spiral fibres.

The *blood supply* of the muscle spindle is well developed. Vessels enter the capsule and give off branches which form a network surrounding the spindle. Other branches proceed to the intrafusal fibres.

(4) *Nerve-endings in Nervous Tissue.*

Under this section the general relation of the neurones to one another in the central nervous system must be considered. Fig. 239 shows the relation of the sensory neurones to the motor. This may involve only two neurones, or there may be

a secondary neurone interposed. In the first case we have the so-called *reflex arc* (Fig. 239, *a*, *b*). The stimulus is carried from the nerve-endings in the skin, through the cellulipetal fibre, to the spinal ganglion cell. From here it is transmitted through the dorsal root to the gray matter of the cord, where

FIG. 239.

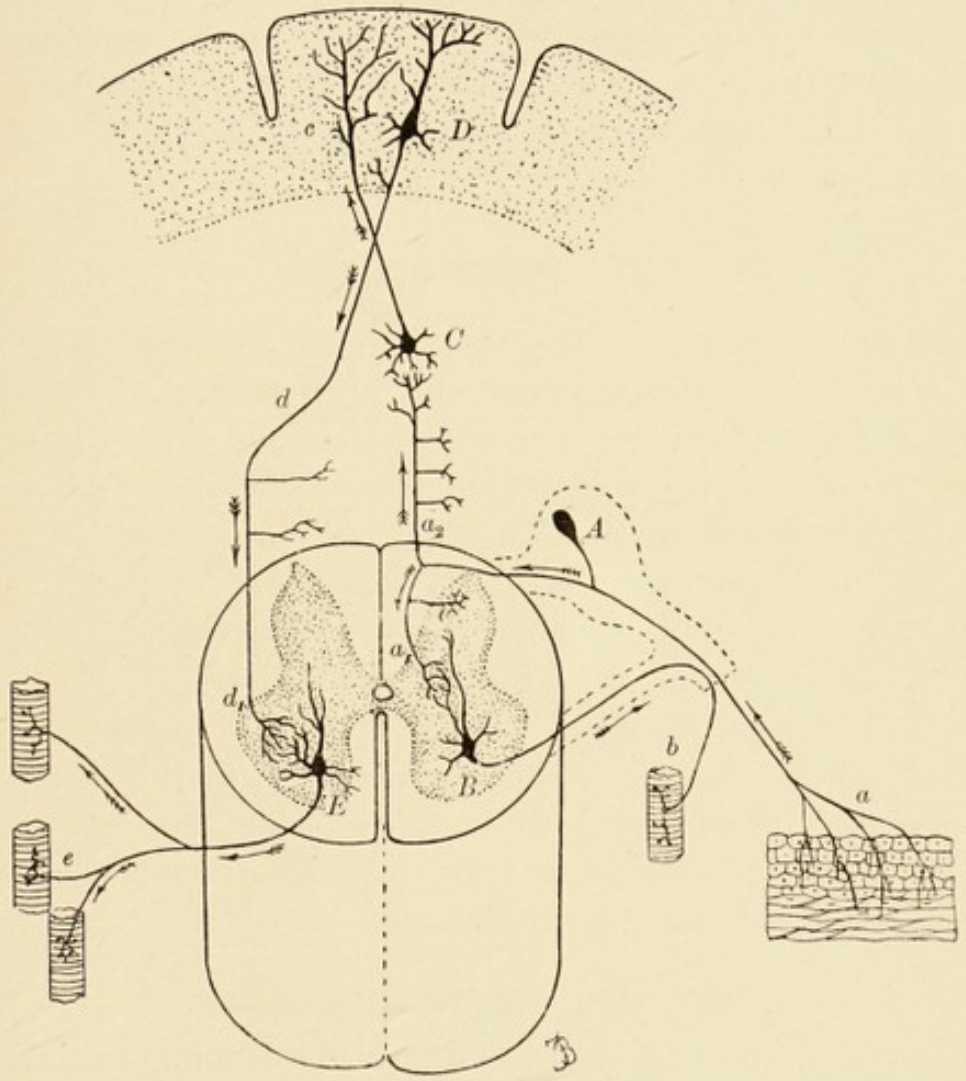


Diagram showing the relations of sensory and motor neurones in the central nervous system. The path of the impulse is indicated by arrows. (After Ramón y Cajal.)

it is passed on to the dendrites of the motor neurone *B*, which lies in the ventral horn. The stimulus then reaches the cell, and is transmitted by means of the axone of that cell to the motor nerve-ending in the muscle *b*. In this way reflex movements take place. This relation is different when the stimulus is transmitted to the cortex of the brain, and a voluntary move-

ment results. In this case at least four neurones form a part of the whole path. The sensory stimulus passes through the cell *A* upward in the white matter of the cord. The fibre a_2 carries it to a neurone of the second order, *C*, which transmits it in turn to the cortex, where the fine branches come into contact with the dendrites of a motor cell, *D*. The axone of this pyramidal cell *d* passes down and crosses over in the pyramidal tract, to come into relation with the dendrites of a motor cell of the first order *E* in the ventral horn of the cord. From this cell the motor impulse is carried out to the nerve-endings in the voluntary muscle *e*.

VIII. SENSE ORGANS.

The sense organs are complex structures, each of which consists not only of the essential end apparatus of the sensory nerve, but also of parts which support and aid this in its function. We distinguish five sense organs, namely:

1. The tactile organ;
2. The organ of sight (visual);
3. The organ of hearing (auditory);
4. The organ of taste (gustatory); and
5. The organ of smell (olfactory).

The tactile sense is located in the skin, so that the latter together with its various nerve-endings forms the tactile organ. We shall, therefore, describe here the skin, which also acts as a protective organ for the whole body.

1. THE SKIN—THE TACTILE ORGAN.

Here must be considered not only the outer skin (integumentum commune), but also its appendages (the nails and the hairs), and its glands (sebaceous and sweat glands).

(*a*) The Outer Skin.

The skin covers the whole outer surface of the human body. It consists of two parts, a connective-tissue part (*derma* or *cutis*) of mesodermal origin, and an epithelial part (*epidermis*) of ectodermal origin (Fig. 241). The cutis may be divided into

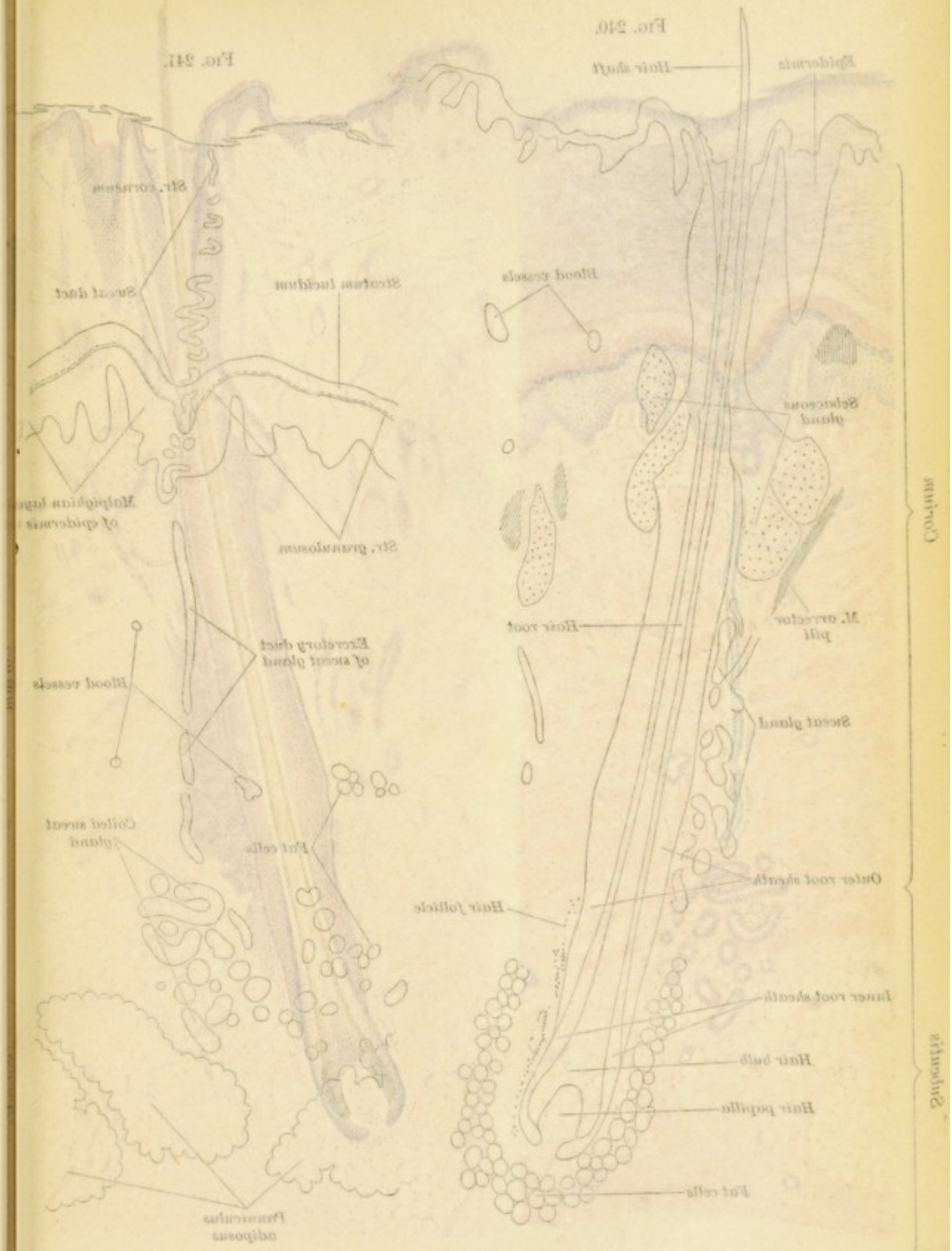


FIG. 240.—From a cross-section of the human scalp. The hair is cut throughout its whole length. Hæma
toxylin and eosin. × 35.

FIG. 241.—Section through skin of adult human finger, cut at right angles to the surface. Hæmatoxylin and
eosin. × 70.

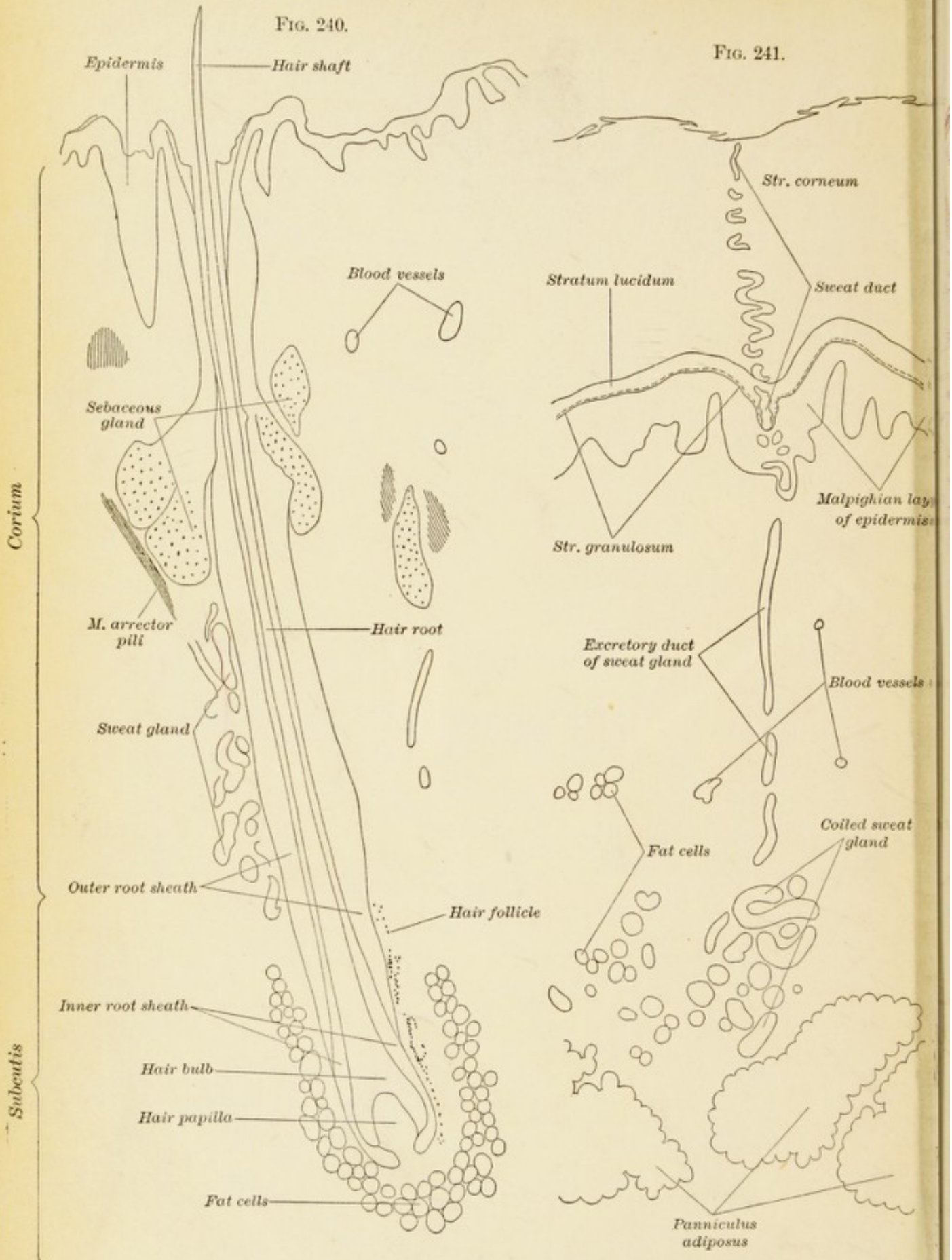


Fig. 240.—From a cross-section of the human scalp. The hair is cut throughout its whole length. Hæmatoxylin and eosin. × 55.

Fig. 241.—Section through skin of adult human finger, cut at right angles to the surface. Hæmatoxylin and eosin. × 70.



Szymonowicz. Histology

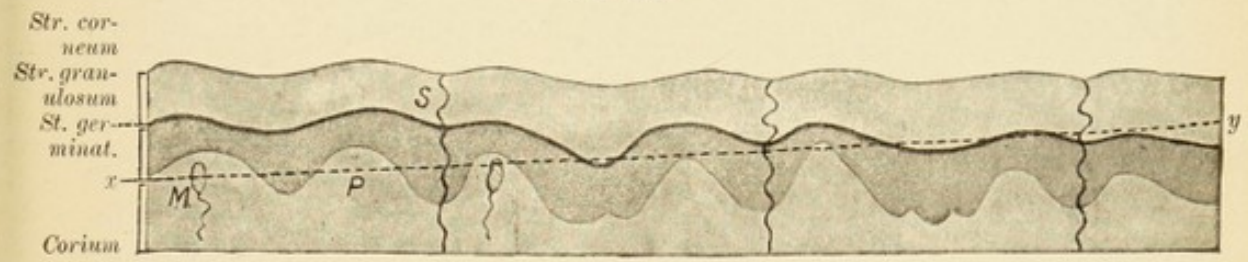
J. Barqcz ad nat. del.

Lith. Anst. v. Werner & Winter, Frankfurt a/M.

a compact layer, the so-called *corium*, and a deeper-lying loose layer, the *tela subcutanea*.

The boundary between the connective-tissue part and the epidermis is usually uneven. This is caused by the fact that the corium immediately under the epidermis is raised into conical or round *papillæ* (Figs. 241, 243, 244). These extend into the epidermis, and are of different size in various parts of the body. The largest are in the planta pedis, vola manus, glans penis, etc., where they reach a height of 0.2 mm. In other

FIG. 242.



Diagrammatic section through the skin. This figure serves to show how the section in Fig. 240 is cut. The line *x–y* gives the direction of the section. *S*, sweat gland; *P*, papilla; *M*, Meissner's corpuscle.

places (*e. g.*, in the skin of the face) they are inconspicuous. We divide the papillæ, according to whether they contain loops of blood capillaries or nerve corpuscles, into vascular and nervous papillæ.

The *corium* consists of white fibrous connective tissue, the fibre bundles of which cross one another in different directions. In the network thus formed we find connective-tissue cells of various kinds, and a plexus of elastic fibres which is denser in the deeper layers.

The corium may be divided into two layers: the *pars papillaris* and the *pars reticularis*. The first, which lies immediately under the epidermis, owes its name to the fact that it contains the papillæ; while the pars reticularis is so named on account of the net-like arrangement of the connective-tissue bundles. These bundles cross one another in such a way that there are left rhomboidal spaces or meshes (Lange's spaces), which are filled with sweat glands or fat. The two layers of the corium pass into one another without any sharp line of demarcation.

In the corium we find in certain places (*e. g.*, in the face) striated muscle fibres, extending up to the pars papillaris. There occur also smooth muscle cells, which run in bundles parallel to the surface and form special networks in the skin of the scrotum (tunica dartos) and the nipple. The smooth muscles of sweat glands and those which are connected with hairs will be spoken of later.

The *subcutaneous tissue* (tela subcutanea) which joins the skin to the neighboring parts is made up of interlacing connective-tissue strands, in the meshes of which fat is found (Fig. 241). When the fat reaches a considerable development, this layer is spoken of as the *panniculus adiposus.* In a few exceptional instances the fat is entirely wanting in the subcutaneous tissue (*e. g.*, in the outer ear, the scrotum, etc.). The more horizontal—*i. e.*, parallel to the surface of the skin—the connective-tissue bundles run, the longer they are and the greater is the movability of the skin. The wrinkling of the skin is dependent on the length of these bundles. If they are short, they run more nearly at right angles to the surface of the skin, and the latter cannot be moved or thrown into folds.

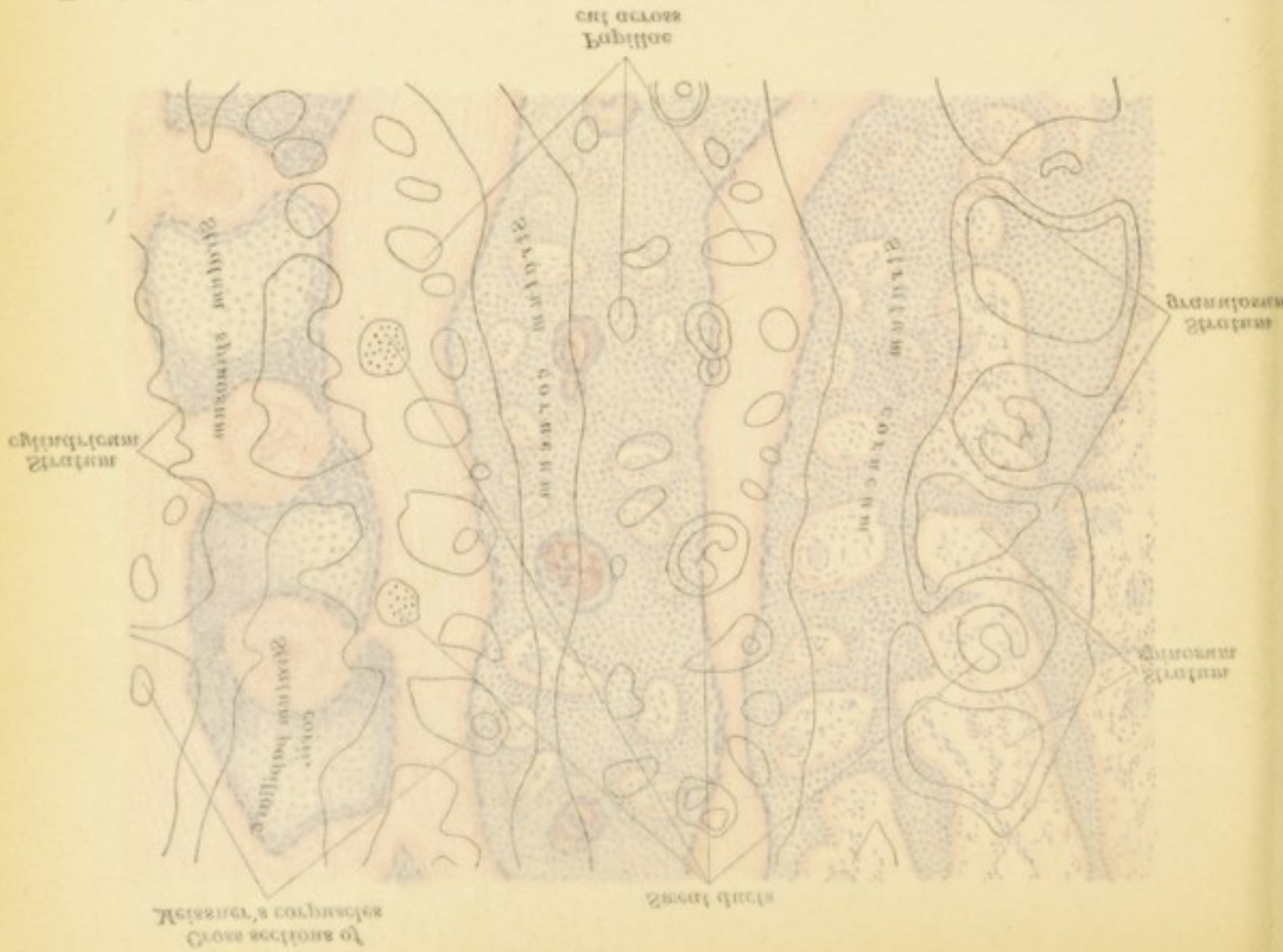
At the boundary between the corium and the epidermis we find a very thin structureless membrane, the so-called *basal membrane.*

The *epidermis* is composed of a many-layered epithelium. Two parts in this may be distinguished: the outer one, which consists of corneous cells (*horny layer, stratum corneum*), and the deeper-lying part, the so-called *Malpighian* layer (stratum Malpighii, stratum germinativum). The latter may again be divided into many layers, which, spoken of from below up, are the *stratum cylindricum, stratum spinosum, stratum granulosum,* and *stratum lucidum* (Fig. 244).

The degree of development of the horny layer and the Malpighian layer differs in various parts of the body. Usually the latter is the thicker of the two, but in the vola manus and the planta pedis the horny layer is greatly thickened. The two lower layers of the stratum Malpighii consist of prickle



FIG. 343.—From a horizontal section through the epidermis of a human finger. The section is almost parallel to the surface of the skin, as shown by the line x in Fig. 345. × 88.



Cross sections of Meissner's corpuscles

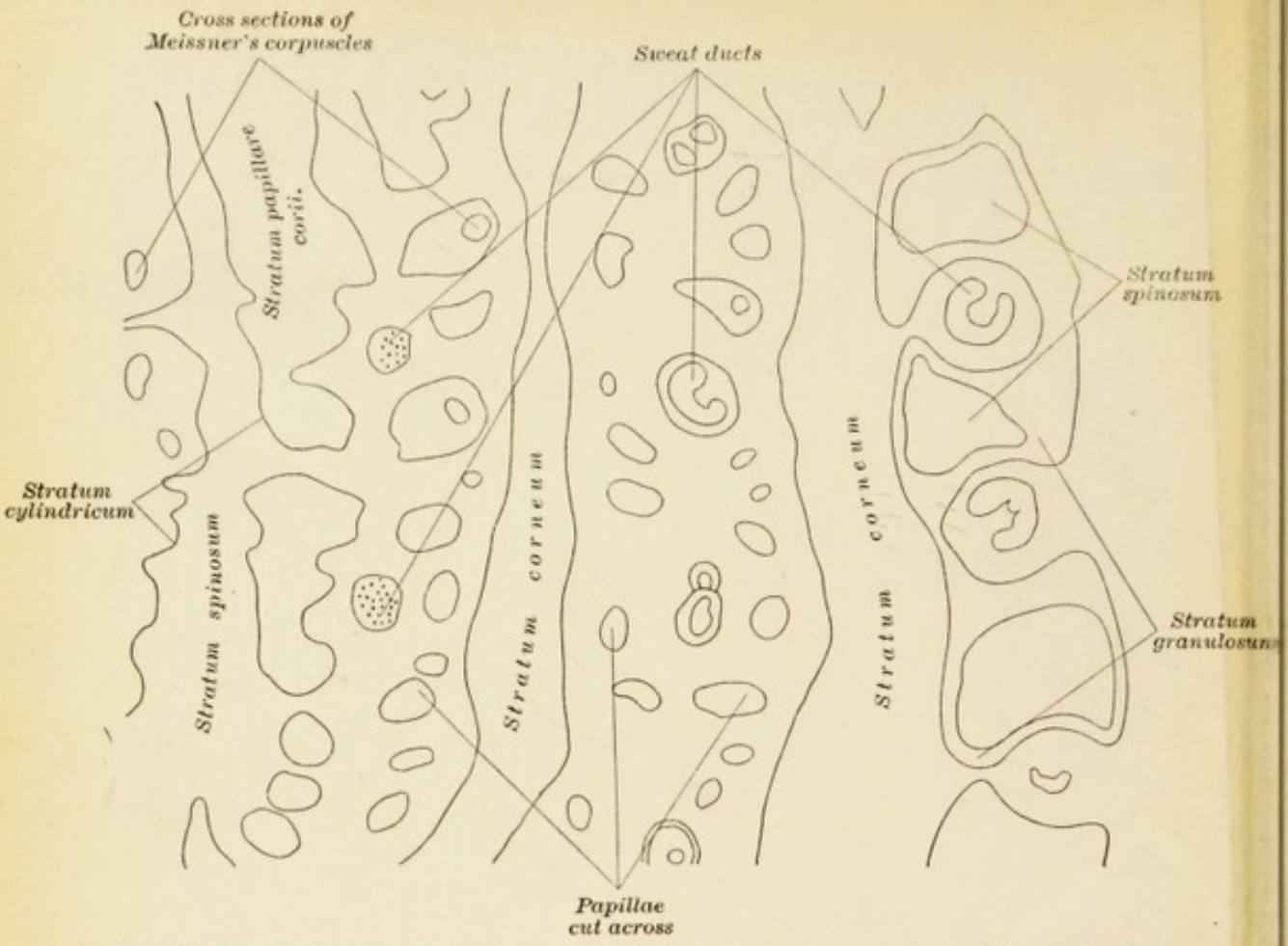


FIG. 243.—From a horizontal section through the epidermis of a human finger. The section is almost parallel to the surface of the skin, as shown by the line *x* in Fig. 242. × 88.

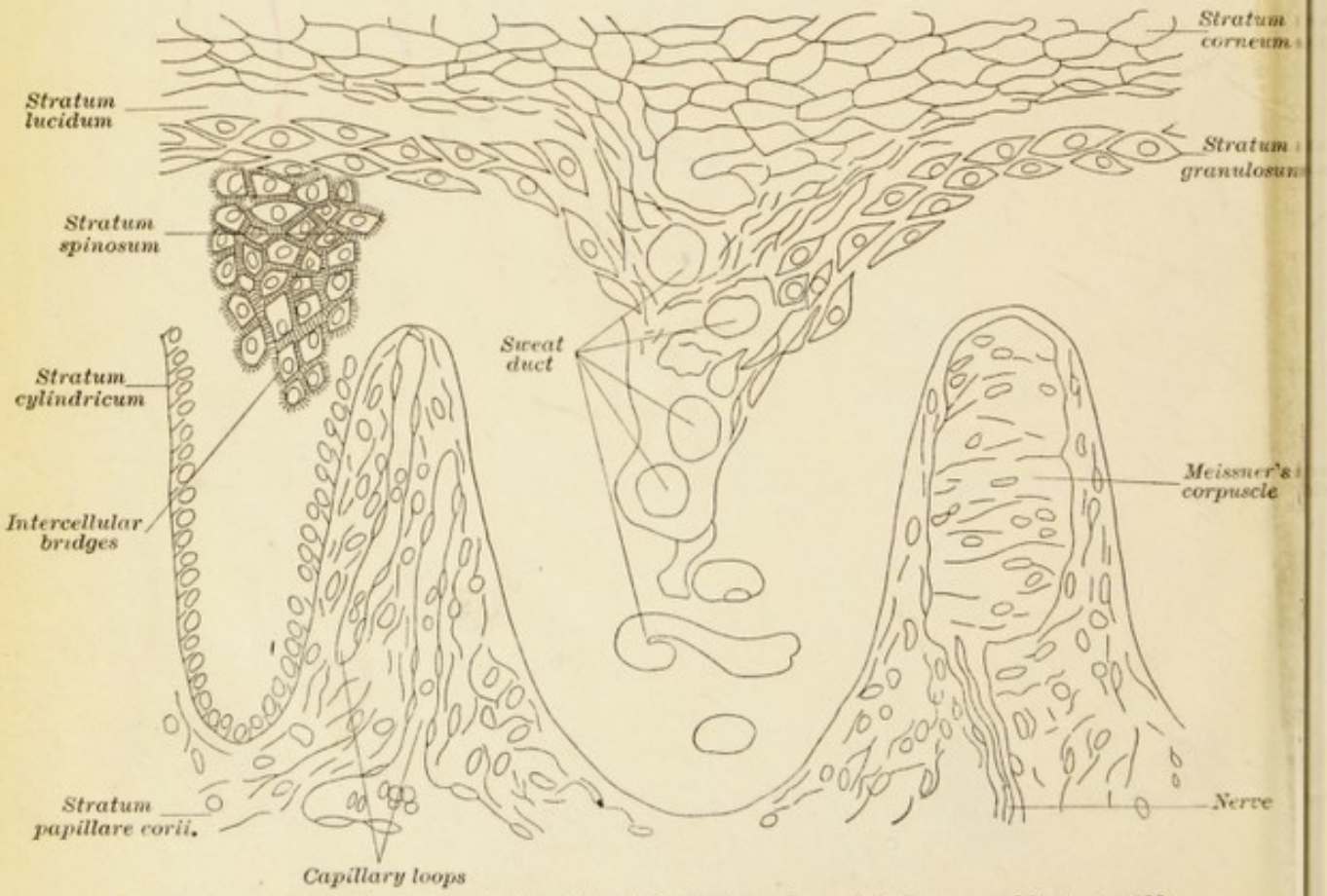


FIG. 244.—From a section through the skin of the hallux of an adult human subject. × 400.





J. Barącz ad nat. del.

Szymonowicz, Histology

Lith. Anst. v. Werner & Winter, Frankfurt a/M.

cells. The lowermost layer has quite high cylindrical cells lying beside one another. The prickles directed downward, with fine fibres extending between them from the corium, as well as the presence of cement substance, provide a means of joining the epidermis firmly to the corium. The *stratum spinosum*, whose cells have been described above, consists of many rows of cells which fill up the free spaces between the papillæ. Above this is the *stratum granulosum*, consisting usually of two or three rows of flattened cells. These possess refractive granules, which indicate the beginning of the process of cornification. They are spoken of as *keratohyaline granules*, and are regarded by some authors as modified cell protoplasm, and by others as a product of the dying nucleus of the cell. This latter view finds some support in the fact that often the development of keratohyaline granules is accompanied by a poverty of the nucleus in chromatin and its final disintegration.

Above the stratum granulosum there is a refractive layer, the *stratum lucidum*, which consists of two or three layers of flat cells. These possess disintegrating nuclei, and contain a homogeneous substance called *eleidin*, which is derived from the keratohyaline granules. The latter increase in size and coalesce to form a semifluid substance, which develops new staining reactions. Keratohyaline stains with hæmatoxylin, while eleidin is colored by eosin or nigrosin. In this layer the boundaries of the cells are often not distinct. The stratum lucidum is often wanting in places where the epidermis is thin. It forms a direct transition to the horny layer.

The cells of the *horny layer* (*stratum corneum*) are like thin scales and show no remains of nuclei. The whole cell is made up of *keratin*, which, as opposed to eleidin and keratohyaline, can be dissolved neither in trypsin nor in pepsin. In sections treated with osmic acid the horny layer shows on its upper and under surfaces, as well as on its sides, a black boundary, which is due to impregnation of the dried layer with fat. The middle part of the horny layer cannot be blackened by osmic acid.

The horny cells are continually rubbed off from the surface of the skin, and new cells are added from the basal layers of the stratum Malpighii. In the lowest layers of the epithelium we meet with karyokinetic figures. The young cells are pushed out by still younger cells toward the surface.

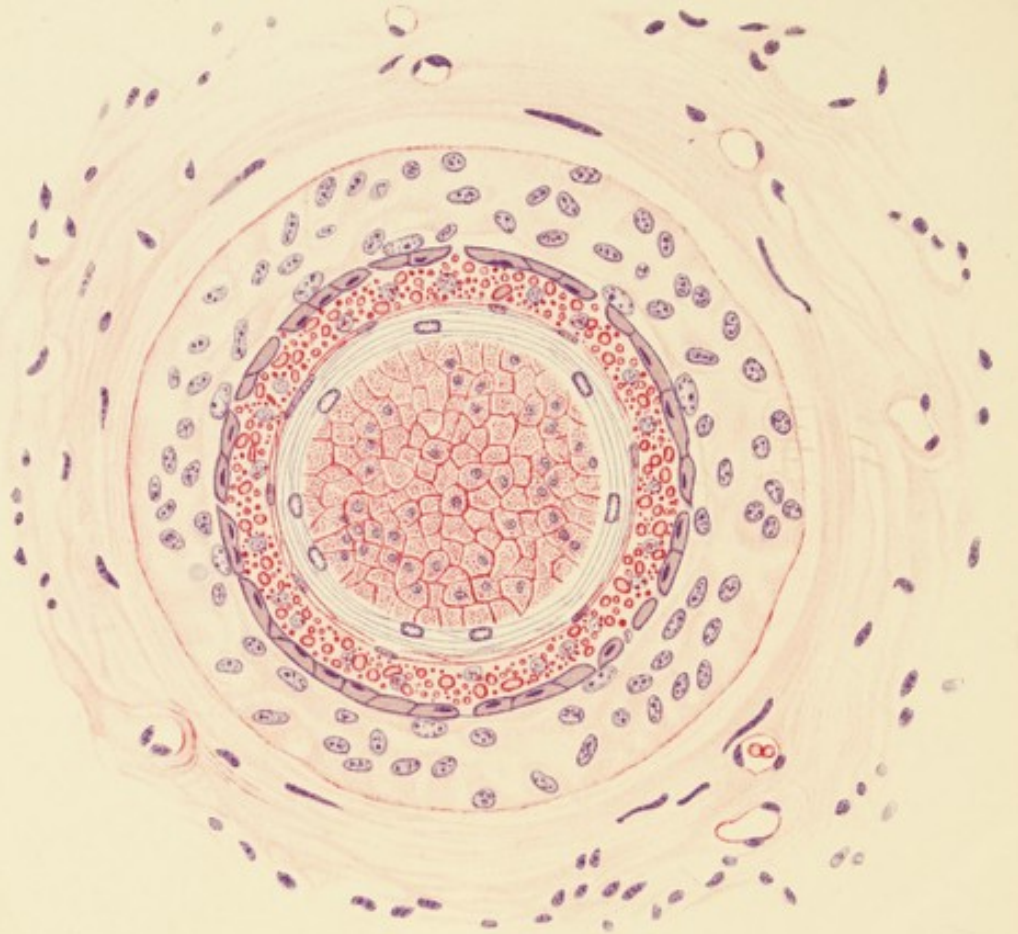
The skin of the white race is in various places colored brown by the deposition of *pigment* (*e. g.*, the skin of the nipple, the labia majora, the scrotum, and around the anus). Much coloring-matter is found in the skin of the negro. Here very fine pigment granules are present between and in the epithelial cells of the lowest layer of the stratum Malpighii, and also in the outer parts of the corium in branched connective-tissue pigment cells. The origin of the pigment is not definitely known. Some authors claim that the epithelial cells have no power of producing pigment, and that the pigment granules are imported by connective-tissue cells. Other authors, on the contrary, hold that the cells of the epidermis are capable of producing pigment granules without the assistance of the connective-tissue cells, since it is an undoubted fact that the pigment of the retina is a product of epithelial cells.

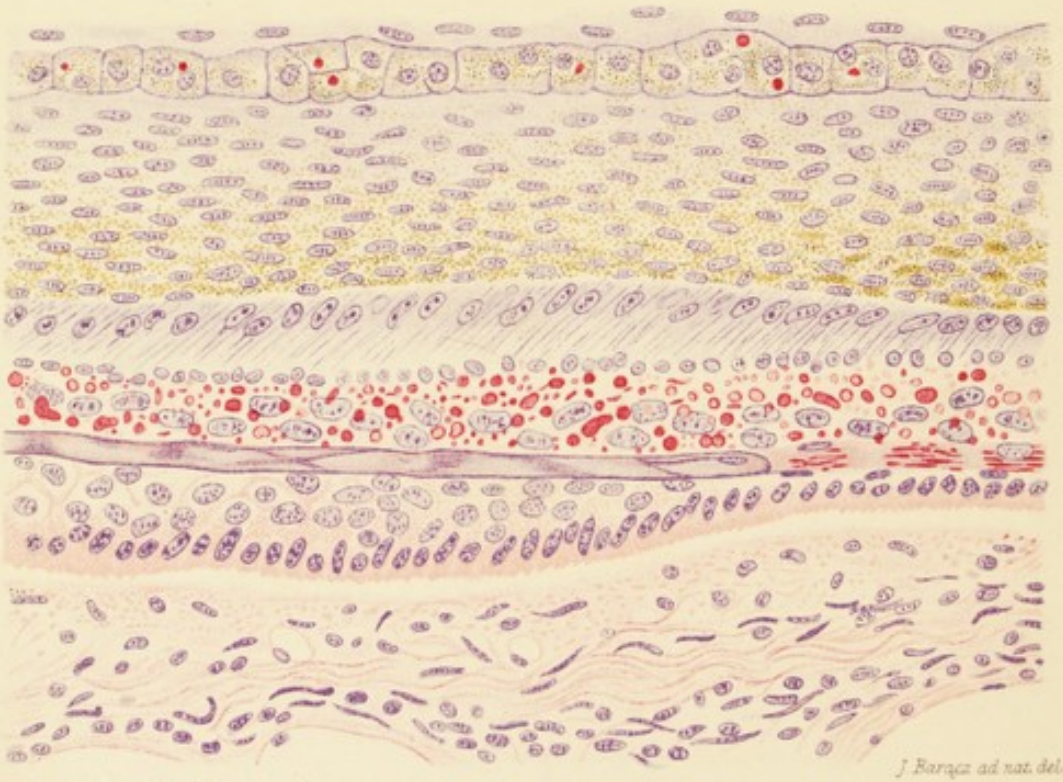
(*b*) Hairs.

The hairs are thread-like structures formed from the epidermis, which are distributed over the whole surface of the body with the exception of the palms of the hands, the soles of the feet, the red borders of the lips, and the inner surface of the præputium.

A part of the hair (*hair root*) is buried in the skin; while a part projects beyond the surface (*hair shaft*) (Fig. 240). The lower part of the hair root is thickened to form a rounded, knob-like structure, the *hair bulb*. Into this there is pushed from below a small round mass of the corium, which is called the *hair papilla*. In small, fine hairs, the root extends into the corium, while the roots of large hairs reach as far as the subcutaneous fat.

A true hair consists of horny epithelium. The part which is situated in the skin is surrounded by several layers of epi-





J. Baraçz ad nat. del.

Szymonowicz, Histology

Lith. Anst. v. Werner & Winter, Frankfurt a/M.

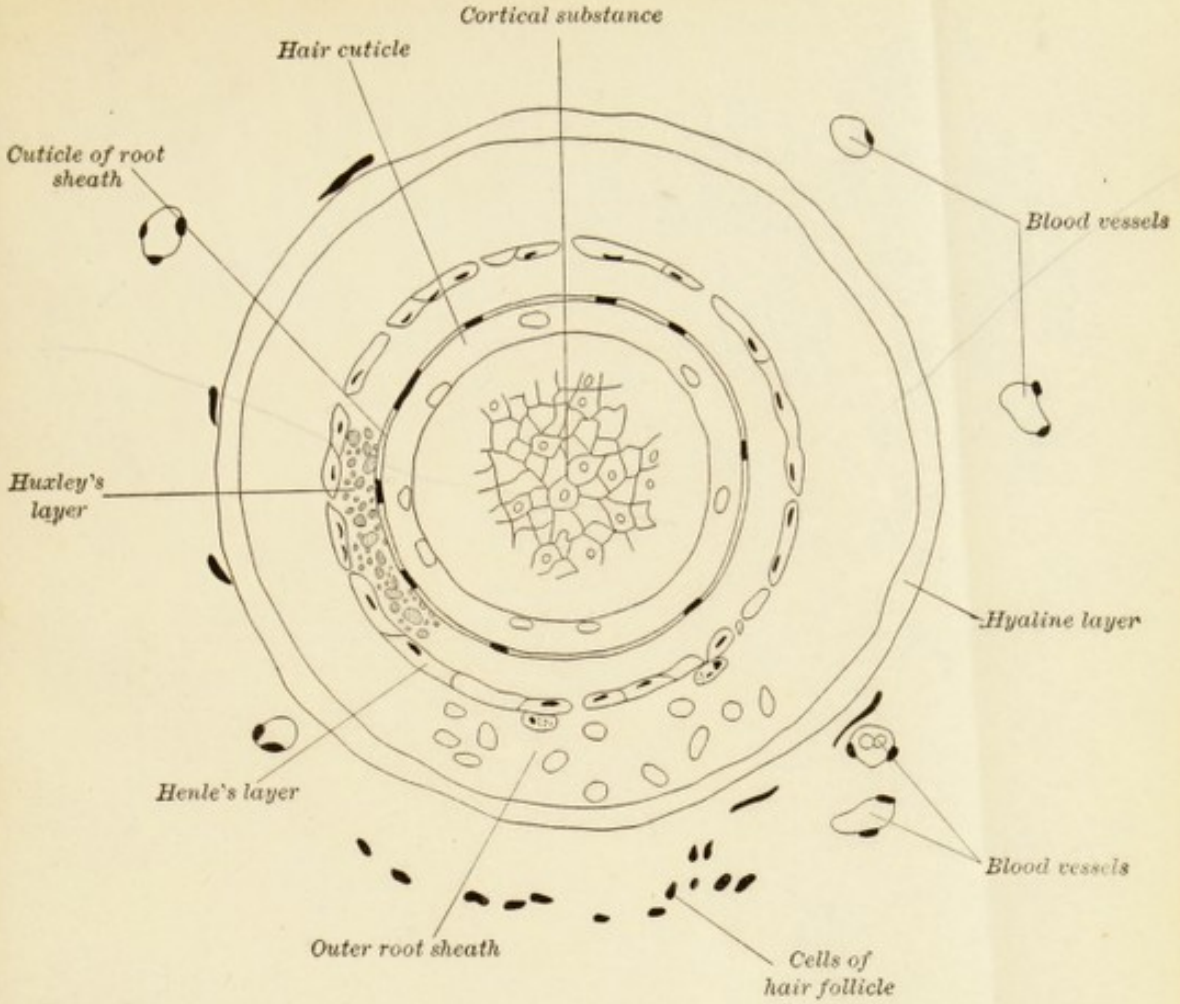


FIG. 245.—Cross-section of a hair and hair follicle in lower half of root. Human scalp. Hæmatoxylin and eosin. × 400.

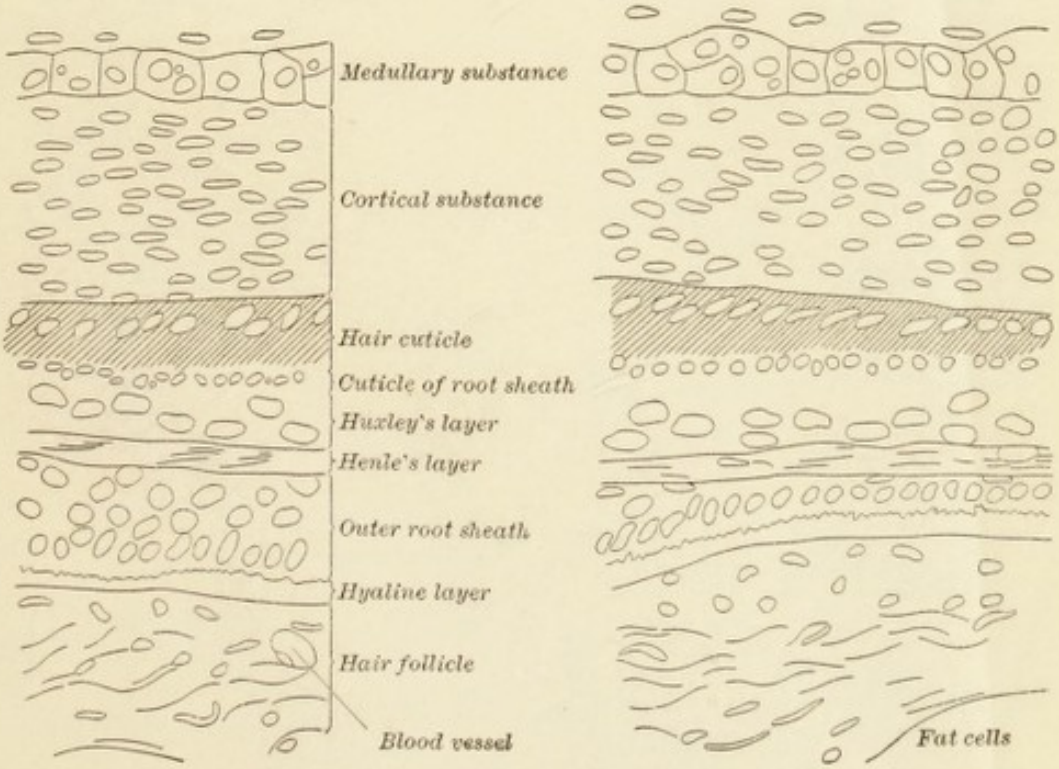


FIG. 246.—From a longitudinal section through the axis of a hair and its root sheath. Human scalp. Hæmatoxylin and eosin. × 550.

FIG. 245.—Cross-section of a hair and hair follicle in lower half of root. Human scalp. Hæmatoxylin and eosin. × 400.

FIG. 246.—From a longitudinal section through the axis of a hair and its root sheath. Human scalp. Hæmatoxylin and eosin. × 250.

thelium, which together form the *sheaths of the hair root.* Outside these we find connective-tissue layers, which enclose them in a saccular structure, which is known as the *hair follicle.* A true hair consists of three parts (Figs. 245 and 246):

1. The medullary substance;
2. The cortical substance;
3. The outer hair membrane (hair cuticle, cuticula pili).

The *medullary substance* lies in the axis of the hairs; but is found usually only in the thicker hairs, and in the lower part of the hair root. It is made up of cubical cells containing large spherical nuclei. As a rule, the whole thickness of the medullary substance is formed by one or two adjacent cells.

The main part of the true hair is composed of the *cortical substance.* This consists of spindle-shaped cells, which show a distinct fibrillar structure and contain oval nuclei. Since these cells lie with their long axes parallel to that of the hair, the whole hair has the appearance of being longitudinally striated. In this part of colored hairs there are pigment granules, inside and between the cells. In the neighborhood of the papilla, however, we find branched pigment cells. There is to be found, likewise, coloring-matter in solution, which infiltrates the cortical cells. The color of the hair is due to these two kinds of pigment. We find also between both cortical and medullary cells small spaces filled with air. In the medulla these may be very abundant, and, when pigment is scanty, they cause the hair to be distinctly white. Hairs which have entirely lost their pigment, but contain no air spaces in the medullary substance, are gray, but never white.

The outermost layer of the true hair is the *hair cuticle.* This is made up of fine, transparent, structureless, and almost rectangular scales, which are placed like tiles in such a way that their lower borders lie on the cortex, while their free edges project toward the outside and the end of the hair. In longitudinal sections of a hair these are directed from the outside downward and inward. They overlie one another, so that four to six cells form the thickness of the cuticle. In cross-

section they are seen to be arranged concentrically. The cells of these layers are without a nucleus in the upper part of the root and shaft; while in the region of the bulb there occur cells which are richer in protoplasm and contain distinct flattened nuclei.

The *root sheaths* consist of an outer and an inner layer (Figs. 245 and 246). The *inner layer* extends from about the upper one-third of the hair root down to the hair papilla. The *outer layer*, which is a process of the whole epidermis, shows in the upper third of the hair root—*i. e.*, up to the orifices of the glands—all the layers of the epidermis. Below this it is made up of only that part which represents the Malpighian layer. The stratum granulosum extends usually as far down as the openings of the sebaceous glands.

The *inner root sheath* consists of three different layers. The innermost layer is the *cuticle of the root sheath* (cuticula vaginæ pili). It lies immediately on the hair cuticle, and has a structure similar to that of the latter. It is, however, thinner than the cuticle, and consists of exceedingly thin, scale-like cells, which possess nuclei in the lower part of the hair root, but not in the upper.

Outside the cuticle of the root sheath there lies the *sheath of Huxley*, which consists of one or two layers of long polygonal cells. In the deeper parts of the hair root there are distinct nuclei, while in the upper parts these are entirely absent or only fragmentary. The third and outermost layer of the inner root sheath is the *sheath of Henle*. This consists of a layer of long flat cells, which in the region of the bulb possess oval nuclei. In the upper parts we find with the progressive cornification only nuclear vestiges. The difference between the cells of the inner root sheath at various places depends on the process of cornification, which increases from below upward.

The *outer root sheath* has the character of the stratum germinativum of the skin. The cells possess intercellular bridges and a fibrillar protoplasm.

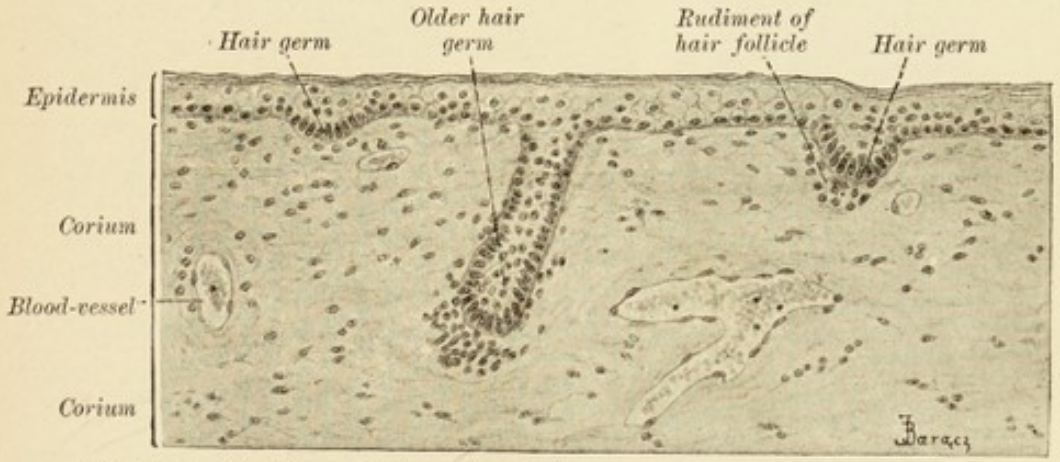
The connective-tissue *hair follicle* consists of three layers,

the innermost of which lies immediately on the outer root sheath, and is known as the *hyaline layer* (Glashaut). This varies in thickness, and is sometimes hardly visible. Its inner surface is distinctly grooved. Outside the hyaline layer we find the *circular sheath*, in which bundles of connective-tissue fibres run around the hair root. This extends from the bottom of the follicle to the level of the sebaceous glands. Outside the circular sheath there are longitudinal bundles of connective-tissue fibres containing vessels and nerves.

Development of Hairs.

Although the hair with its root sheaths is a somewhat complicated structure, all the various parts are found to have a common origin in the *stratum germinativum* of the skin. Toward the end of the third month of fœtal life epithelial thickenings appear in those places where hairs are to develop (Fig. 247). In consequence of the farther increase of cells

FIG. 247.

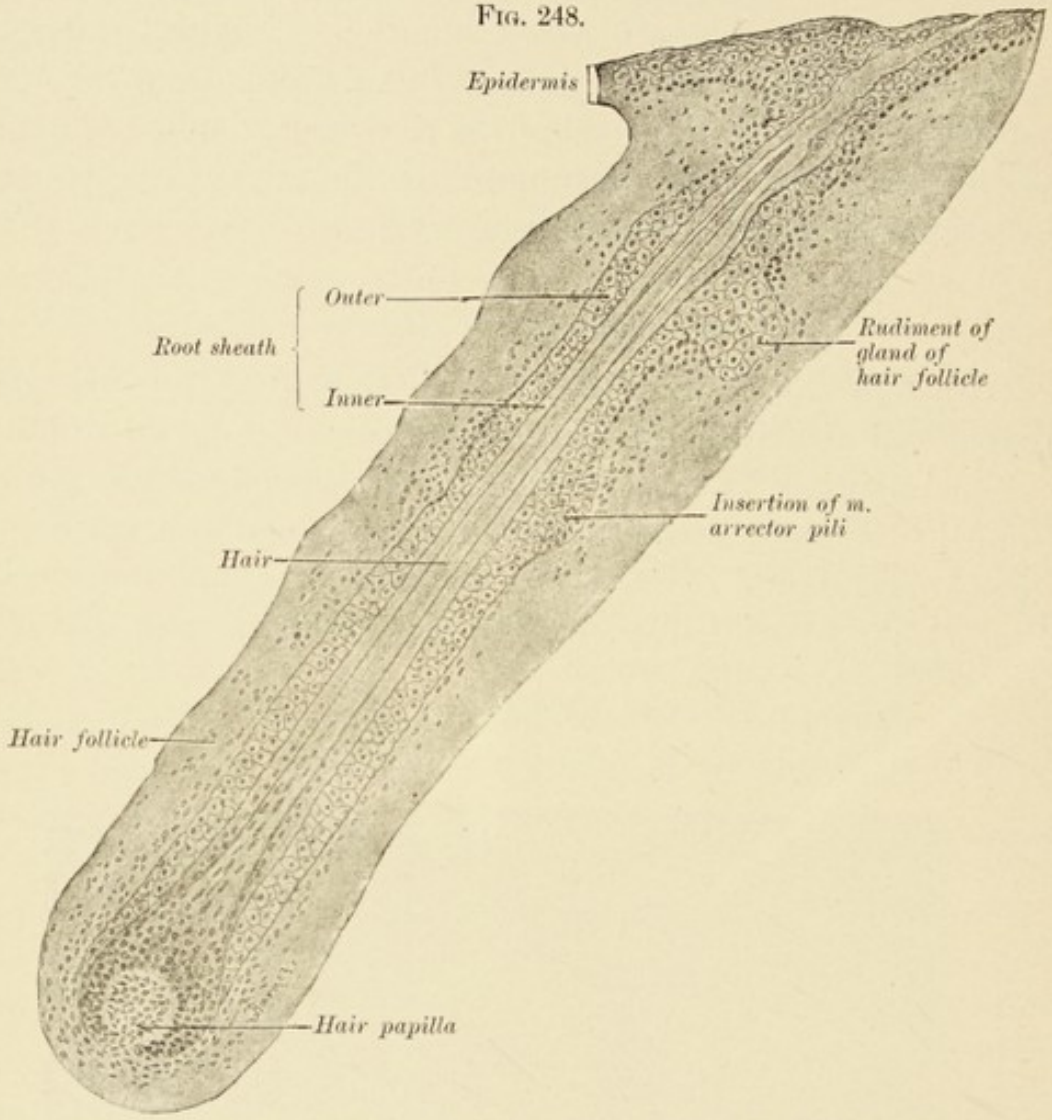


Vertical section through the scalp of a human embryo of the fifth month. × 230.

the epidermis dips down into the corium in the form of solid epidermal columns, each of which forms a hair germ. This increases in length and becomes thicker at its lower end. At this time we notice that the corium is differentiated to form the hair follicle; and the connective-tissue papilla grows up from the corium into the bulb of the hair. Various differentiations now take place in the cells of the hair germ. The axial cells

give origin to the true hair; while the cells lying around this form the inner root sheath. The more peripheral cells go to make up the outer root sheath (Fig. 248).

FIG. 248.



From a vertical section through the scalp of a human embryo of the sixth month. × 150.

The growth of the hair and the inner root sheath takes place from the region of the papilla to the outer surface of the skin; while the outer root sheath grows from the hair follicle toward the axis of the hair. The mother cells for the outer root sheath are the cells of the outermost layer of this sheath; while the matrix of the hair and inner root sheath is made up of the cells at the lower end of the hair bulb immediately bordering on the hair papilla. These *matrix cells* are the same at this stage for the various layers of the hair and inner root

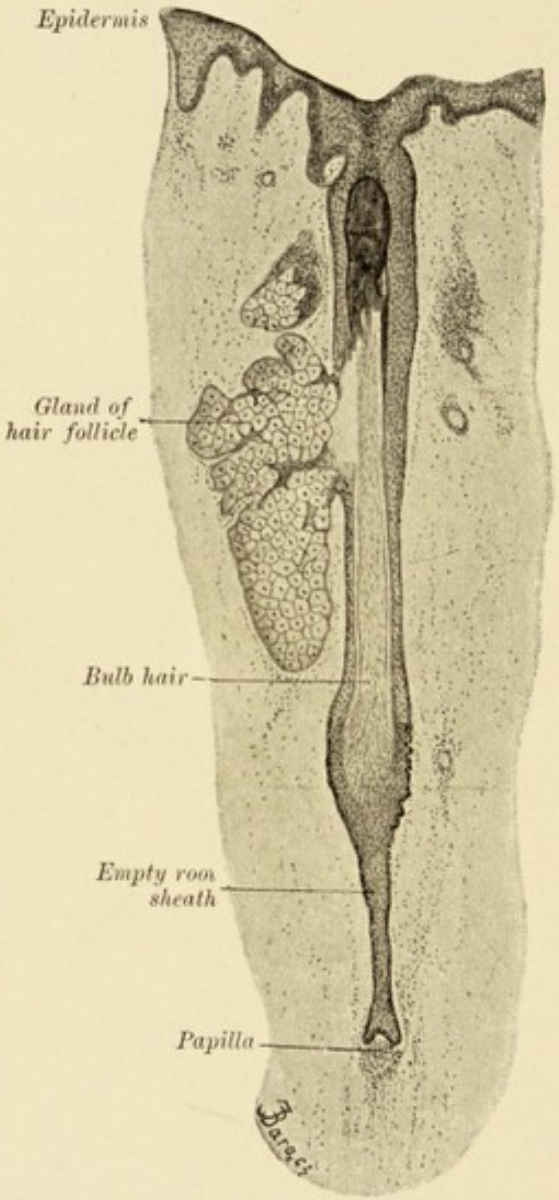
sheath. They are undifferentiated, and do not yet show the characteristics by which the cells of these individual layers are distinguished. The matrix cells of all layers are cylindrical or polygonal cells, rich in protoplasm. All the sheaths do not show a cornification at the same level, and the keratohyaline granules or eleidin droplets cannot be recognized in all of them. The cortical substance and cuticula pili become corneous without the presence of keratohyaline granules, while in the medullary substance there can usually be recognized droplets of keratohyaline. We find this substance in all three layers of the inner root sheath (Fig. 246). In the deeper parts the granules are present in Henle's sheath. Farther toward the surface they are more abundant, until finally we come to cells with rudimentary nuclei and corneous contents. We thus see that in the inner root sheath the growth as well as the process of cornification takes place from below upward to the surface of the skin.

The bulb of the hair which is about to fall out becomes corneous, separates from the papilla, and splits up into many fibres. Such a dying hair loses its connection with the papilla in consequence of an increase in the cells of the root sheaths. The root sheaths, being empty, form between the papilla and the lower thickening of the dead hair a cord-like mass of cells (Fig. 249). In place of such a hair there appears a new hair, formed by a multiplication of epithelial cells. This rests on the papilla and grows upward until the first hair is forced out.

In connection with hairs, we must speak of the bundles of smooth muscle cells making up the so-called *arrectores pilorum*, since these are connected directly with the hair follicle. These bundles have their origin in the stratum papillare of the corium, and are inserted at the lower part of the hair follicle. The hairs are inserted always in the skin at an angle to the surface. On the side where the hair follicle forms an obtuse angle with the skin surface there is fastened a bundle of smooth muscle fibres. The contraction of these fibres causes an erection of the hair. The simultaneous formation of a de-

pression at the place where the upper end of the muscle is fastened, and the elevation of the parts immediately surrounding the hair, give rise to the appearance commonly known as goose-skin. Since the sebaceous glands are found between the hair and the muscle, the contraction of the latter may assist

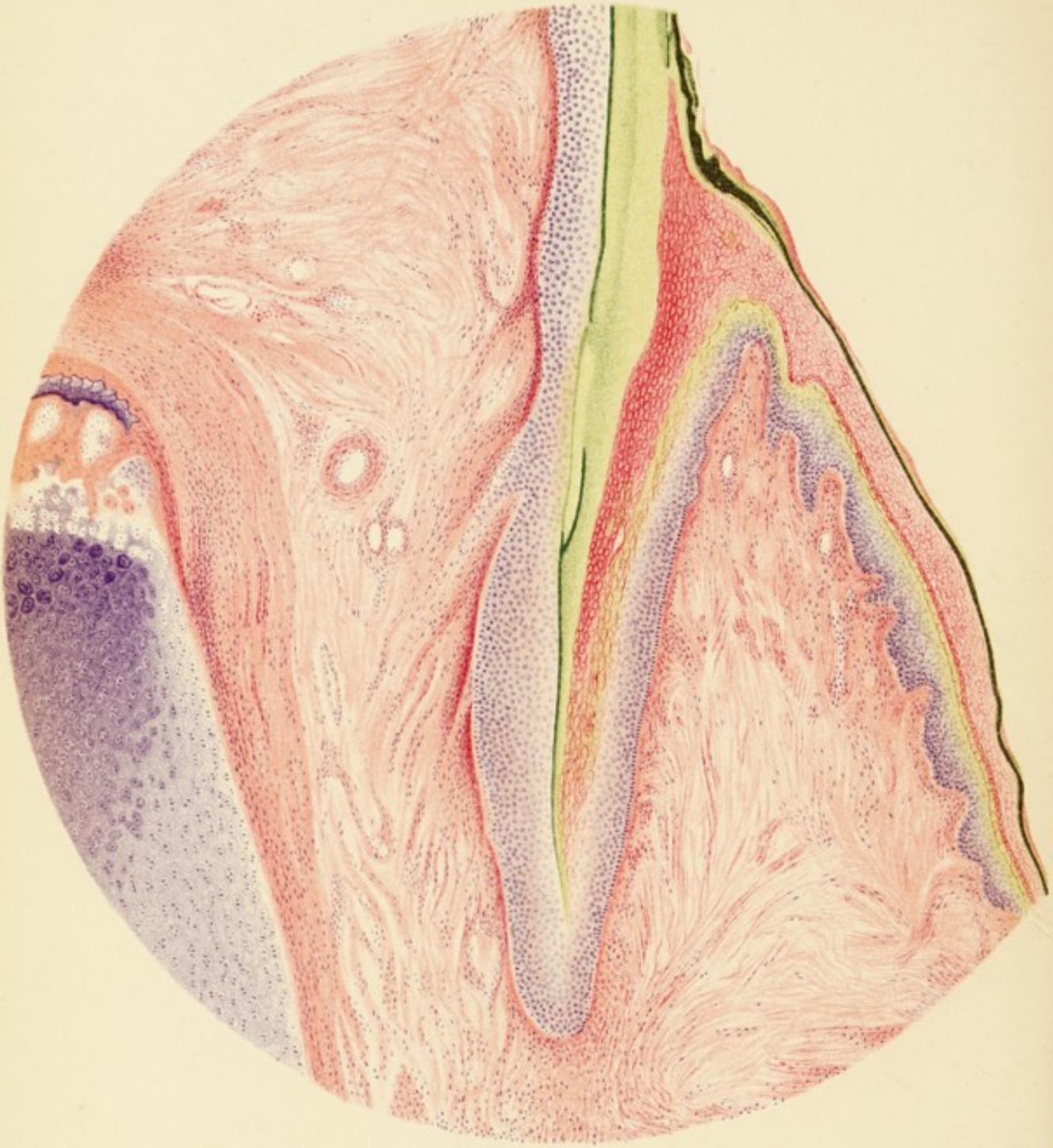
FIG. 249.

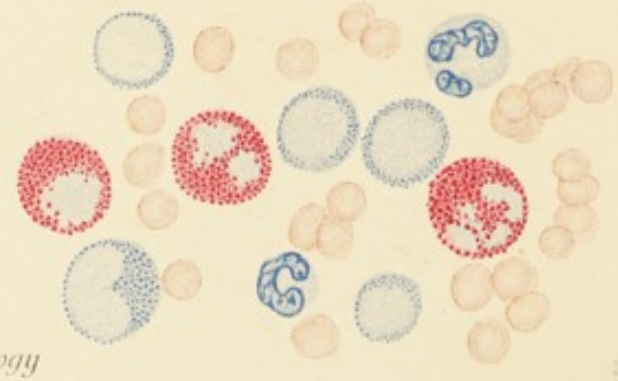


From a vertical section of the scalp of a human adult. In the centre there is a hair falling out (club hair). × 43.

also in the discharge of the contents of the gland into the hair follicle.

The hair follicle is supplied with blood through a thick network of capillary vessels, which is situated in the region





Szymonowicz. Histology

J. Barraja ad nat. del.
Lith. Anst. v. Werner & Winter, Frankfurt a/M.

FIG. 250.

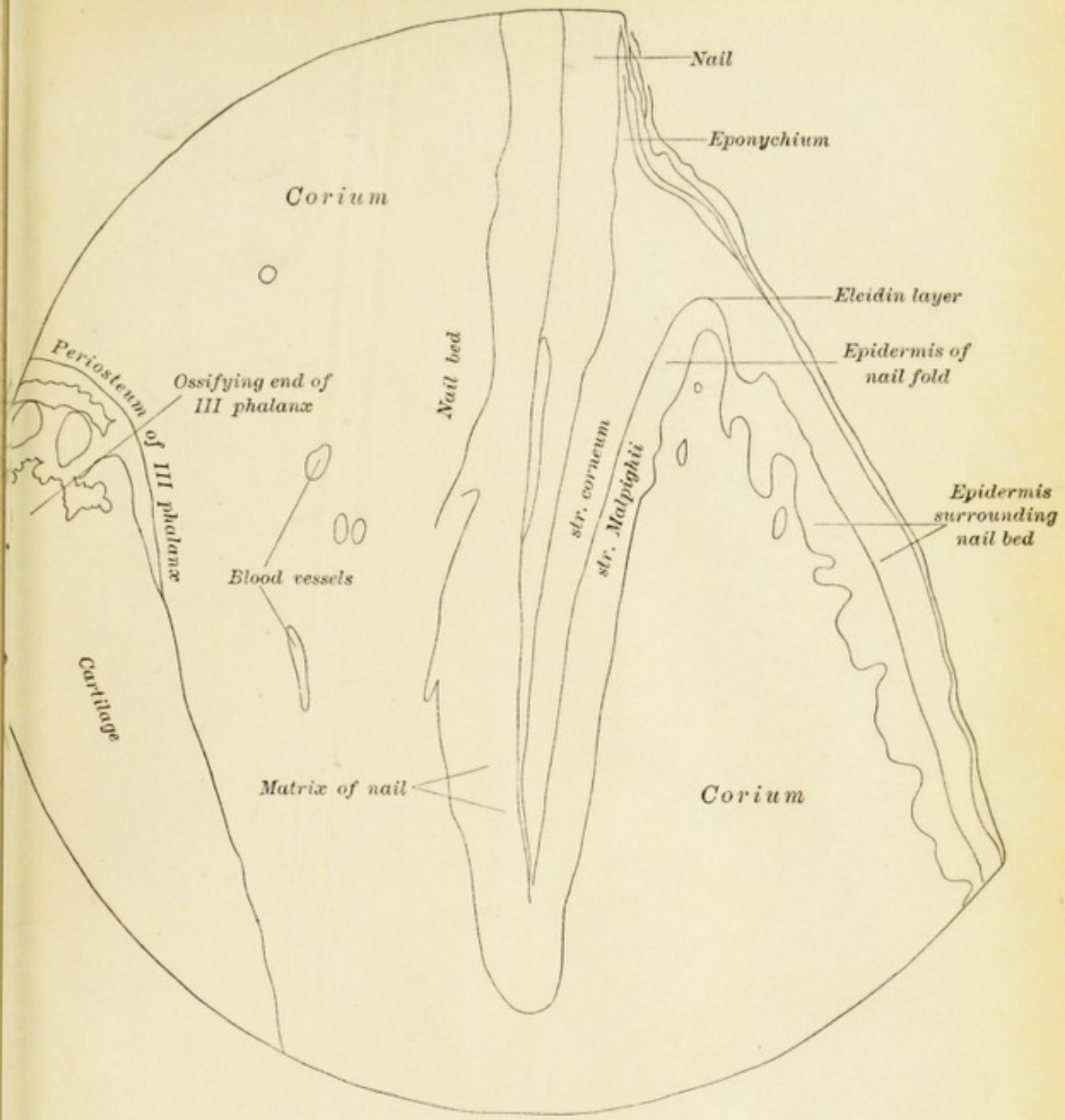
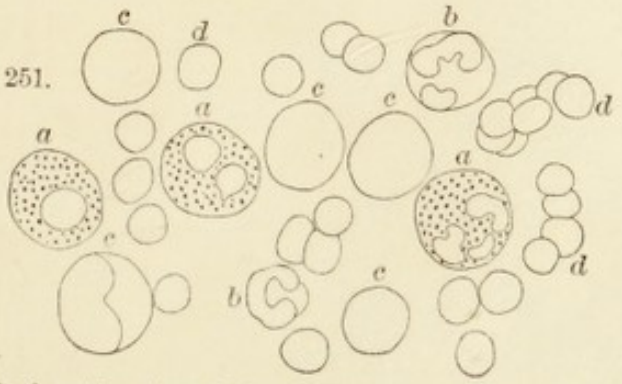


FIG. 251.



a = *acidophile granules.*
b = *neutrophile* "
c = *basophile* "
d = *erythrocytes*

FIG. 250.—Longitudinal section through the nail, and nail fold of a child. Hæmatoxylin and picro-carmine hardened in Flemming's fluid. × 60.

FIG. 251.—From human leukæmic blood. Methylene-blue and eosin. × 660.

FIG. 250.

FIG. 251.

a = acidophile granules.
b = neutrophile ,,
c = basophile ,,
d = erythrocytes

FIG. 250.—Longitudinal section through the nail and nail fold of a child. Haematoxylin and picro-carmine hardened in Flemming's fluid. × 60.

FIG. 251.—From human leukæmic blood. Methylene-blue and eosin. × 600.

of the hyaline membrane, and by capillary loops which enter the papilla.

Little is known concerning the nerve-endings of the human hair. In other mammals the nerves end below the sebaceous glands. Medullated fibres lose their medullary sheaths, divide, and penetrate to the hyaline membrane. Here some of the branches encircle the hair, while others end freely on the hyaline membrane as naked axis cylinders. These branch regularly and run parallel to the long axis of the hair.

The so-called *tactile hairs* of many mammals show an especially rich innervation. They are characterized by the presence of well-developed blood spaces in the walls of the hair follicle, and are therefore known also as *sinus hairs.* In these hairs especially two kinds of nerve-endings are to be noted:

(*a*) The endings on the outer surface of the hyaline membrane in the form of free arborizations; and

(*b*) The endings under the hyaline membrane in the outer root sheath. These terminate by means of tactile menisci, which are in contact with tactile cells. They resemble strongly the tactile corpuscles of Merkel.

(*c*) Nails.

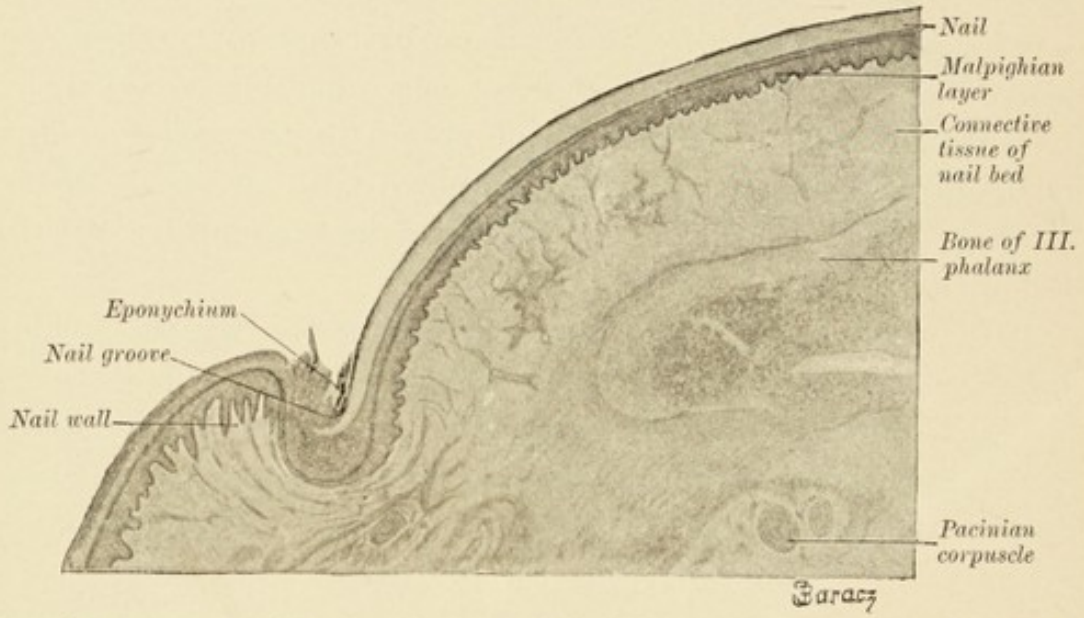
The nail is an epidermal structure. It lies on the corium, which forms the so-called *nail bed*, and is surrounded by the *nail wall*, which is formed from the skin (Figs. 250 and 252). Between the nail wall and nail bed there is a groove, called the *nail groove.* The part of the nail visible to the naked eye is called the *nail body*, while the posterior portion which lies under the skin is the *nail root.*

The connective-tissue nail bed forms ridges running forward along the nail and from the middle line out to the sides. These become higher toward the free end of the nail, where they are about 0.22 mm. Where the nail bed ends, in front, we usually find skin papillæ.

In the nail bed lies the nail, which consists of two parts: a soft layer, which represents the Malpighian layer of the skin;

and the hard, corneous part or true nail. The Malpighian layer of the nail, which consists of polygonal prickle cells, fills the spaces between the furrows of the nail bed and covers it with several layers of cells (Figs. 252 and 253). The Malpighian layer of the nail under the nail root is much more strongly developed, and is known as the *matrix unguis* (Fig. 250), because from this place the growth of the nail takes

FIG. 252.



Part of a transverse section through the terminal phalanx of the finger of a child sixteen days old. × 22.

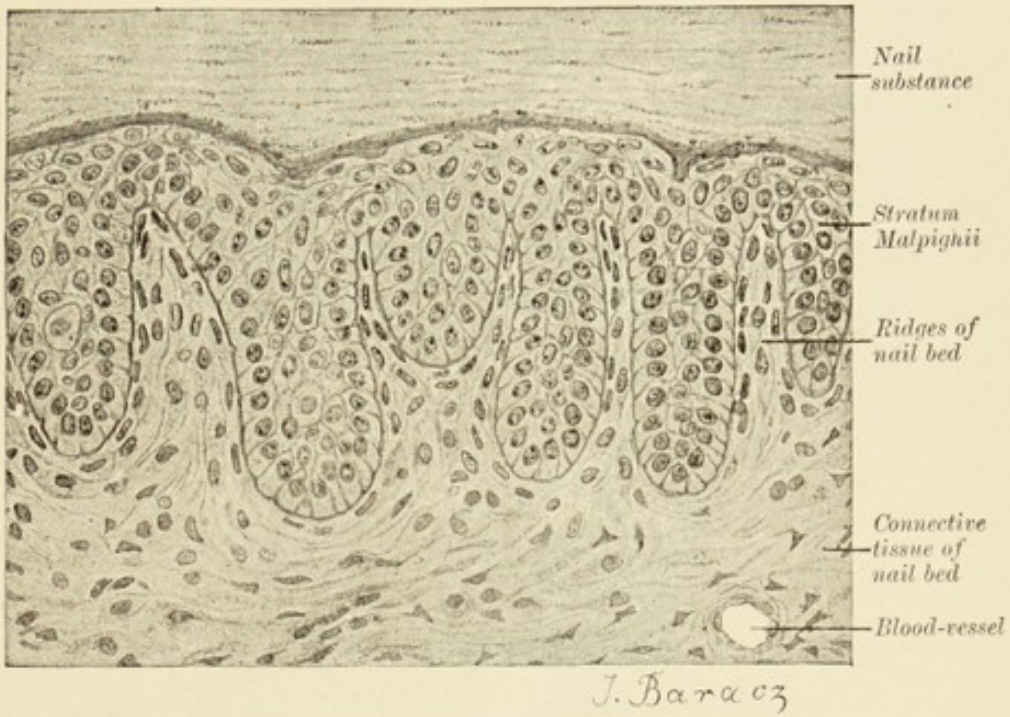
place. The matrix is conspicuous as the whiter part of the nail, and ends anteriorly in a curved line, and forms the so-called *lunula*. Here we find a stratum granulosum, which does not occur in the nail region.

The cells of the nail itself are flat and horny, and in them can be seen distinct nuclear remains. By the joining together of many of such cells the so-called *nail leaves* are formed. These overlie one another like tiles. The white areas often seen in nails are due to air bubbles which collect between the leaves.

As the Malpighian layer of the nail groove passes over into that of the skin in the nail wall, a stratum corneum appears, which covers a part of the upper surface of the nail and forms the *eponychium*. At the anterior border of the

nail the Malpighian layer of the skin passes over into that of the nail. The latter is covered over at this place of transition by a horny layer, which extends along on the lower surface of the free nail border, and is known as the *hyponychium*.

FIG. 253.



Transverse section through the nail body. × 280.

The growth of the nail proceeds, from behind, forward, by a progressive transformation of the matrix cells into true nail cells. This takes place at the posterior and lateral borders, as well as the lower and often the upper surface of the nail root. In consequence of this the nail is pushed forward, while the Malpighian layer does not change its position.

(*d*) Glands of the Skin.

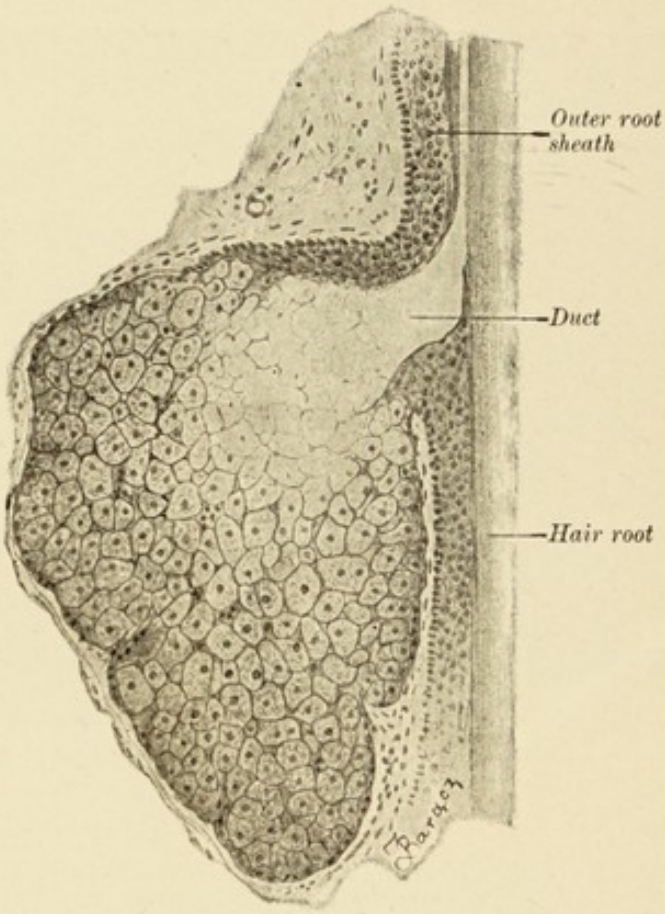
Sebaceous Glands.

The *sebaceous glands*, which are distributed over almost the entire surface of the body, are found usually in connection with hair follicles; hence the name hair follicle glands. Only exceptionally do we find them in parts which are devoid of hairs (*e. g.*, the red borders of the lips, the labia minora, the glans

penis, and prepuce (Tyson's glands)). They are wanting in the palms of the hands and soles of the feet.

They are simple or branched alveolar single glands, club-like or pyriform. Their size varies from 0.2 mm. to 2.2 mm.

FIG. 254.



Sebaceous gland from the human scalp. × 120.

in length. The largest are found often associated with small, thin hairs, such as those in the nose. Their ducts open into the upper third of the hair follicle.

Sebaceous glands are surrounded by a connective-tissue capsule which originates in the hair follicle or in the corium itself. The glands consist of epithelial cells which come from the outer root sheath; or, if the gland is not in connection with a hair, from the epidermis of the skin. The epithelial cells forming the neck of the gland retain unchanged the characteristics of the cells from which they arise. In the body of the gland, however, they are modified somewhat by

the collection of fat globules in the protoplasm of the cells. The cells lying in the middle of the gland and in the lumen of the duct are most markedly changed. Here almost the entire protoplasm is converted into fat, the small globules of which coalesce to form larger drops. The nuclei of these cells become shrunken and dead; while the cell itself disintegrates and goes to form a part of the glandular secretion. We see that the death of the cells is necessary for the production of the secretion, which is in part formed in the cells during life. While the cells in the middle of the gland are destroyed to form the sebum, other cells are added by the division and multiplication of the peripheral cells. At the end of the fourth month of fœtal life these glands begin as solid outgrowths of the outer root sheath. Those which have no connection with hairs appear as down-growths of the Malpighian layer of the epidermis into the corium.

Sweat Glands.

Sweat glands (glandulæ sudoriparæ) are distributed over the whole surface of the skin, with the exception of the inner surface of the prepuce, the glans penis, and the red border of the lips. They are as a rule simple tubular glands, and only exceptionally are branched (*e. g.*, the axillary and circumanal glands). The name *coil gland* is applied to them on account of the shape of their lower part.

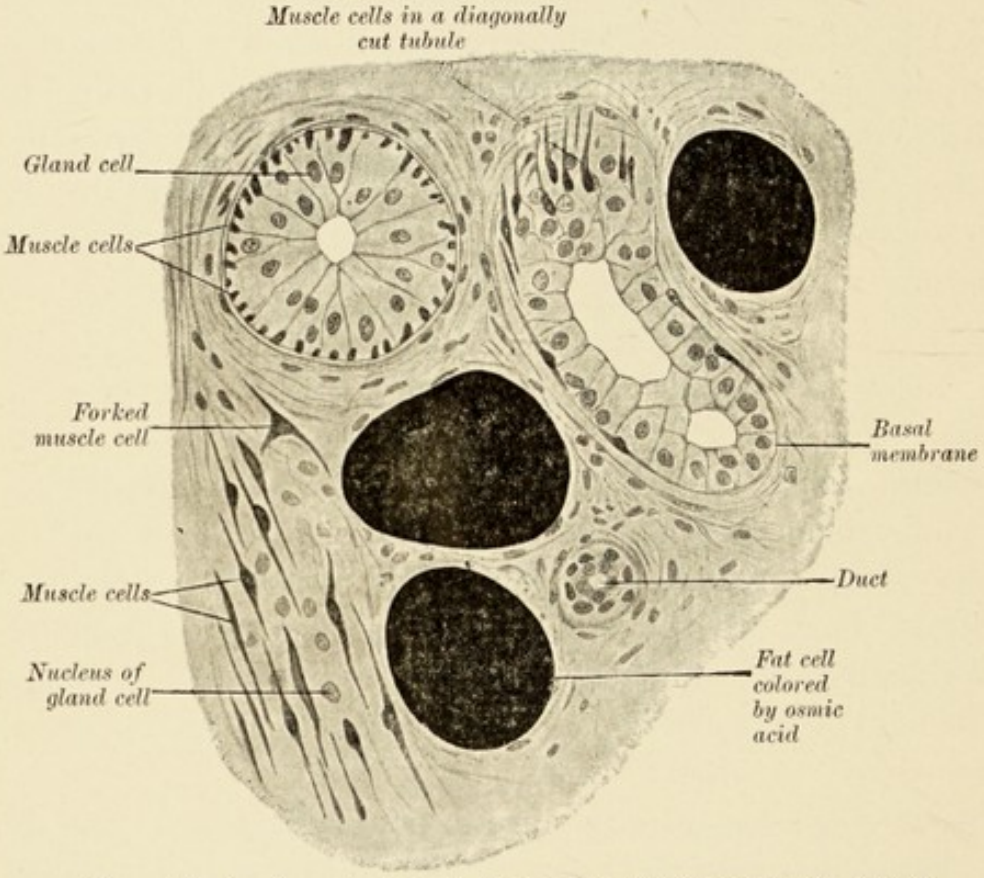
In these glands two parts are to be distinguished: the duct, and the lower secreting part, which forms a coil and ends blindly (Fig. 241). The body of the gland is found at the border between the corium and the subcutaneous tissue, or may be situated entirely in the subcutaneous fat. The lumen of the secreting part of the tubules is greater than that of the duct.

In the duct there are two parts; one in the corium, and the other in the epidermis. The former is coiled slightly, and possesses true walls; while the part in the epidermis presents no walls of its own. The duct always enters the

epidermis between the papillæ and opens on the surface of the stratum corneum by a round sweat pore (Fig. 241).

In the secreting coiled portion of the gland (Fig. 255) the wall of the tubule consists of a layer of cubical epithelium, the cells of which contain a finely granular protoplasm. This often includes fat droplets and brown pigment granules, and possesses on the free surface of the cell a cuticle. Outside these gland cells we always find in the larger glands a longitudinal layer

FIG. 255.



Some tubules of sweat glands from the skin of a human finger. × 350.

of spindle-shaped smooth muscle cells. Outside this there is a connective-tissue *membrana propria* surrounding the whole tubule. That part of the membrana propria immediately adjacent to the gland is thin and homogeneous, and forms the *basal membrane.*

The part of the duct which is present in the corium differs from the secreting tubules in that there is a second layer of epithelial cells in place of the smooth muscle elements. The

PLATE L.

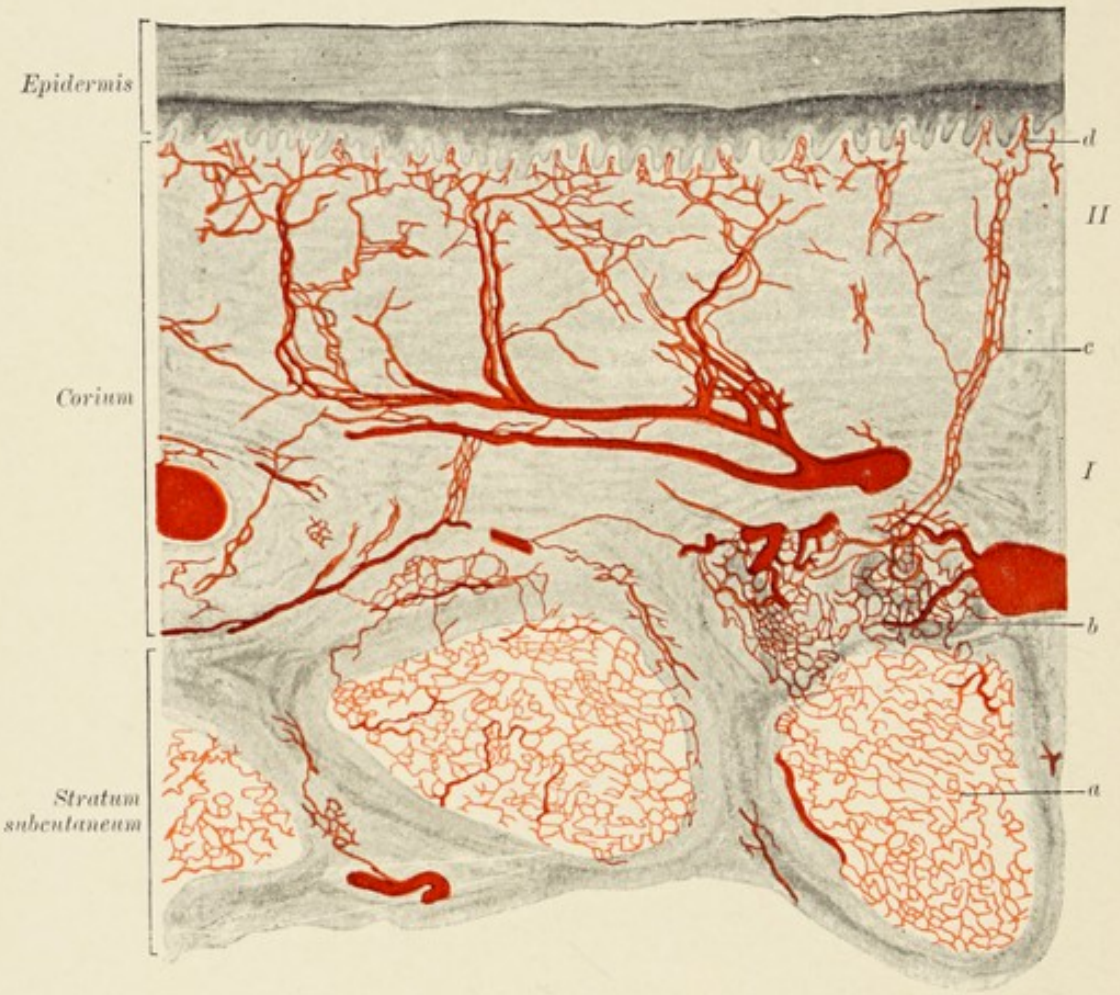


FIG. 256.—From a vertical section of the skin of the human hand. Blood-vessels injected red. × 35.

a, fat; *b*, coiled sweat glands; *c*, duct of sweat gland; *d*, papillæ; I., cutaneous network; II., subpapillary network.

whole wall consists of two layers of epithelial cells and a tunica propria. On entering the epidermis the duct becomes spirally coiled. It loses its own wall and is bounded by the cells of the epidermis in which it lies. The cells of the Malpighian layer of the epidermis arrange themselves concentrically around the lumen. The stratum granulosum turns and follows the duct downward for a short distance (Fig. 244).

The sweat glands develop in the fifth month of embryonic life as a solid outgrowth of the Malpighian layer. In the course of growth they become slightly coiled, and in the seventh month possess a lumen.

Sweat glands are supplied richly with nerves. Non-medullated fibres form a fine network on the outer surface of the membrana propria, from which fine fibres pass through the basal membrane. These end on the surfaces of the gland cells by means of fine end bulbs.

(*e*) Vessels and Nerves of the Skin.

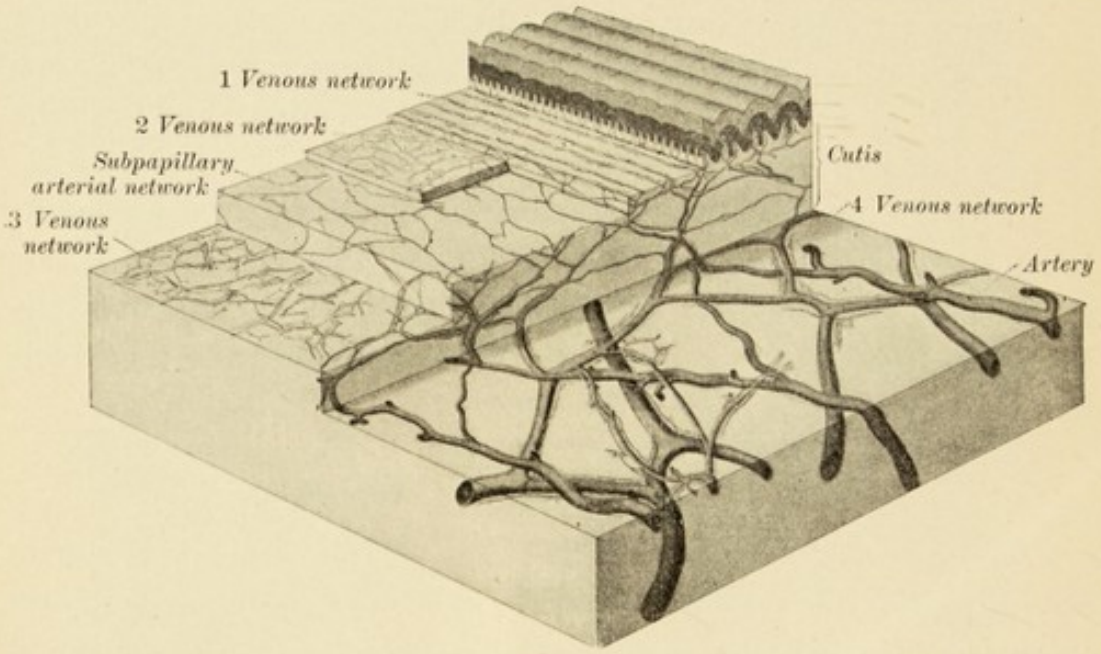
The number and diameter of vessels in the skin varies according to the region studied. The blood supply is greatest in those places which are subject to pressure (*e. g.*, the gluteal regions, the palms of the hands, and the soles of the feet). The branching is greatest in parts which are most movable. (Spalteholz).

The *arteries* enter the corium and anastomose to form the *cutaneous network.* From this, branches arise, which pass upward toward the epidermis, and before reaching it anastomose with one another to form the *subpapillary network* (Figs. 256 and 257). Small capillary end branches proceed from the latter network into the papillæ, forming *capillary loops.* These give origin to the veins. Branches from the cutaneous network form a dense plexus around the subcutaneous fat, and around the bodies of the sweat glands (Fig. 256).

The *veins* begin in the papillæ and form four distinct networks parallel to the surface. The most superficial lies immediately under the papillæ. From this, irregular branches run down to the second plexus, the meshes of which are small and

quadrangular. Passing deeper, the veins form a third network in the lower part of the corium, with large irregular meshes. The fourth plexus is formed between the corium and subcutis. These are all shown in the reconstruction taken from the work of Spalteholz (Fig. 257). The circular muscle layer disappears

FIG. 257.



Reconstruction of blood-vessels of the skin of the human foot. (Spalteholz.)

in the arteries in the middle of the cutis, and in the veins appears in the fourth plexus, where valves also are found first.

The *lymph-vessels* form a fine, close plexus spread out in the stratum papillare, from which loops are sent to the papillæ. The larger vessels passing into the depths from this plexus anastomose in the stratum subcutaneum, to give rise to a second coarser network.

Nerves are present everywhere in the skin, while certain regions are supplied specially (*e. g.*, soles of the feet, palms of the hands, external genitals). Numerous forms of nerve-endings are present. We find free intra-epithelial nerve-endings, and Merkel's tactile corpuscles in the epidermis; Meissner's tactile corpuscles, and end bulbs in the papillæ; and Vater-Pacinian, Ruffini's, and other corpuscles in the subcutis.

(*f*) Mammary Gland.

The mammary gland is a cutaneous gland, which is present in both sexes, and up to the beginning of puberty is not well developed. Its epithelial beginning (milk line or ridge) is seen in the first months of embryonic life. After the commencement of puberty the gland continues to develop in the female, but undergoes a retrogression in the male. The highest development in the female is reached at the end of pregnancy. Shortly after the birth of the child the milk secretion or lactation begins. The function of the mammary gland is thus dependent on the sexual life.

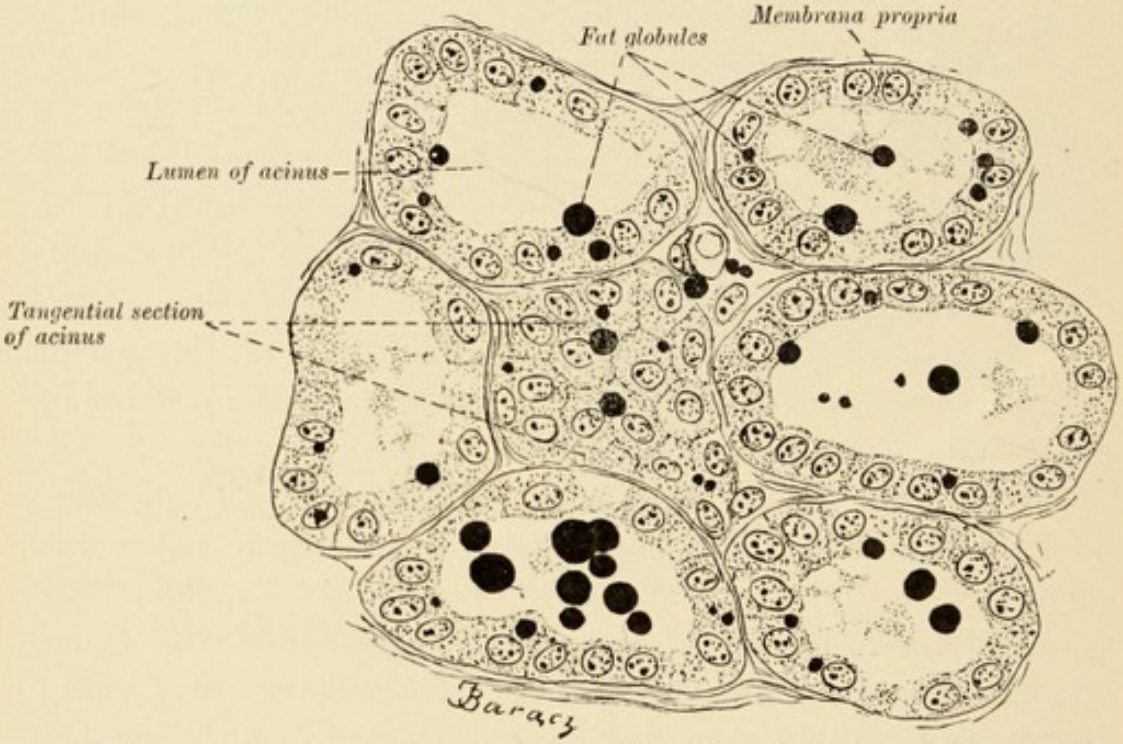
Before puberty this whole organ, in both sexes, consists of connective tissue in which branched tubules are imbedded. These represent the ducts of the completely developed gland, and end blindly in saccular dilatations. In the adult female there occur branched tubular gland bodies, but it is only during pregnancy that these develop in large quantities at the sides of the branched ducts. The newly formed branches of the gland bodies possess also side twigs.

The well-developed mammary gland (at the end of pregnancy and during lactation) consists of fifteen to twenty conical *lobes*, which are arranged radially. Each lobe consists of numerous smaller *lobules*, which represent a large group of gland bodies lying close together. These have the form of alveoli, and lead into small ducts, which join to form the duct of the mammary gland. Before the latter opens to the outside through the nipple, it is widened to form the *sinus lactiferus*. Each individual lobe represents really a separate compound alveolar gland, since it opens into the nipple by an orifice of its own, the *porus lactiferus*. The individual lobes are separated from one another by loose connective tissue, which often contains a quantity of fat.

The finer structure of the alveolus (Fig. 258) differs according to whether it is at rest or secreting. When at rest, the round or pyriform alveoli are small and lined with cubical granular epithelial cells. During the transition to the active

state (at the end of pregnancy) the alveoli increase in size, numerous leucocytes find their way into the lumena of the alveoli, and the granular epithelial cells begin the formation of fat. These fat globules are taken up by the leucocytes, which are thus converted into *colostrum corpuscles*. After the birth of the child the gland cells become larger and the production of fat increases. The walls of the alveoli now consist of high cylindrical gland cells full of secretion, and also lower cells which have been emptied of their contents. The part of the

FIG. 258.



Part of a transverse section of the mammary gland of a guinea-pig during lactation. × 500.

cell bordering on the lumen especially undergoes fatty change. When this secretion escapes, the part of the cell containing the nucleus regenerates the whole cell. This process may take place many times. The whole cell does not disintegrate, as is the case in the sebaceous glands. Mitotic division is observed often in these cells, while, on the contrary, extruded nuclei are found free in the lumen of the alveolus.

The *membrana propria* of the alveolus is homogeneous, and contains on its inner surface stellate *basket cells*, which surround the gland cells by long processes.

In a gland which has ceased to function, the interstitial connective tissue becomes relatively more abundant and the gland alveoli tend to disappear.

The *ducts* are lined with a single layer of cylindrical epithelium, which in the neighborhood of the external orifice passes over into stratified flat epithelium. Outside, the duct is clothed with a circular layer of connective tissue containing elastic fibres.

During the climacteric the gland undergoes involution, the alveoli and ducts decreasing greatly in number and size.

The skin of the nipple and its near neighborhood is strongly pigmented. It contains large papillæ and smooth muscle cells which run in part circularly around the openings of the ducts and in part longitudinally in the nipple. The skin of the region immediately around the nipple (areola) contains, besides large sweat glands, many (about twelve) sebaceous glands of considerable size, the so-called *Montgomery's glands* (glandulæ areolares). The structure of the latter forms a transition between the sebaceous and mammary glands. They increase in size during pregnancy.

The *blood-vessels* entering the gland parenchyma from different sides break up into a fine capillary plexus, which surrounds the gland ducts and alveoli. The *lymph-vessels* run in the form of capillary networks, both in the interstitial connective tissue and in the skin of the nipple and areola. The *nerves* entering the mammary gland in part supply the blood-vessels, and partly end in the gland parenchyma, as in the salivary glands. In the skin of the nipple and in the end dilatations of the larger ducts there are found Meissner's and Vater-Pacinian tactile corpuscles (W. Krause).

The secretion of the mammary gland—the milk—is an emulsion of fat droplets, whose size varies from 1 to 5 μ in diameter. Each fat globule is surrounded by a layer of casein, which prevents their coalescence with one another.

The *colostrum*, which is present in the mammary gland before and in the first two or three days after the birth of the child, contains fat drops and colostrum corpuscles. These

cells are nucleated, and include in their protoplasm many free fat globules. They are derived probably from leucocytes which have wandered into the lumen of the alveolus. Some authors regard them as gland cells which have undergone fatty change.

2. VISUAL ORGAN.

The true organ of vision consists of the *eyeball* (bulbus oculi) and the *optic nerve*. Besides these there are protective structures, the *eyelids* and the *lachrymal apparatus*.

(*a*) Eyeball.

In the walls of the eyeball there are three layers:

(1) *Tunica externa seu fibrosa*, which consists of the opaque *sclera* and the transparent anterior part, the *cornea*.

(2) *Tunica media seu vasculosa*, which is made up of the *choroidea*, the *ciliary body*, and the *iris*.

(3) *Tunica interna*, which consists of the *retina*.

The eyeball contains in its interior the *aqueous* and *vitreous humors* and the *lens crystallina*.

(*1*) *Tunica Externa.*

The *cornea* (Fig. 259) is a membrane varying in thickness from 0.8 to 1.1 mm. In it can be made out five layers, which from in front backward are as follows:

(1) The anterior epithelial layer (corneal epithelium);
(2) The lamina elastica anterior;
(3) The substantia propria corneæ;
(4) The lamina elastica posterior;
(5) The posterior epithelial layer (corneal endothelium).

(1) The most superficial sheath consists of five to eight layers of epithelial cells; the deepest of which are cylindrical. These pass over into lower polygonal cells, which at the surface become flat, but are always nucleated. Regeneration takes place in the basal cylindrical cells, in which karyokinetic figures are found not infrequently. The cells are bound together by intercellular bridges, as in the skin. The lower

PLATE LI.

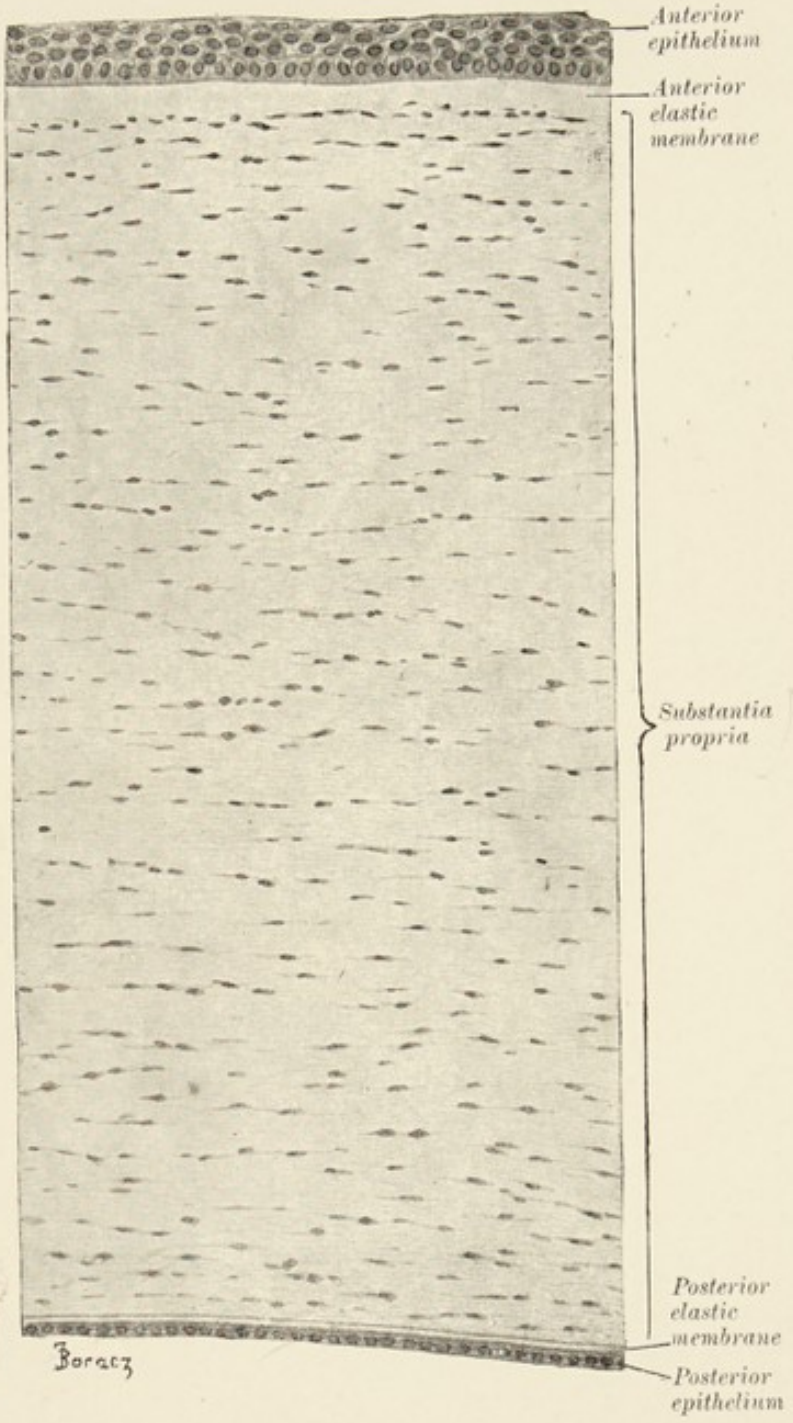


FIG. 259.—Vertical section through the cornea of a newborn child. × 200.

surface of this epithelium is smooth, since the connective tissue there is wanting in papillæ. At the border of the cornea this epithelium passes over into that of the conjunctiva.

(2) The *lamina elastica anterior* (Bowman's membrane, anterior basal membrane) is strongly developed in man, varying from 0.01 to 0.02 mm. in thickness. It is a homogeneous refractive membrane. By means of certain reagents (potassium permanganate) fibrillæ can be demonstrated in it. The anterior surface presents minute inequalities, which correspond with projections and depressions on the under surface of the basal cells.

(3) The *substantia propria* forms the main mass of the cornea. It consists of connective-tissue fibrillæ, which are bound together into flat lamellæ by means of interfibrillar cement substance. There are in man about sixty of these lamellæ overlying one another and running parallel to the surface of the cornea. They are joined together by interlamellar cement substance. The fibrillæ run in different directions and cross one another at various angles. A few bundles run obliquely and join the individual lamellæ with one another. These are the so-called *fibræ arcuatæ*.

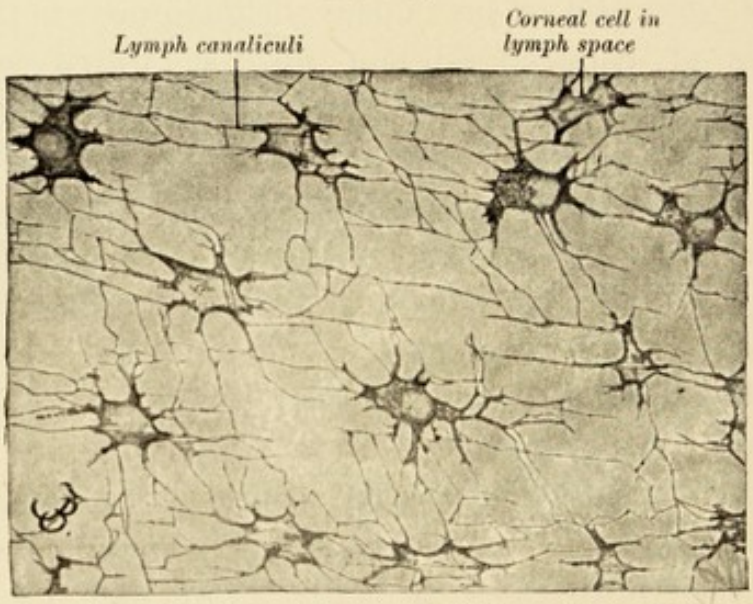
Through the entire substantia propria there runs a system of *canals* and *spaces* which contain a serous fluid. This system can be demonstrated most easily by impregnation with silver or chloride of gold. The former gives a negative picture—*i. e.*, the canals and spaces are colorless on a brown background. By the gold method, on the contrary, a positive picture is obtained, in which the canal system is colored violet (Fig. 260). In the spaces lie flat connective-tissue cells possessing many processes and large nuclei. These so-called *fixed corneal cells* lie close to the walls of the spaces. Wandering cells also occur in the cornea.

(4) The *lamina elastica posterior* (Descemet's membrane, posterior basal membrane) is a refractive membrane only 0.006 mm. thick. It has been described as an elastic membrane, but, according to Mall, does not stain by Weigert's elastic stain.

(5) The *corneal endothelium* (posterior epithelial layer) consists of a layer of low hexagonal cells, whose protoplasm is rich in fibrils. These seem to pass from one cell to another, as in the stratum spinosum of the epidermis.

The *sclera* has a structure similar to that of the substantia propria corneæ. It possesses, however, numerous elastic fibres, of which a part form networks. The flat connective-tissue cells lie in irregularly branched spaces. The connective-tissue fibrils are arranged in layers in such a way that those of one layer have a meridional and those of another an equatorial

FIG. 260.



From a horizontal section of an ox's cornea. Positive picture of the canal system demonstrated by the gold chloride method. × 450.

direction. The sclera shows in certain places collections of pigment (*e. g.*, at the border of the cornea, and in the neighborhood of the entrance of the optic nerve).

On the inner surface of the sclera we find a loose connective tissue arranged in thin layers. This contains branched pigment cells and joins the sclera to the chorioidea. In separating these layers a part of the connective tissue remains with the sclera, and a part adheres to the chorioidea. We distinguish this connective-tissue layer as the *lamina fusca sleræ* or *lamina suprachorioidea.* At the place where the optic nerve penetrates the sclera we find only a remnant of the layer in the

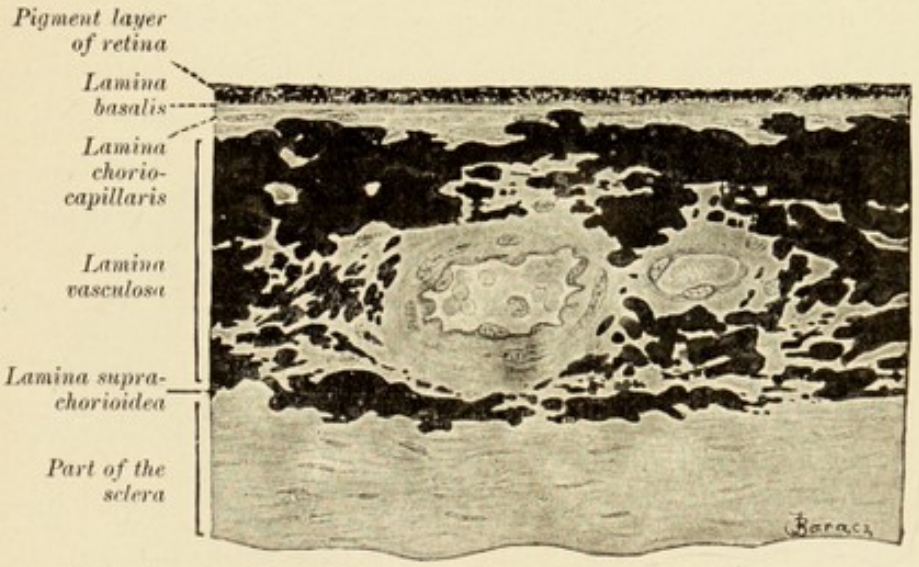
form of a reticular network, the so-called *lamina cribrosa*. The eye muscles attach themselves to the sclera in such a way that their tendons pass over into the fibril bundles of the sclera. The outer surface of the sclera borders on the conjunctiva scleræ, with which it is bound by the loose subconjunctival connective tissue.

(2) *Tunica Media.*

In the *chorioidea* we distinguish several layers (Fig. 261):

1. The *lamina vasculosa* is the outermost layer, and is adjacent to the lamina suprachorioidea. It contains large blood-vessels, the branches of the venæ ciliares posticæ, and the arteriæ ciliares posticæ brevis. The ground substance consists

FIG. 261.



Vertical section through the chorioidea and a part of the sclera of an ape. × 440.

of connective tissue with fine elastic fibre networks. In it there are veins surrounded by lymph spaces. Numerous pigment cells are present, and running along the arteries are bundles of smooth muscle cells and flat branched cells.

2. The *lamina choriocapillaris* lies internal to the lamina vasculosa. It consists of a small amount of ground substance containing a capillary plexus, which is more dense in the region of the macula lutea. No pigment is present.

3. The *lamina basalis* is a highly refractive, delicate mem-

brane which lies on the inner surface of the chorioidea and borders on the pigment epithelium of the retina.

The *corpus ciliare* is to be regarded as a process of the chorioidea, which reaches from the ora serrata to the outermost borders of the iris. It consists of the so-called *orbiculus ciliares*, the *processus ciliares* (corona ciliaris), and the *musculus ciliaris*.

The *orbiculus ciliaris* differs in structure from the chorioidea in that it contains no lamina choriocapillaris. The lamina basalis is thickened to form intercrossing ridges, with depressions between which are filled with retinal pigment epithelium. The vessels and muscle bundles belonging to this region run in a meridional direction.

The *corona ciliaris* (Fig. 262) consists of seventy to eighty ridge-like processes running meridionally (processus ciliares). These are arranged around the lens, and are about 2 mm. long and 1 mm. high. They are highest at the end toward the lens. Toward the outside the ground substance of the processes border on the ciliary muscles. The inner surface, on the other hand, is covered by the lamina basalis, which rests on the pigment layer of the pars ciliaris retinæ.

The *musculus ciliaris* (Fig. 262) has the form of a flat ring about 3 mm. in thickness. It consists of smooth muscle cells, which may be divided into three groups according to the direction in which they run :

1. The outermost (*meridional*) part (tensor chorioideæ) contains bundles of muscle cells which run meridionally and lie next to the sclera. They reach from the canal of Schlemm to the orbiculus ciliaris.

2. Outside these fibres there is a middle (*radial*) layer of the ciliary muscle. Its bundles of fibres have a radial arrangement, so that some of them are spread out toward the centre of the eyeball, like the rays of a fan (Fig. 262).

3. The innermost (*circular*) portion of the muscle takes an equatorial or circular course, so that the name Müller's ring muscle is applied also to it.

The *iris* is to be regarded as a process of the chorioidea.

PLATE LII.

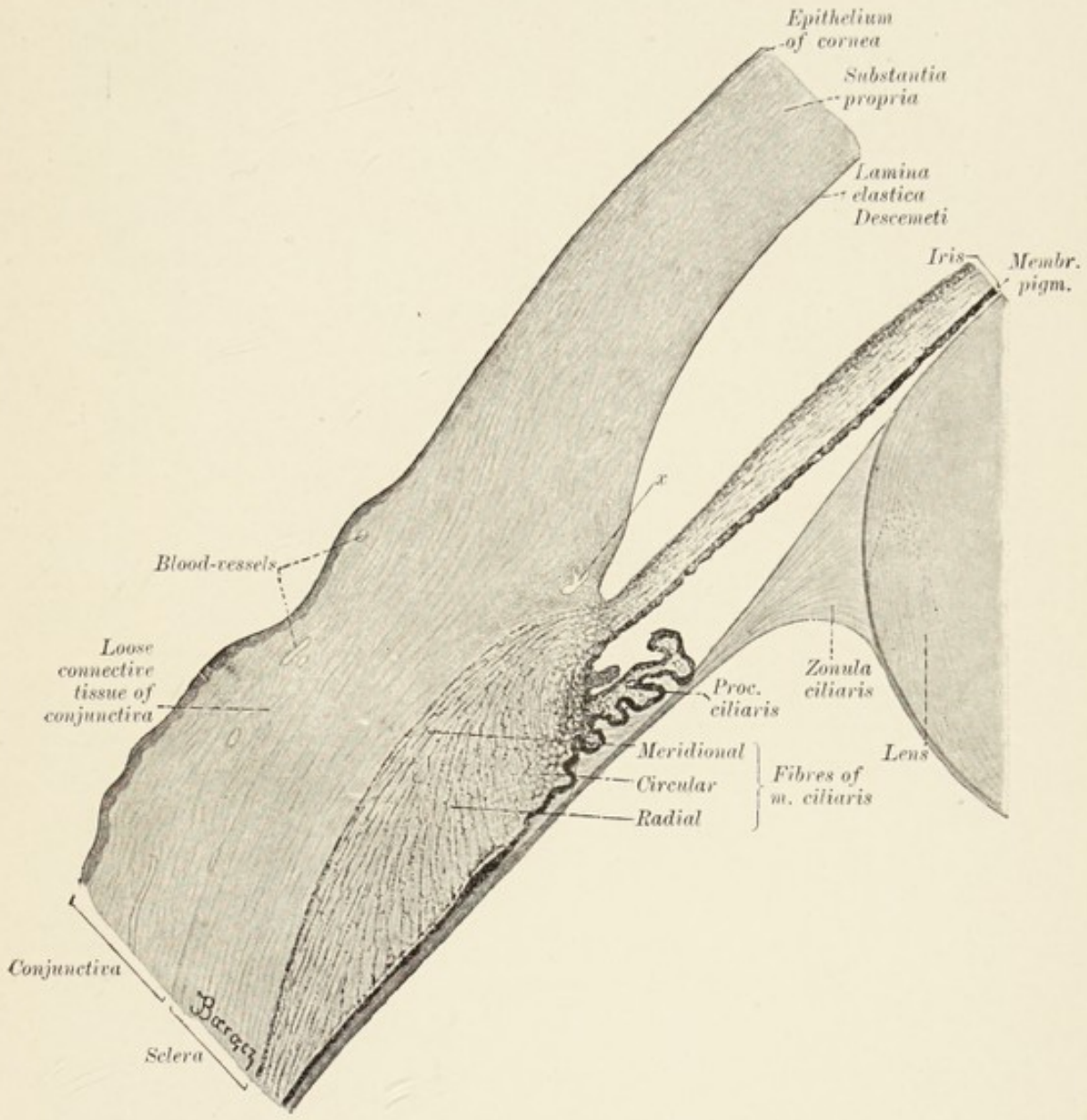


FIG. 262.—Meridional section through the ciliary body of an ape's eye. *x*, sinus venosus scleræ. × 30.

It consists of four layers: the anterior epithelium, the stroma iridis, the posterior limiting layer, and the pigment layer.

1. The *anterior epithelium* is made up of a simple layer of flat cells, which cover the anterior surface of the iris. In old individuals this layer is no longer to be made out.

2. The *stroma iridis* consists, in its anterior half, of reticular connective tissue (*anterior limiting layer*), and in its posterior half of loose connective tissue which contains numerous blood-vessels (*vascular layer*). The vessels, which here have a radial arrangement, possess no muscular sheaths, but are enclosed by a strongly developed adventitia. In this part of the iris the smooth muscle cells are collected to form the *musculus sphincter pupillæ* and the *musculus dilatator pupillæ*. The first is formed of bundles of fibres, which are arranged circularly around the pupillary edge of the iris in the form of bands about 1 mm. broad. The second muscle is made up of bundles of fibres running radially. The pigment which is present in the connective tissue of the iris stroma in varying quantity lends color to the iris. In light eyes it is not abundant.

The posterior limiting layer (Bruch's membrane), which is a process of the lamina basalis, is a refractive membrane 2 μ thick.

4. The *pigment layer* of the iris (pars iridica retinæ) presents two layers of cells. The cells of the posterior layer are cubical and strongly pigmented, while those of the anterior layer are flat and contain only a little pigment.

Special note must be made of those places where the cornea passes over into the sclera, and where the iris and corpus ciliare are connected with the outer coats of the eye. The sclera passes directly over into the cornea, its fibril bundles running without interruption from one coat to the other. The hardly noticeable line of separation passes obliquely backward and inward. In this region the ciliary border of the iris is attached to the outer coats of the eye. This attachment takes place by means of the so-called ligamentum pectinatum iridis, which in man is developed much less strongly than in many lower animals. The ligament is made up of a network of fibres

situated in the angle of the anterior chamber, between the cornea and iris. The fibres pass over into Descemet's membrane, which in this region shows a fibrillar structure. There occur here also, on the one side, free connective-tissue bundles from the substantia propria corneæ, and on the other side connective tissue and elastic fibres of the intermuscular tissue of the ciliary muscle and processes from the iris stroma. These fibres form a network whose strands are covered with flat epithelium continuous with the corneal endothelium and the epithelium of the anterior surface of the iris. Between the strands of tissue there are free spaces, the so-called *spaces of Fontana.*

(3) *Tunica interna.*

The *retina* is the third and innermost coat of the eyeball, and contains the terminations of the optic nerve fibres. It lines the whole posterior part of the eye, and ends at the pupillary border of the iris. We can distinguish it in three zones: 1. The *pars optica retinæ*, which extends from the place of entrance of the optic nerve, to the neighborhood of the ciliary body, where it ends in a zig-zag line, the *ora serrata;* 2. The *pars ciliaris retinæ*, from the ora serrata to the ciliary border of the iris; and 3. The *pars iridica retinæ*, which extends from the ciliary border to the pupillary border of the iris.

1. The *pars optica retinæ* (Figs. 263 and 265) is the only part of the retina which is sensitive to light. It consists of several layers, the elements of which have been studied by the newer methods, such as the vital methylene-blue staining, and the Golgi impregnation. Three main layers can be made out: the outermost *pigment layer*, the *middle layer* (Gehirnschicht), and the innermost *neuro-epithelial layer.* The middle layer is made up of six, the neuro-epithelial layer of four sheaths, so that the retina possesses altogether eleven layers:

1. Pigment layer.
2. Layer of rods and cones;
3. Membrana limitans externa;
4. Outer granular layer;
5. Henle's fibre layer.

} Neuro-epithelial layer.

6. Outer reticular (molecular) layer;
7. Outer ganglionic (inner granular) layer;
8. Inner reticular (molecular) layer;
9. Inner ganglionic layer;
10. Nerve-fibre layer;
11. Membrana limitans interna.

} Middle layer (Gehirnschicht).

We shall begin the description of the individual layers with the outermost one. The elements of the *pigment sheath* are usually regular hexagonal cells, which are arranged in a simple

FIG. 263.

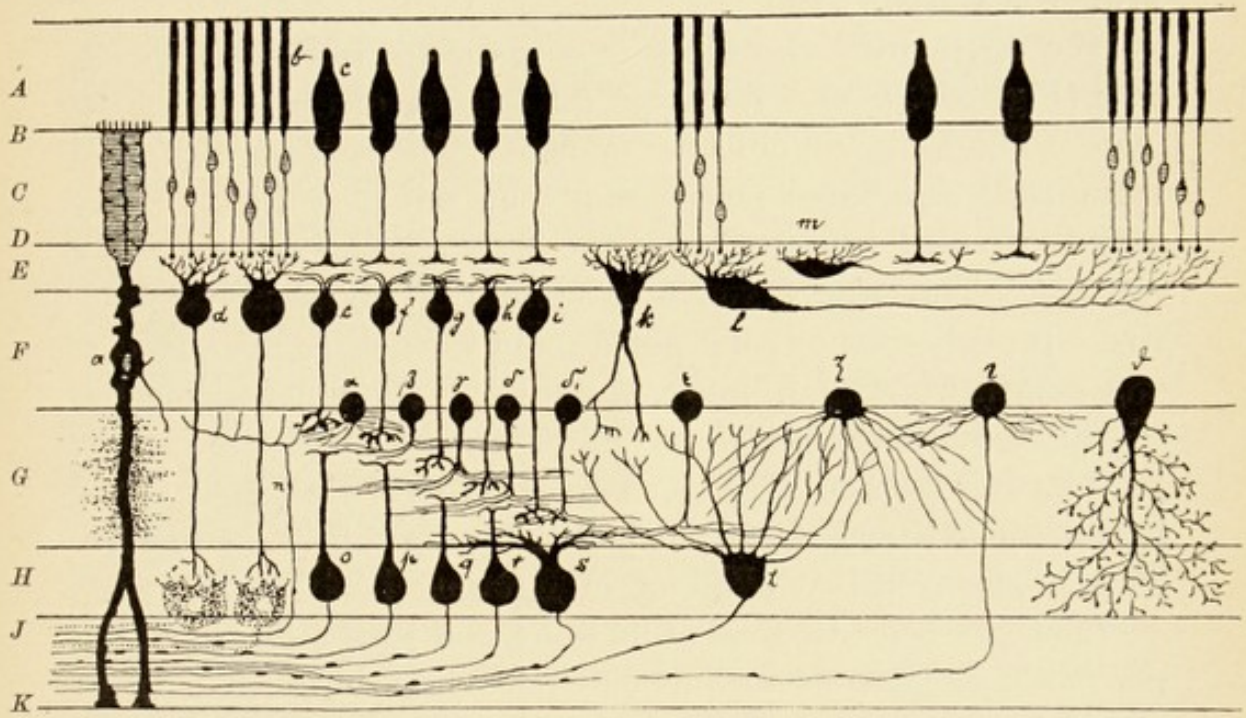


Diagram of the retina, compiled by Kallius, from the work of Ramón y Cajal.

A, layer of rods and cones; *B*, membrana limitans externa; *C*, outer granular layer; *D*, Henle's fibre layer; *E*, outer reticular layer; *F*, outer ganglionic layer; *G*, inner reticular layer; *H*, inner ganglionic layer; *J*, nerve-fibre layer; *K*, membrana limitans interna; *a*, Müller's supporting cell; *b*, rods; *c*, cones; *d*, bipolar cell belonging to rods; *e–i*, bipolar cell belonging to cones; *k–m*, horizontal cells; *n*, centrifugal nerve fibre; *o–t*, ganglion cells of optic nerve; *α–ε*, spongioblasts (amarkrine cells); *ζ–ϑ*, diffuse amakrine cells; *η*, nervous spongioblast. (From Merkel-Bonnet, *Ergebnisse d. Anat. u. Entwick*, Bd. II. S. 251.)

layer. The somewhat flattened nucleus lies in the outer pigment-free half of the cell. The inner strongly pigmented part of the cell possesses long, fine, fringe-like processes, which penetrate between the outer segments of the visual cells. The pigment, in the form of small dark-brown granules and rods, may change its position under the influence of light, so that

it is distributed equally throughout the cell. In consequence of this the rods and cones become surrounded by pigment granules in the region of the external limiting membrane. After exposure to stronger light the pigment moves to the outer part of the cell and collects in a thin layer there, so that the visual cells are quite free from it.

The *neuro-epithelial layer* is formed of the *visual cells.* Of these, there are three layers: the layer of rods and cones, the outer granular layer, and the sheath of Henle. The external limiting membrane is derived from the supporting cells of Müller (see below).

We distinguish two kinds of visual cells, *rod cells* and *cone cells* (Fig. 263, *b*, *c*). Each *rod cell* consists of a *rod* and a *rod fibre.* The latter contains the nucleus. The *rods* are elongated cylindrical structures, about 50 μ long and 2 μ thick. They may be divided into two parts, the *outer segment* and the *inner segment.* The outer segment is cylindrical and doubly refractive. It contains the visual purple, and when acted upon by certain reagents breaks up into many discs. The inner segment is slightly spindle-shaped, finely granular, and singly refractive. In the outer part of the inner segment there is in most vertebrates an ellipsoidal body which shows a fibrous structure. This is the so-called *ellipsoid* of Krause.

Each rod is continuous at its inner end with a fine fibre, the *rod fibre.* This ends in the outer reticular layer in a small globular thickening. Each rod fibre shows somewhere in its course a nucleated enlargement, the *rod nucleus.* This may occur at various levels, so that the outer granular layer contains many rows of nuclei. In some animals (cat, rabbit, guinea-pig, horse, etc.) the nucleus shows a distinct transverse striation, which is due to the arrangement of the chromatin substance in two to four plate-like segments. In man the nucleus shows a reticular structure, and only seldom do we see an indistinct cross-striation, which is due to annular thickenings of the chromatin network on the surface of the nucleus.

The *cone cells* consist also of two parts, the *cone* and the *cone fibre.*

The *cones* are shorter than the rods, measuring only about 30 μ. Like the rods, they show an *outer* and an *inner segment*. The outer segment is much shorter than that of the rod, and is slightly conical in form. It sometimes presents cross-striations. The inner segment is somewhat shorter and much thicker (6 μ) than that of the rod, and is rounded. The *ellipsoid* of the cone is larger than that of the rod, and lies in the peripheral part of the inner segment, occupying about two-thirds of this.

Each cone is continuous with a *cone fibre*. At the junction of these two parts of the cone cell, immediately inside the external limiting layer, lies the *cone nucleus*. The cone fibres end in the outer reticular layer by means of a conical expansion, from which fine fibres spread out.

The number of rods is far greater than that of the cones. They are distributed less uniformly, so that in a section taken at right angles to the surface two or three rods are found between each two cones.

The rods and cones lie in a row, the lower boundary of which is the membrana limitans externa (Fig. 263, *B*). This membrane is a product of the Müller's fibres. Outside these lie the rod and cone fibres, together with their nuclei, forming the outer granular layer (*C*). This consists usually of granules crowded closely together. In the region of the macula lutea the inner segments of the rod and cone fibres are elongated, and form the so-called *Henle's fibre layer* (*D*), which contains no granules.

The *outer reticular layer* (*E*) is made up of the thickened ends of the visual cell fibres and the end arborizations of cells whose bodies lie in the outer ganglionic layer.

The main constituents of the *outer ganglionic layer* (inner granular layer) (*F*) are the bipolar ganglion cells, whose processes end in the outer and inner reticular layers. Some cells (Fig. 263, *d*) establish a communication between the rod cells and the optic nerve fibres in such a way that the outer arborizations come in contact with the ends of the rod cells, and the inner processes reach to the inner border of the inner reticular layer to surround the ganglion cells there. Other

cells (*e–i*) are associated, by means of the processes which are sent into the outer reticular layer, with the broad conical ends of the cone fibres. The inner processes, on the contrary, enter the inner reticular layer, where they come into contact at various levels with the branched protoplasmic processes of the ganglion cells.

Besides these cells, we find at the inner border of this layer, cells which are known as *spongioblasts* (W. Müller) or *para-reticular cells* (Kallius). The processes of these cells end in the inner reticular layer. With these cells must be classified, according to Ramón y Cajal, those in which no axis-cylinder process is to be seen (amakrine cells, *α–ζ* and ϑ). Some of these give off end arborizations only at certain levels (*α–ε*, cells in which the dendrites are arranged in layers). Others, on the contrary, send their processes diffusely through the whole thickness of the inner reticular layer (*ζ* ϑ).

Besides the amakrine cells, we find at this level, in certain animals, cells giving off axones which pass over into optic nerve fibres. Finally, there are cells (*m*, *l*) which possess one or more main processes spreading out on the outer surface of the inner reticular layer. They resemble the so-called *horizontal cells* (Ramón y Cajal), which lie in the outer part of the outer ganglionic layer at the boundary of the outer reticular substance. These cells owe their name to the fact that their long axis lies parallel to the surface of the retina. They are ganglion cells whose bodies give off numerous short dendrites, branching abundantly in the outer reticular layer, and also a long, fine, horizontal axis-cylinder process, which breaks up at the end into numerous branches. Two kinds of these cells can be distinguished: the *outer smaller* cells (*m*), whose axis-cylinder processes come in contact by end arborizations with the ends of the cone fibres; and the *inner large* cells (*l*), whose long processes are connected with the end bulbs of the rod fibres. These cells join together distant parts of the retina.

We find also in this region cells (*K*) which send out processes which end above in the outer and below in the

inner reticular layer. The nuclei of Müller's fibres also lie at the level of the outer ganglionic layer.

The inner reticular (molecular) layer (*G*) consists of a fine network, which is derived mainly from the branched processes of cells of the outer ganglionic layer, as well as the dendrites of cells of the inner ganglionic layer. This layer shows striations parallel to the surface of the retina. This appearance is due to the fact that the end arborizations of the cells lie at different levels (Fig. 263). Between the most external arborizations of the bipolar cells (*e–i*) belonging to the cones, and between the innermost branched dendrites of the ganglion cells (*o–s*), there run the fine branches of the amakrine cells. Fine side branches of the Müller's fibres (*a*) also take part in this network.

The *inner ganglion-cell layer* (Fig. 263, *H*) consists of multipolar ganglion cells with many protoplasmic processes, which extend toward the outside, and at certain levels of the inner reticular layer break up into fine branches. Retzius and Cajal claim that each ganglion cell branches without forming anastomoses with other cells. Dogiel believes, on the contrary, that the protoplasmic processes of all ganglion cells of the retina join with one another and form a network. The axis-cylinder process extends inward and comes to lie in the nerve-fibre layer as an independent nerve fibre.

In the human retina a ganglion cell is sometimes found to be bound to another by a short bridge. These are the so-called *twin cells* (Dogiel, Greeff). Such a bridge may vary in length, and is only a thick protoplasmic process which is continuous with that of another cell. Only one of two cells thus connected possesses an axis-cylinder process, which passes over into the nerve-fibre layer.

In the inner ganglion-cell layer there lie cells (*t*) whose dendrites pass diffusely through the whole thickness of the inner reticular layer, but have no connection with the rods and cones.

The *nerve-fibre layer* (Fig. 263, *J*) contains the fibres of the optic nerve, which diverge from one another in all direc-

tions at the papilla nervi optici. This layer is thickest at the place of entrance of the optic nerve (Fig. 264). It contains only naked axis cylinders. The great majority of these are centripetal fibres, which are derived from the cells of the adjacent layer (*H*) of the retina. It is highly probable that there are a few (*n*) centrifugal fibres (Cajal), which are processes of ganglion cells situated in the brain. The greater number of these fibres form by their end arborizations a pericellular network around the cells which lie in the outer part of the inner reticular layer—*i. e.*, around the parareticular cells Some of them, on the contrary, end freely after penetrating to the more external layers of the retina (Dogiel).

The *membrana limitans interna* (*K*), which forms the innermost layer of the retina, is a product of the supporting cells of Müller (supporting fibres, radial fibres).

These *supporting cells of Müller* are somewhat similar to the ependymal cells of the embryonic spinal cord. They are elements of an epithelial nature (of ectodermal origin), and consist of elongated cells which extend through the whole thickness of the retina. The inner end of the cell is widened into a cone-shaped body, which shows a fibrous structure (radial fibre cone). In consequence of the fusion of these conical bodies, a membrane is formed, the membrana limitans interna. From this place the supporting cells extend toward the outer surface. In both reticular layers delicate fibres are given off in all directions. At the level of the outer reticular layer each cell presents an ellipsoidal nucleus. In the outer ganglionic and outer granular layers the cells show numerous cup-like depressions on their surfaces, caused by pressure exerted by other kinds of cells. At the bases of the rods and cones is found the membrana limitans externa, which is formed by a membranous widening of the supporting fibres. From its surface there run fine processes, which form the so-called *fibre-baskets*, which surround the bases of the rods and cones.

In the supporting tissue of the retina there are, in addition to the Müller's fibres, *neuroglia cells* (spider cells), which occur abundantly in the optic nerve.

Fig. 264.
Optic fibre sheath
Ganglion cell sheath
Inner molecular layer
Inner granular layer
Outer molecular layer
Henle's fibre sheath
Outer granular layer
Rods and cones
Pigment layer
Blood vessels
Lamina cribrosa
Bundles of optic nerve fibres
Fig. 265.
1. Pigment epithelium
2. Rods and cones
3. External limiting membrane
4. Outer granular layer
5. Henle's fibre sheath
6. Outer reticular layer
7. Inner granular layer
8. Ganglion cell layer
9. Nerve fibre sheath
10. Blood vessel
Fig. 266.
External sheath
Internal sheath
Blood vessels
Sclera
Blood vessels
Fig. 267.—Longitudinal section of optic nerve of man.
Hlondi's stain. × 30.
Hlondi's stain. × 70.
Fig. 268.—Section of retina at right angles to the surface.

FIG. 264.

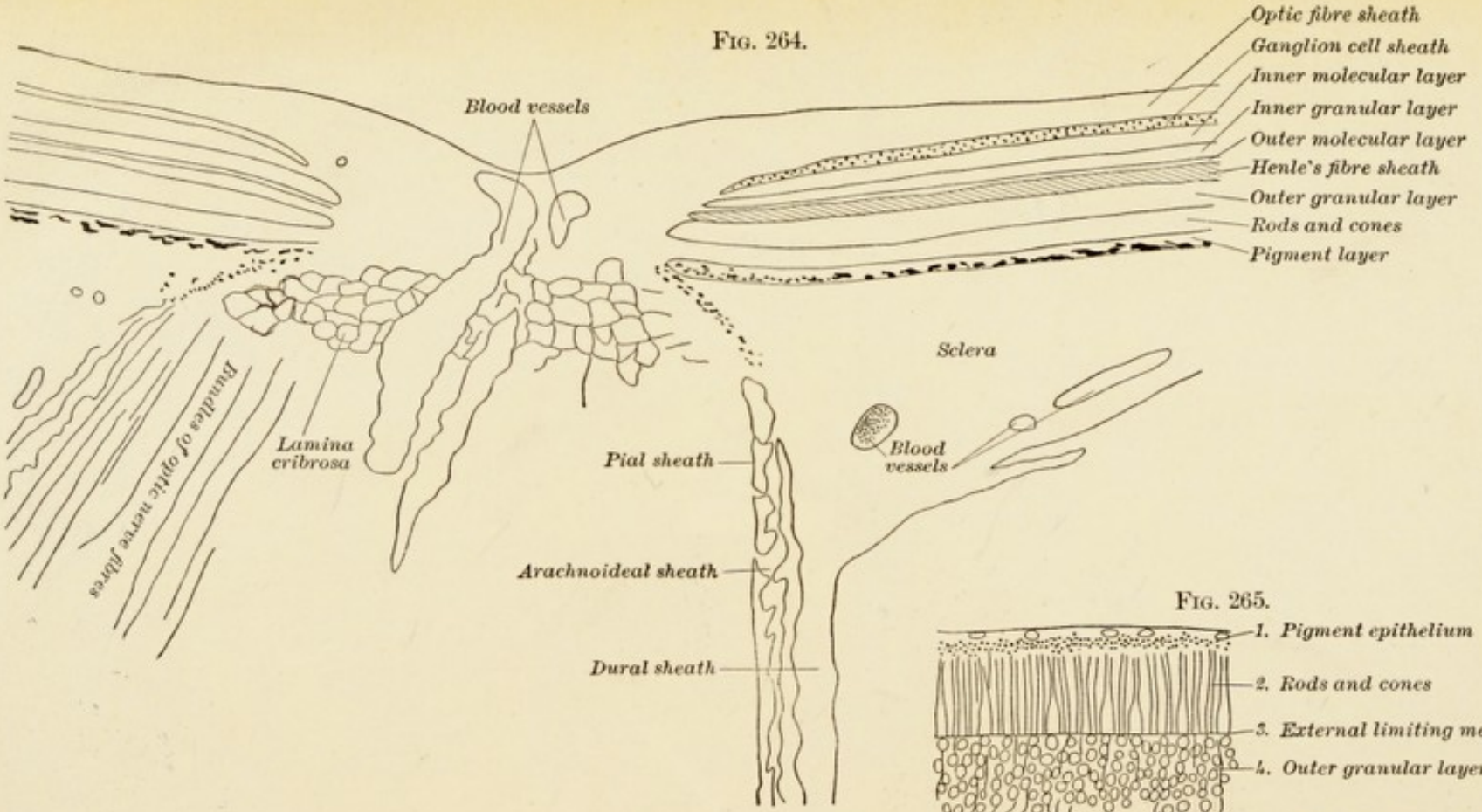


FIG. 265.

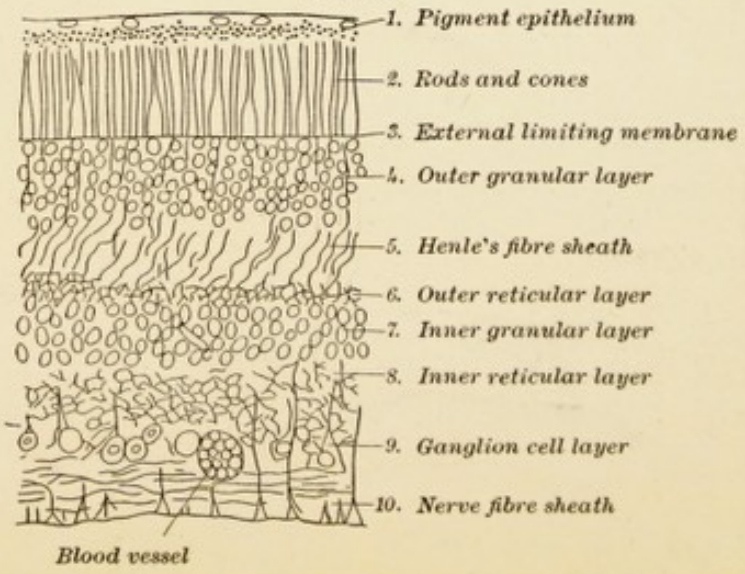
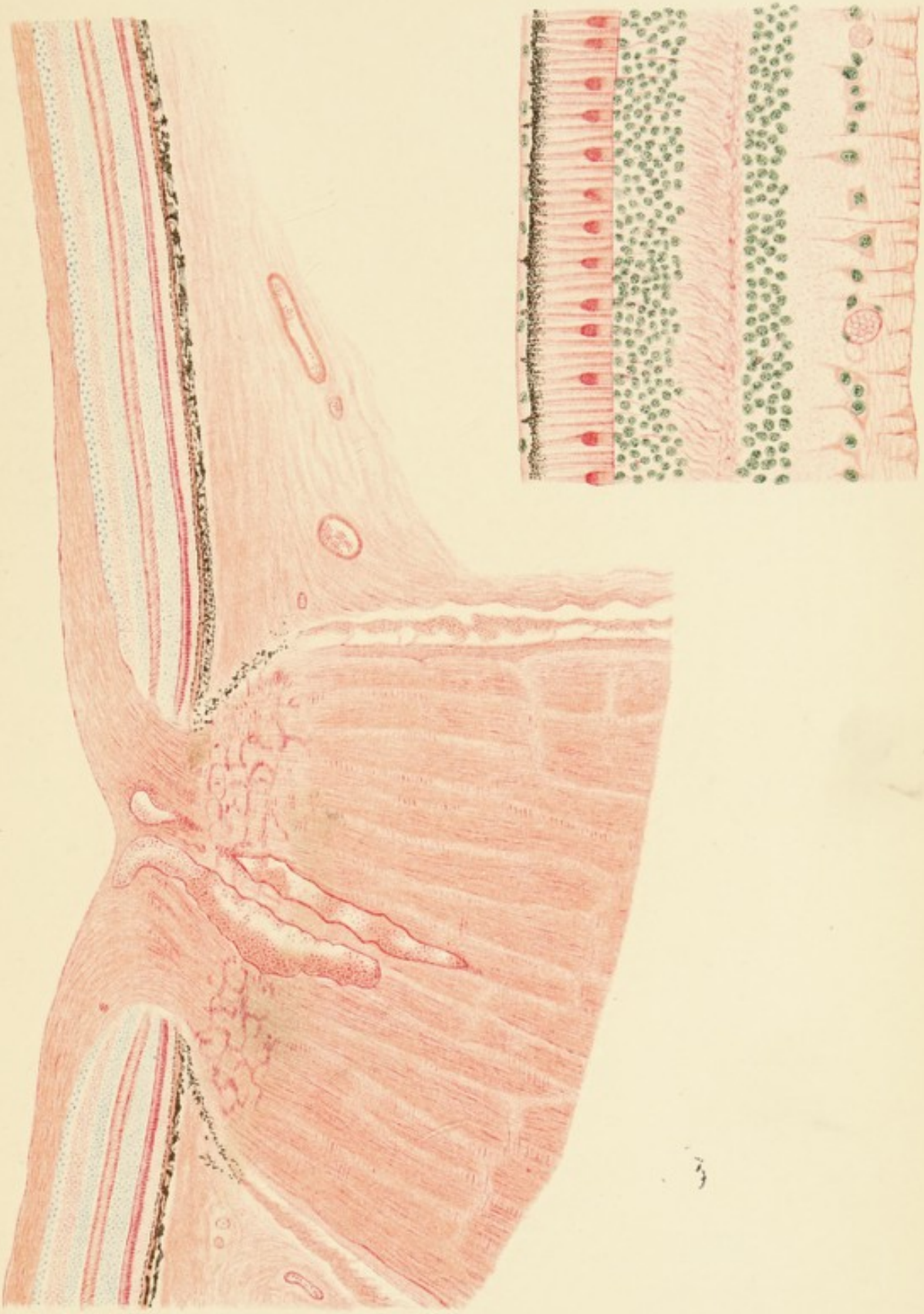


FIG. 264.—Longitudinal section of place of entry of optic nerve of man. Biondi's stain. × 70.

FIG. 265.—Section of retina of ape, taken at right angles to the surface. Biondi's stain. × 330.



Szymonowicz, Histology

J. Barącz ad nat. del.

Lith. Anst. v. Werner & Winter, Frankfurt a/M.

From the above description of the retina, it is seen that the light stimuli reach the brain in the following way: The rod and cone visual cells, which one may call the first neurones, receive the stimulus. From here it is transmitted to the bipolar cells of the outer ganglionic layer (second neurones), and thence to the cells of the ganglion-cell layer (third neurones), which send fibres through the optic nerve to the brain. The connection between these cells is by contact in the two reticular layers.

The retina has a somewhat different structure in the macula lutea, the papilla n. optici (see Optic nerve), and the ora serrata.

In the region of the *macula lutea* the middle or cerebral layer contains a yellow pigment, which is distributed diffusely, so that this part has a yellowish color on the surface. In this neighborhood the inner ganglion-cell layer is distinctly thicker, consisting of as many as nine layers of ganglion cells. The outer ganglionic layer is also wider here. The layer of rods and cones becomes poorer in rods as the macula lutea is approached, so that in this region itself only cone cells are present. In the macula lutea Henle's fibre sheath is especially well developed.

In the centre of the macula lutea on its inner surface there is a depression, the *fovea centralis*, in which the retinal layers are distinctly thinner than elsewhere. The nerve-fibre sheath ends here, and both ganglion-cell layers disappear, so that in the fundus foveæ itself only a neuro-epithelial layer is found. Owing to the entire absence of the pigmented cerebral layer of the retina, the fundus foveæ appears colorless.

In the region of the *ora serrata* a marked decrease in thickness of the retina takes place in consequence of the disappearance of the retinal layers. The nerve-fibre and ganglion-cell layers are the first to disappear. The structure of the visual cell layer is altered and the two reticular layers are lost. The outer granular layer fuses with the outer ganglionic layer. At a certain distance from the ora serrata the rod cells disappear, and the cone cells change their typical character and

become finally a single layer of cylindrical epithelium. The supporting cells of Müller are well developed here.

2. In the *pars ciliaris retinæ* we find only two layers of cells. Toward the outside there is pigmented epithelium, while on the inner side there is a layer of high cylindrical cells, which are derived from the neuro-epithelial layer. These cylindrical cells take the place of the layer of visual cells and the outer granular layer, which is still to be seen at the ora serrata.

3. Pars iridica retinæ, see Iris.

(4) *The Optic Nerve.*

The optic nerve possesses three sheaths, which are to be regarded as continuous with the membranes of the brain. The dura mater forms the outermost sheath, the arachnoidea the second, and that which lies immediately on the nerve is derived from the pia mater and sends septa between the individual fibre bundles. Between the processes of the dura mater and the arachnoidea, and between the arachnoidea and the pia mater, there are two spaces, of which the first is in communication with the subdural space, and the second with the subarachnoid space. All three sheaths are bound together by connective-tissue strands, which cross over through the spaces.

At the entrance of the optic nerve into the eyeball the dural and pial sheaths pass over into the sclera. The arachnoidea, on the contrary, breaks up into fibres before it reaches the sclera, so that the subdural and subarachnoidal spaces communicate with one another.

Where the optic nerve enters the eye, the sclera and choroid are pierced and perforated, so that they are reduced to a lattice-work tissue, which we call the *lamina cribrosa.*

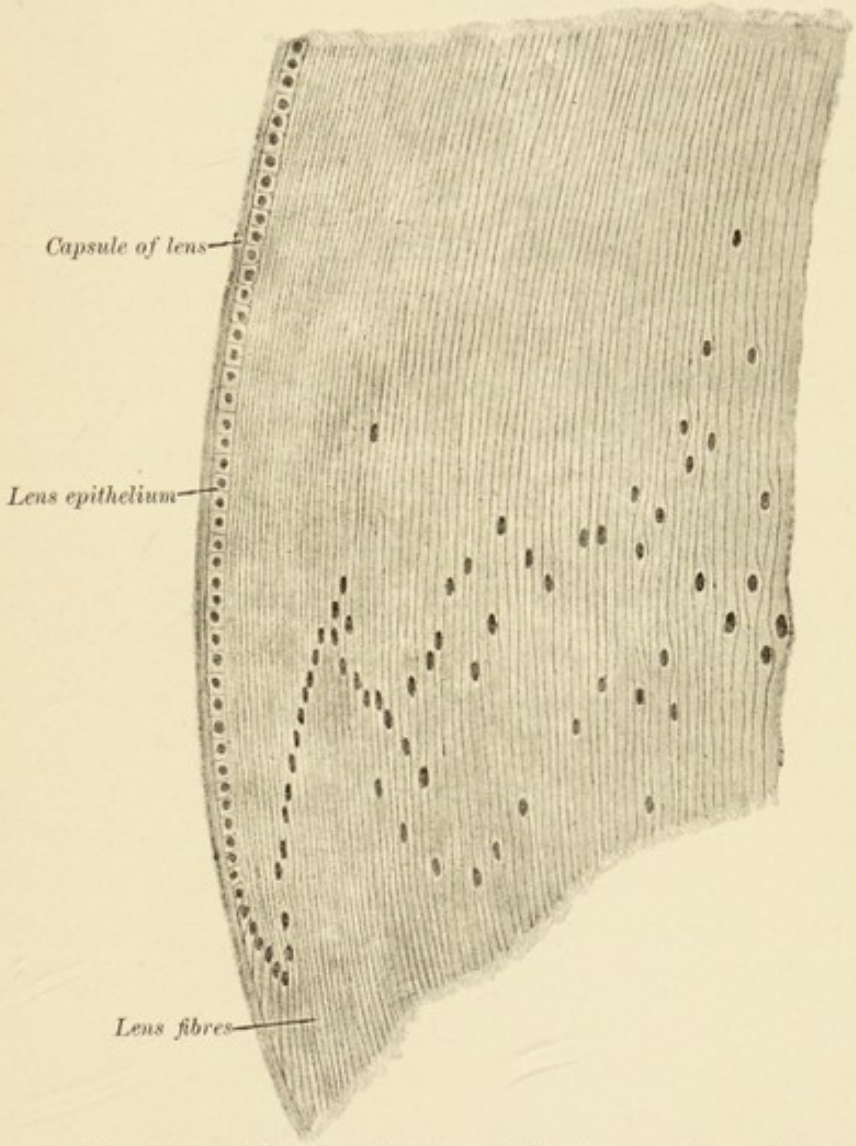
The fibres of the optic nerve are medullated but possess no sheath of Schwann. As the fibres pass through the chorioid and sclera they lose their medullary sheath and pass over on the inner surface of the retina as naked axis cylinders, which form the optic nerve-fibre layer. In consequence of the loss

of the myelin sheaths the nerve becomes considerably thinner on entering the eyeball.

(5) *The Lens.*

In the lens we may distinguish the *substantia lentis* and the *lens capsule.* The lens is an epithelial structure formed from the ectoderm. It consists in the beginning of cylindrical cells,

FIG. 266.



Part of a meridional section through the border of an ape's lens. × 200.

which during subsequent development increase in height at the posterior surface of the lens. This increase goes on until exceedingly long cells are formed, the *lens fibres.*

In adults the *substantia lentis* consists of lens fibres, which

at the anterior surface are covered by a single layer of cubical *lens epithelium*. This reaches as far as the equator of the lens, where the cells increase in height to form lens fibres. The lens fibres are flattened hexagonal prisms, which are thickened at the posterior end. They run in a meridional direction from the anterior surface backward. A small quantity of cement substance joins the fibres together. The outer fibres in the region of the equator possess oval nuclei, while in the centre of the lens no nuclei are present.

The *lens capsule* is a clear refractive membrane, which is thicker on its anterior (10–15 μ) than on its posterior surface (5–7 μ). On its outer surface it shows parallel striations and is lamellated. In its behavior toward reagents it resembles neither white fibrous nor elastic tissue. It is probably partly cuticular and partly connective tissue in nature.

(6) *The Vitreous Body and the Zonula Ciliaris.*

The vitreous body is made up of a tissue which contains about 98 per cent. of fluid substance, the *vitreous humor*. The firm parts have the form of fine intercrossing connective-tissue fibrils, connective-tissue cells of various kinds, and wandering cells (leucocytes).

The entire vitreous body is surrounded by a refractile homogeneous membrane, the *membrana hyaloidea*, which touches on the outside the membrana limitans interna retinæ.

In the region of the ora serrata fine fibres run from the surface of the hyaloid membrane and the ciliary processes in a meridional direction toward the lens and insert themselves in its capsule. The insertion of the fibres in the lens occupies a wide zone at the equator, which reaches some distance on the anterior and posterior surfaces. Taken together, these (*fibræ zonulares*) form the *zonula ciliaris*, which serves to hold the lens in place.

The fibres of the zonula and the equatorial zone of the lens form the boundaries of a whole system of large and small spaces, the *spatia zonularis* (canal of Petit), which are in communication with the posterior chamber of the eye.

PLATE LIV.

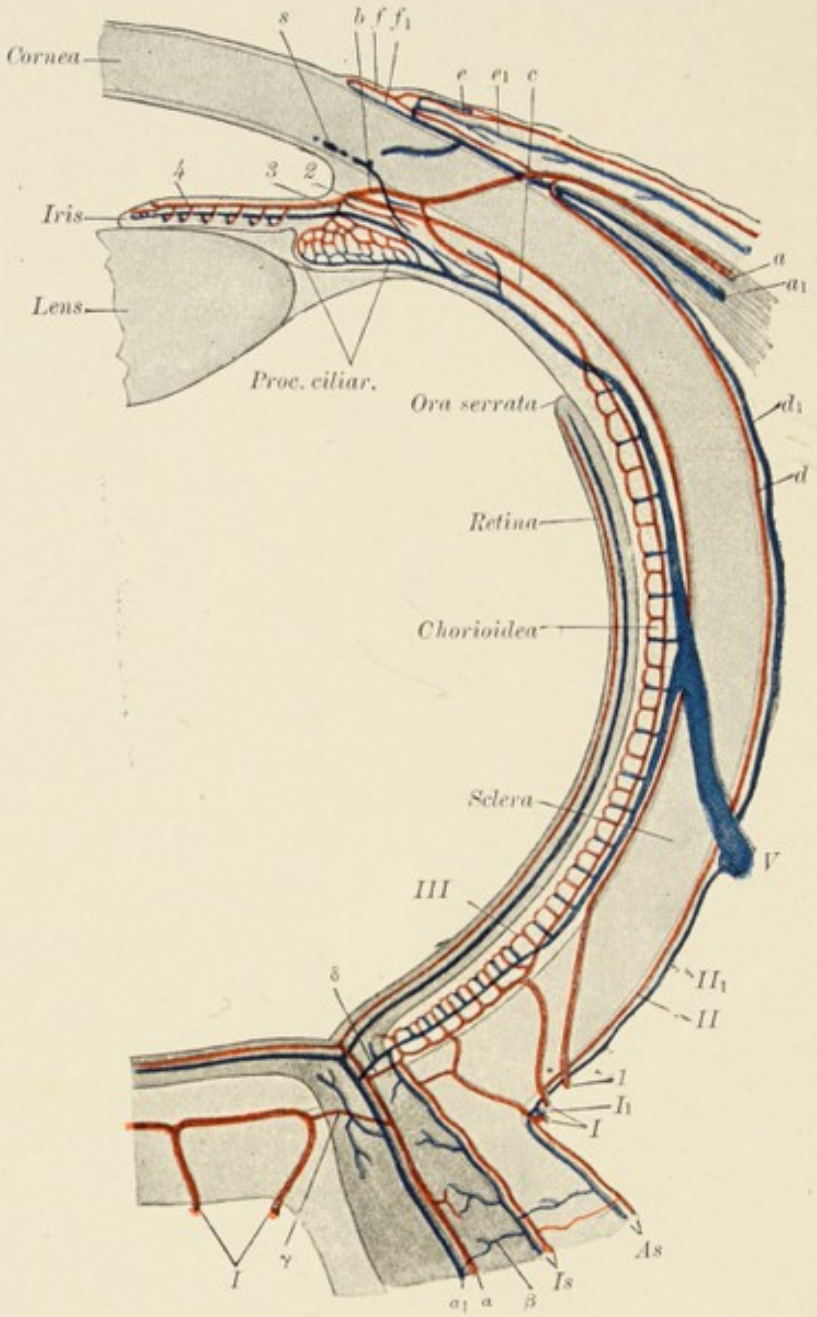


FIG. 267.—Diagram of the blood-vessels of the eye, as seen in a horizontal section. (Leber, after Stöhr.)

Arteries red, veins blue.

Course of vasa centralia retinæ: α, arteria, α_1, vena centralis retinæ; β, anastomosis with vessels of outer coats; γ, anastomosis with branches of short posterior ciliary arteries; δ, anastomosis with chorioideal vessels.

Course of vasa ciliar. postic. brev.: I., arteriæ, and I_1, venæ ciliar. postic. brev.; II., episcleral artery; II_1, episcleral vein; III., capillaries of lamina choricapillaris.

Course of vasa ciliar. postic. long.: 1, a. ciliar. post. longa; 2, circulus iridis major cut across; 3, branches to ciliary body; 4, branches to iris.

Course of vasa ciliar. ant.: a, arteria, a_1, vena ciliar. ant.; b, junction with the circulus iridis major; c, junction with lamina choriocapill.; d, arterial, and d_1, venous episcleral branches; e, arterial, and e_1, venous branches to conjunctiva scleræ; f, arterial, and f_1, venous branches to corneal border; V, vena vorticosa; S, transverse section of sinus venosus scleræ.

(7) *Blood-vessels of the Eyeball.*

There are to be distinguished in the eyeball two systems of blood-vessels, the *retinal system*, and the *ciliary system* (Fig. 267). These systems are marked off sharply from one another, and anastomose only at the place of entry.

The *retinal system* of vessels is formed by the *vasa centralia retinæ*. The central retinal artery (Fig. 267, *α*) runs in the axis of the optic nerve until it reaches the papilla, where it divides into two main branches. One of these runs forward and the other posteriorly. Each breaks up in the nerve-fibre layer of the retina into numerous small branches, which in turn form capillary networks. These supply the cerebral layer of the whole pars optica retinæ as far as the ora serrata. The neuro-epithelial layer and the fovea centralis are non-vascular. The branches of the retinal artery form so-called end arteries, for they anastomose with one another only by means of their larger twigs.

The veins arising from the capillaries run parallel with the arteries, and join finally, giving origin to two main trunks, which form the *central retinal vein*, *α*, in the axis of the optic nerve. The arteries give off on the way small twigs between the fibre bundles of the optic nerve. Some of these anastomose with the vessels of the outer coats of the eye, while others join with branches of the arteriæ ciliares posticæ breves (*γ*). Also the branches of the central retinal vessels form a connection with the smaller vessels and capillaries of the chorioid (*δ*).

In the eyes of embryos we meet with a vessel, the *arteria hyaloidea*, which is really a branch of the central retinal artery. This hyaloid artery runs through the vitreous body up to the posterior surface of the lens. It supplies the capsule of the lens and sends branches into the vitreous body. This vessel begins to degenerate before birth, and remains only as the so-called *Cloquet's canal* (canalis hyaloideus), which is filled with fluid.

The *ciliary system* of vessels is formed of:

(*a*) The arteriæ ciliares posticæ breves;

(*b*) The arteriæ ciliares posticæ longæ; and

(*c*) The arteriæ ciliares anticæ.

The first group supplies the smooth part of the chorioidea; the two latter supply especially the ciliary body and iris.

(*a*) The *arteriæ ciliares posticæ breves* (I.) break through the sclera in the region of the entrance of the optic nerve. They number eighteen or twenty, and give rise to the dense capillary network of the lamina choriocapillaris (III.). On the way they give off branches which supply the scleral surface of the posterior half of the eyeball, and form anastomoses with branches of the arteria centralis retinæ (γ), the arteriæ ciliares posticæ longæ, and the arteriæ ciliares anticæ.

(*b*) The *arteriæ ciliares posticæ longæ* (1) break through the sclera and run between the chorioidea and the sclera up to the ciliary body, where they form at the ciliary border of the iris the *circulus arteriosus iridis major* (2). From this there proceed branches which supply the ciliary processes (3) and the iris, and at the pupillary border of the iris form the *circulus iridis minor*.

(*c*) The *arteriæ ciliares anticæ* (*a*) arise from the arteries of the four straight muscles of the eye, and give off branches for the anterior half of the sclera (*d*), the conjunctiva scleræ (*e*), and the edge of the cornea. They then break through the sclera and send branches to the ciliary muscles, while others join with the circulus iridis major (*b*) or the lamina choriocapillaris (*c*).

The capillary loops supplying the edge of the cornea arise also from arteries of the anterior part of the conjunctiva scleræ. Here they form a network of capillaries which pass over into the underlying veins. The central parts of the cornea are in adult mammals entirely non-vascular.

Almost all the blood brought in by the arteriæ ciliares posticæ collects in the *venæ vorticosæ*. These veins (Fig. 265, V) are characterized by the fact that they have a course entirely different from that of the arteries. There are usually four to six trunks, which arise by the coalescence of numerous branches from all sides. They penetrate the sclera and open into one of the venæ ophthalmicæ.

Besides these main paths for the draining of blood from the

chorioidea, the ciliary body, and the iris, there are other veins, the *venæ ciliares posticæ breves* (I,) and the *venæ ciliares anticæ*, which take a course more or less parallel to that of the arteries. The *venæ ciliares anticæ* (*a*) drain the blood from the ciliary muscle and from the veins of the annular canal of Schlemm (S). They take the blood also from the episcleral connective tissue (*d*,) (except some which flows into the venæ vorticosæ), from the conjunctiva scleræ (*e*,) and from the edge of the cornea (*f*,).

(8) *The Lymph Paths of the Eyeball.*

The eyeball contains no true lymph-vessels, but a system of spaces which, according to Schwalbe, may be divided into the *anterior* and the *posterior lymph paths.*

The system of anterior lymph paths forms:

1. The lymph canals of the cornea and sclera;

2. The anterior chamber of the eye, which is filled with the aqueous humor. With this there communicates by means of a capillary space between the iris and lens:

3. The posterior chamber of the eye. With this in turn there are connected:

4. The spatia zonularia (canal of Petit).

The system of posterior lymph paths consists of:

1. The subdural and subarachnoideal spaces, separating the sheaths of the optic nerve;

The perichorioideal space between the chorioidea and the sclera;

3. The Tenon's lymph space, which is found between the dural sheath of the optic nerve and the sclera, and between the fibres of the fascia of Tenon; and, finally,

4. The lymph spaces of the retina. These appear as perivascular spaces, and as interlaminar spaces between the pigment layer and the rest of the retina.

The perichorioideal space is connected, by means of the spaces surrounding the venæ vorticosæ, with the lymph space of Tenon.

(9) *The Nerves of the Eyeball.*

The nerves which, in addition to the optic nerve, terminate in the eyeball penetrate the sclera in the region of the optic nerve, and run forward in the suprachorioidea. On their way they give off branches to the chorioidea, and form on the outer surface of the ciliary muscle a plexus which contains numerous groups of ganglion cells (*plexus gangliosus ciliaris*). From this, small branches run to the ciliary body, the iris, and the cornea.

The nerves to the ciliary body end in the walls of the blood-vessels, in the ciliary muscle, and in the lamina suprachorioidea, in the form of extremely fine end arborizations.

The nerves to the iris form an annular plexus in the iris stroma. They lose their medullary sheaths and supply the smooth muscle and the vessels of the iris, and form a fine plexus on its anterior surface.

The nerves to the cornea form a network in the sclera around the corneal border—the *plexus annularis*, from which branches proceed to the cornea and conjunctiva. The corneal branches enter from the sclera into the substantia propria of the cornea, where they lose their medullary sheaths and form plexuses at different levels. Of these, we distinguish four:

(*a*) The *ground plexus*, in the deeper layers of the substantia propria;

(*b*) The *subbasal plexus*, just under the lamina elastica anterior;

(*c*) The *subepithelial plexus*, in the deeper layers of epithelium; and

(*d*) The *intra-epithelial plexus*. The last plexus is made up of fine fibres running between the epithelial cells to the outermost layers, where they end freely in knob-like swellings.

According to Dogiel, some of the nerves in the substantia propria corneæ terminate by means of end plates. Some, on the other hand, end at the edge of the cornea in terminal bulbs (Krause), which are to be found also in great numbers in the conjunctiva.

(*b*) Protecting Organs of the Eye.

(*1*) *The Eyelids and the Conjunctiva.*

The skin which covers the outer surface of the eyelids passes over into the conjunctiva palpebralis, which lines the inner surface. Between these two layers we find the main portion of the eyelid, which contains the m. orbicularis palpebrarum and the tarsus. The relation of these constituents is shown best in a sagittal section of the lid, as represented in Fig. 268.

On the outer surface the skin is thin and contains numerous fine hairs, small sebaceous glands, and sweat glands. The papillæ of the corium are small and weakly developed, with the exception of those at the edge of the lid. The subcutaneous tissue is very loose and poor in fat cells. Along the anterior border of the lid there are thick hairs, the *eyelashes*, arranged in two or three rows and deeply sunk in the corium.

In connection with the eyelashes at the border of the lid we find two kinds of glands: the ordinary small *sebaceous glands*, and *Moll's glands* (glandulæ ciliares). The latter resemble the coil glands in form. Their ducts open often into the follicles of the eyelashes.

Behind the subcutaneous tissue there lies a layer of cross-striated muscle, the *m. orbicularis palpebrarum*, whose bundles run from one angle of the lid to the other. In a sagittal section the bundles are cut transversely. Near the border of the lid, behind the eyelashes, lies the *musculus tarsalis* (*Riolani*).

Farther in, there is a layer of connective tissue (fascia palpebralis), with which the tendon of the *musc. levator palpebræ* in the upper lid is fused. A part of this muscle, which also contains smooth muscle cells (*m. palpebralis superior*), is attached to the tarsus. In the lower lid we find in this region the tendon of the *m. rectus inferior*, of which the *m. palpebralis inferior* is a process. The latter contains smooth muscle cells.

Farther back, there occurs a firm plate of fibrous connective tissue, the so-called *tarsus*, which occupies about two-thirds of the height of the whole eyelid. It contains about thirty *tarsal*

glands (*Meibomian glands*), which are distributed throughout its whole height. They are alveolar glands, through the entire length of which there is seen a duct lined with stratified flat epithelium. The ducts open out at the border of the lid, as shown in Fig. 268. Opening into all sides of the duct there are round alveoli. Their cells undergo fatty change and give out a fat-containing secretion. The finer structure of these glands is like that of sebaceous glands.

At the upper border of the tarsus, in the lateral half of the eyelid, there are, especially in the upper lid, branched tubular glands (*Krause's glands*), which are to be considered as accessory tear glands. The ducts pierce the conjunctiva and open into the conjunctival sac.

The conjunctiva borders directly on the tarsus. It consists, like other mucous membranes, of epithelium and a tunica propria. The epithelium is made up of two or three layers of cylindrical epithelium with a cuticular border on the free surface. Among these cells there are vesicular cells containing mucous material. These differ from ordinary goblet cells, in not lying altogether on the surface. According to Pfitzner, they represent the so-called Leydig's cells, such as are found in the epidermis of the larvæ of fishes and amphibians. At the posterior edge of the lid this epithelium passes over into stratified pavement epithelium. Only in the upper part is the conjunctiva not smooth. Here it forms small furrows and folds. The connective-tissue tunica propria contains plasma cells and leucocytes in varying quantity.

The conjunctiva palpebralis passes over onto the eyeball at the fornix conjunctivæ and becomes the *conjunctiva scleræ*. In the fornix there often occur many small lymph nodules. The epithelium of the fornix and conjunctiva scleræ is similar to that of the cojunctiva palpebralis. The epithelium of the scleral conjunctiva passes over into stratified pavement epithelium in the neighborhood of the corneal border.

The *plica semilunaris*, which represents the rudimentary third eyelid, consists of connective tissue and stratified pavement epithelium. If it is strongly developed, it may contain

PLATE LV.

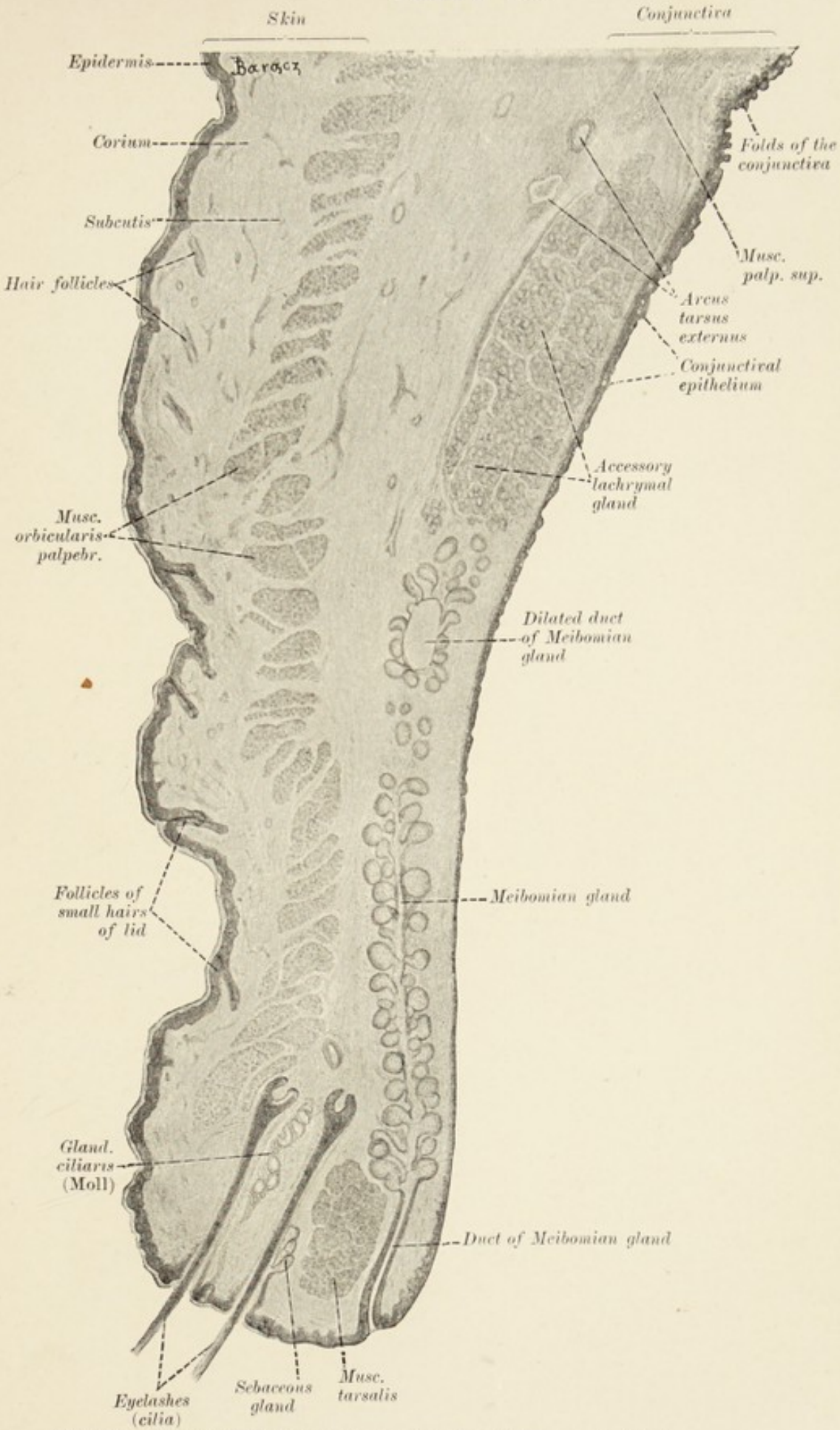


FIG. 268.—Section through the upper eyelid of a child two and a half years old. × 22.

a small plate of cartilage. The small glands which usually are found here probably represent the glands of Harder of lower mammals.

The *caruncula lachrymalis* is covered with stratified pavement epithelium, and may contain small hairs, sebaceous glands, coil glands (accessory tear glands), etc.

Into each eyelid there enter two *palpebral arteries*, one from the outer and the other from the inner angle of the eye (lateral and medial arteries). The two arteries join together on the anterior surface of the tarsus in the neighborhood of the lid border. This gives rise to the *arcus tarseus*. At the upper edge of the tarsus the arterial branches may form a second arch, which is often the case in the upper lid. Both arches break up into numerous branches which supply the skin, the muscle, the glands, and the whole conjunctiva. The vessels of the bulbar conjunctiva join at the border of the cornea with the arteriæ ciliares anticæ by numerous anastomoses.

The *lymph-vessels* form two plexuses which anastomose with one another. One lies in front of, the other behind, the tarsus. The bulbar conjunctiva contains in the tunica propria a capillary plexus of lymph-vessels which, according to Teichmann, Toldt, and others, is entirely closed at the border of the cornea. According to others (Waldeyer), it is in communication with the lymph system of the cornea.

The *nerves* form dense plexuses in the tarsus and also in the conjunctiva. The fibres derived from these supply the skin, muscle, vessels, and Meibomian glands. The latter become surrounded by fine networks of fibres. In the conjunctiva some of the fibres end in blood-vessels, others by free intra-epithelial arborizations; while the great majority terminate in round or oval end bulbs, which lie in the papillæ of the border of the lid and the neighboring conjunctiva, and in the tunica propria immediately under the epithelium in other parts of the conjunctiva.

(2) *The Lachrymal Apparatus.*

The *lachrymal gland* is a compound tubular gland which, from the nature of its secretion, must be regarded as serous. The ducts, which are numerous, are clothed with cylindrical epithelium, and receive the secretion directly from the intermediate portion of the gland. This intermediate portion, or neck, is lined with lower epithelium, and is continuous with the end portion or body of the gland. The latter is made up of granular serous cells surrounded by a membrana propria. In this there are stellate basket cells, which form a network around the gland tubules. The interstitial connective tissue contains a great many elastic fibres.

The walls of the *lachrymal canals* consist of stratified pavement epithelium and a richly vascular connective-tissue layer, which contains numerous elastic fibres. The walls lie on the longitudinal cross-striated muscle bands of the orbicularis muscle.

The *tear sac* and *nasal duct* are clothed with a double layer of cylindrical epithelium which may contain goblet cells. The tunica propria contains many leucocytes.

The *nerves* of the lachrymal glands are almost entirely non-medullated. They form a network in the membrana propria of the tubules, and from this fine fibres run through the membrana propria. These form a plexus at the bases of the cells, and a second one between the gland cells. These come into immediate contact with the gland cells.

3. AUDITORY ORGAN.

In the auditory organ we distinguish three parts: the *inner ear*, the *middle ear*, and the *outer ear*.

(*a*) The Inner Ear.

The inner ear is the most essential part of the auditory organ, for it contains the end apparatus of the auditory nerve. It is an organ of extremely complicated structure, and is known as the *labyrinth*. In it two main sacs are to be noted, the *sacculus* and the *utriculus*, which are joined by a narrow canal,

the *ductus utriculo-sacculari*s. The sacculus communicates by means of the *ductus reuniens* (Henseni) with a long spiral structure, the *cochlea* (ductus cochlearis). The utriculus, on the other hand, is connected with the three *semicircular canals*, each of which is dilated to form an ampulla at its point of communication with the utriculus.

These membranous structures, taken together, form the *membranous labyrinth*, which is surrounded by firm *bony labyrinth*. The membranous labyrinth contains a fluid, the *endolymph*, while its outer surface is bathed in the *perilymph* which fills up the space between the bony and membranous labyrinths.

(*1*) *Sacculus, Utriculus, and Semicircular Canals.*

All of these parts possess a somewhat similar structure, which in comparison with that of the cochlea is quite simple. They all incompletely fill the bony spaces in which they lie, and only in certain places are fixed to the periosteum. The free spaces are traversed by connective-tissue strands (ligamenta sacculorum et ductuum), which, on the one hand, are fastened to the wall of the canal, and, on the other, to the periosteum. These strands are covered with a layer of flat epithelial cells similar to those of the periosteum and labyrinth.

The walls of these sacs and canals consist of three layers, namely, a connective-tissue sheath rich in elastic fibres, a structureless basal membrane, and an epithelial layer. The last consists of a single layer of flat epithelium.

Along the concave side of each semicircular canal there is a line, the so-called *raphe*, where the cells increase considerably in height. Also in the ampullæ the cells bordering on the cristæ acusticæ are cylindrical, and form the *plana semilunata*.

Where the auditory nerve ends, the epithelial layer is more complicated. In the sacs there are found the *maculæ acusticæ*, and in the ampullæ the *cristæ acusticæ*. The low epithelium becomes in these regions much higher. It shows a cuticular

border and passes over into the neuro-epithelium. In the latter we can distinguish two kinds of cells: 1, supporting cells; and 2, hair cells.

1. The *supporting cells* are long structures somewhat widened at each end and split at the lower extremity. The oval nucleus lies, as a rule, in the lower half of the cell.

2. The *hair cells* are cylindrical cells which do not occupy the whole thickness of the epithelial layer. The thickened, bulged end, which contains a spherical nucleus, reaches only as far as the middle of the layer. The free upper end of the cell presents a cuticular border with a number of fine hairs, which are shorter in the macula than in the crista. The hair cells are elements which are in close contact with the sensory nerves. The relation of the nerve fibres to the hair cells is as follows: The nerve fibres break through the basal membrane, lose their medullary sheaths, and at the bases of the hair cells break up into three or four branches, which go to form a horizontal plexus (stratum plexiforme). These surround the hair cells like the calyx of a flower, and give off ascending branches, which, however, do not reach the surface. In this way one branch usually comes in contact with many hair cells (Retzius, Ramón y Cajal, and others).

The maculæ acusticæ are covered by a layer of soft gelatinous substance, the so-called *otolith membrane*, which encloses numerous small prismatic *otoliths* (statoliths, otokonien crystals). These consist of calcium carbonate. The otolith membrane is to be regarded as a cuticular structure.

In the ampullæ we find on each crista a conical structure, the *cupola*, which corresponds with the otolith membrane. This is seen plainly in fixed preparations, where the semifluid substance between the auditory hairs is coagulated. In the neighborhood of the cristæ and maculæ the whole wall of the sacculus utriculus and canals is distinctly thicker, owing to the increased thickness of the connective-tissue sheath and basal membrane.

PLATE LVI.

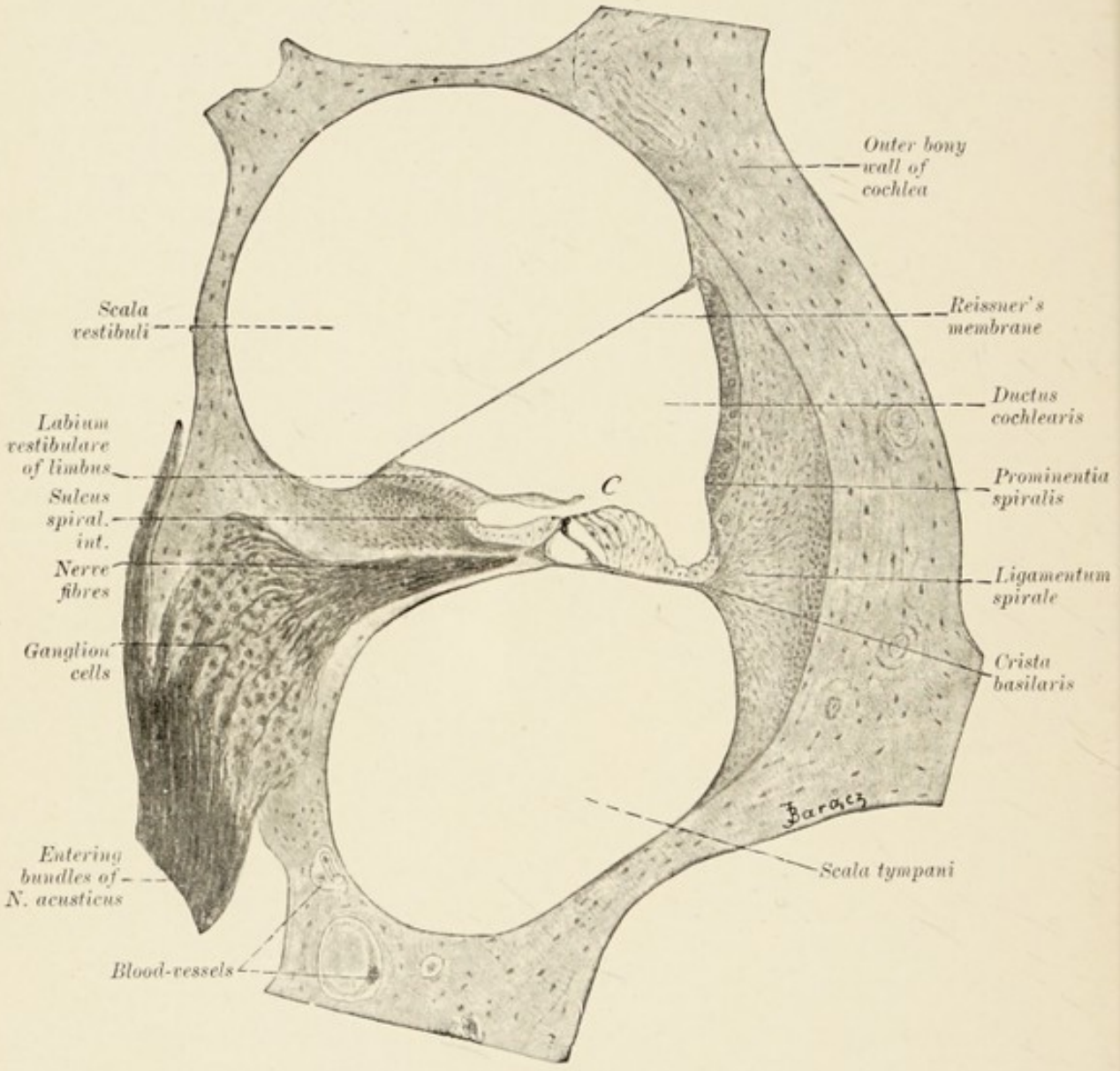


FIG. 269.—Section through the second coil of a guinea pig's cochlea. *C*, Cortis organ. × 95.

(2) *The Cochlea.*

The membranous cochlea, or ductus cochlearis, is a long sac which fills up only a small part of the bony cochlea and follows the spiral turns two and three-quarters times. The ductus cochlearis (Fig. 269) lies between the perilymphatic sacs, the *scala vestibuli* and *scala tympani*. It touches on the former with its upper wall the *membrana vestibuli* (*Reissneri*); and on the latter with its lower wall the *lamina spiralis membranacea*.

For convenience in description, we shall consider the cochlea as not lying horizontally, but with its axis vertical, so that its base is down and its apex up. If then an axial section be taken, the ductus cochlearis has in cross-section a triangular outline. Two of these sides form the upper and lower walls, while the outer wall lies against the periosteum of the outer bony cochlea. The periosteum is here distinctly thickened, so that it forms on cross-section a semilunar mass of connective tissue (*ligamentum spirale*). The angle where the upper (vestibular) and lower (tympanal) walls come together lies at the apex of the triangle opposite the external wall, in the region of the outer free border of the lamina spiralis ossea. At this point the connective tissue forms a projection on the lamina spiralis ossea, the *limbus spiralis*. This begins at the attachment of Reissner's membrane, and forms a ridge protruding into the lumen of the ductus cochlearis. This is called the *labium vestibulare*. Farther outward there is a process which overhangs the free border of the lamina spiralis ossea and lies on the wall of the scala tympani. This is the *labium tympanicum*. Between these two labia there is the *sulcus spiralis internus*.

The walls of the membranous cochlea consist of a very fine connective-tissue sheath and an epithelial layer. The latter lines the inner surface of the ductus cochlearis and shows some peculiarities in structure in certain places. The outer and upper walls are formed quite simply. The *membrana vestibularis*, which forms the upper wall of the ductus cochlearis, is a very

thin membrane, which is a process from the periosteum of the scala vestibuli. It therefore consists of a thin connective-tissue layer covered on the upper surface with flat cells, and on the side toward the ductus with a single layer of flat polygonal epithelial cells.

The *outer wall* lies directly on the periosteum. The outer layer, which consists of loose connective tissue, fuses with the periosteum and forms together with this the ligamentum spirale. From this, two processes extend toward the lumen of the ductus cochlearis: the *prominentia spiralis*, which contains a vein, the *vas prominens;* and the so-called *crista basilaris*. Between these processes there is a depression, the *sulcus spiralis externus*. The outer layer of loose connective tissue immediately under the epithelium contains a dense network of blood-vessels (*stria vascularis*). It reaches from the insertion of the membrana vestibularis to the prominentia spiralis. Its capillaries play an important rôle in the secretion of the endolymph of the cochlea. They are situated so close to the surface that they enter the epithelial layer, and we have here to do with a vascularized epithelium. The cubical epithelium covering the stria vascularis is not sharply marked off from the connective tissue. At the prominentia the epithelial cells are much lower than elsewhere. They increase in height below, and pass over into the cylindrical cells of the lamina basilaris.

While the upper and outer are comparatively simple, the lower (tympanal) wall shows a very complicated structure (Fig. 270). It is formed partly by the limbus spiralis, which rests on the free border of the lamina spiralis, and partly by the lamina spiralis membranacea.

The limbus is connected closely with the periosteum of the underlying lamina spiralis ossea. It shows on its surface more or less irregular papilla-like protuberances, and at the top of the labium vestibulare a series of radially arranged plates, the so-called Huschke's auditory teeth. The entire surface of the limbus is covered with a layer of cubical epithelial cells. At the free border there is in the lamina spiralis ossea a series of oval holes, the *foramina nervina*, through which the bundles

PLATE LVII.

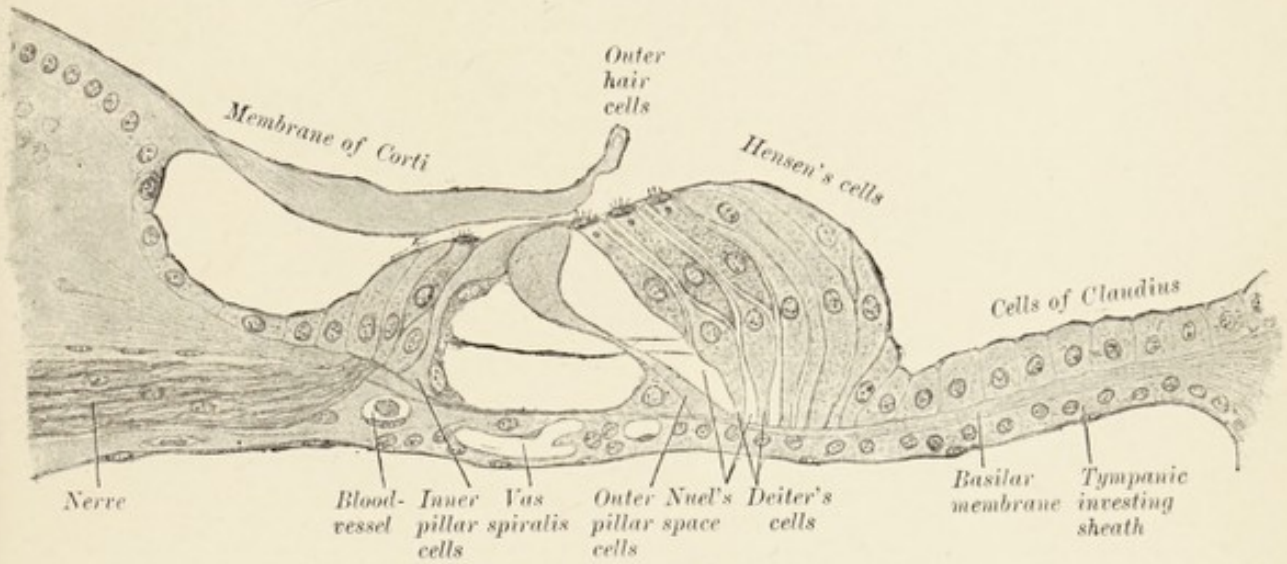


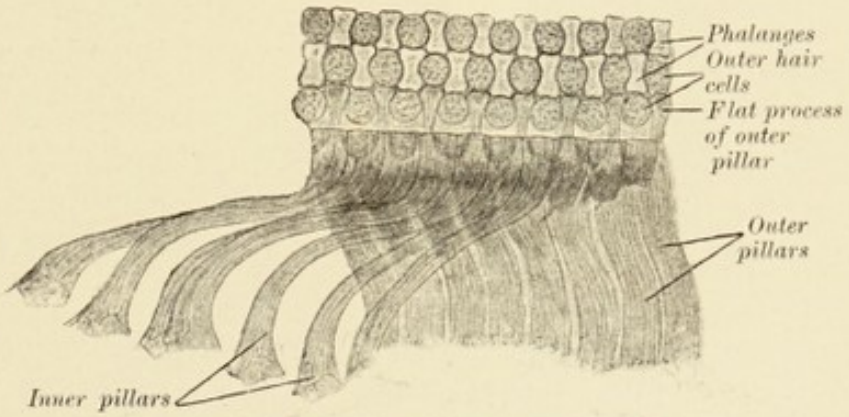
FIG. 270.—Vertical section through the organ of Corti of a guinea-pig. × 350.

of the cochlear nerve pass. The number of these holes is estimated as about 4000. The zone is known as the *habenula perforata.*

We pass on to the second, more complicated part of the tympanal wall, the *lamina spiralis membranacea.* The base of this part forms the so-called *membrana basilaris*, which is a process of the connective tissue occurring in the labium tympanicum of the limbus, and attaches itself to the crista basilaris of the ligamentum spirale. It has the form of a fine tightly stretched membrane of a connective-tissue nature. The membrana basilaris possesses on its lower (tympanal) surface a layer which is a process of the periosteum of the lamina spiralis ossea, and consists of an inner connective-tissue sheath and a layer of flat epithelial cells.

The surface directed toward the lumen of the ductus cochlearis is covered with epithelium, which is in large part differentiated into neuro-epithelium. It forms the so-called *organon spiralis* or *Corti's organ*, in which lie the terminal ramifications of the cochlear nerve.

FIG. 271.



Fragment of the organ of Corti of a rabbit. × 470.

Corti's organ covers the inner part of the membrana basilaria. The part is called the *zona tecta*, as opposed to the outer part, which is striated on its surface, and is known as the *zona pectinata.*

If we observe the organ of Corti in a radial section of the cochlea, we see that it is made up of an inner and an outer part, which are made up of *auditory cells* and *supporting cells.*

These parts are the inner and outer segments of the organ of Corti, and are situated on either side of *Corti's arch.*

In Fig. 270 it is seen that the epithelial cells from the sulcus spiralis internus outward become higher and pass over into the inner segment of the organ of Corti. Two kinds of cells can be recognized in this region. Those of one kind are provided with fine hairs on the upper free surface, and are known as the *inner hair cells* or *auditory cells.* They are arranged in a row bordering on the arch of Corti. They are cylindrical structures, whose lower thickened parts contain large nuclei. They do not reach to the membrana basilaris.

The upper free surface of these cells is marked by a cuticular border which is broader than the upper end of the cell body; and carries about twenty fine stiff hairs. These are essentially sense cells, entering into communication with the terminal ramifications of the cochlear nerve fibres.

Just internal to the hair cells we find three or four rows of high cells which act as supports for the hair cells. These are called the *supporting cells* or *inner roof cells.*

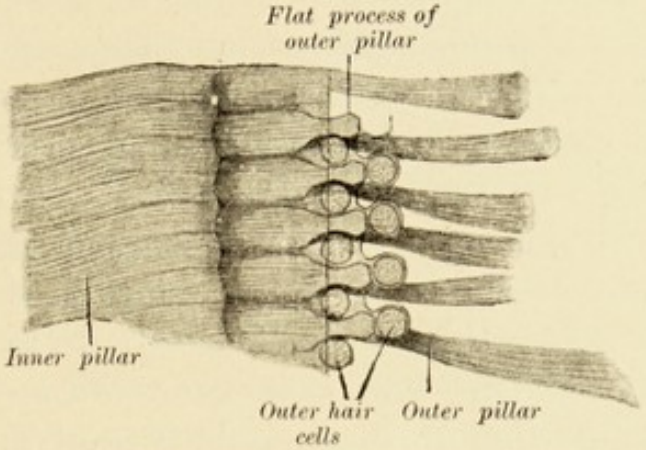
Toward the outside the hair cells lie on the cells of Corti's arch. The latter consist of two rows of so-called *pillars* (pillar cells). We distinguish the *inner pillars* and the *outer pillars* of the arch (Figs. 271 and 272). These are somewhat S-shaped, and lean toward one another, so that their upper ends are joined, and lower ends resting on the membrana basilaris are far apart. In this way they form an arch—*arcus spiralis*—which partly encloses the *canal of Corti.*

The *inner pillars* are strong fibres, each spread out at its base to form a foot-plate resting on the membrana basilaris. The upper end (head end) is thickened and hollowed to form a socket, in which the head of the outer pillar fits. The lengthened upper part forms a flat process or head-plate overlying the head of the outer pillar. The middle part or body of the pillar is thin, and shows on close examination a striation which indicates a fibrous structure.

The *outer pillars* are constructed similarly. They are somewhat larger and broader than the inner pillars, so that, for

example, in the guinea-pig, ten inner pillars correspond with eight outer pillars (Fig. 271). The inner pillars are more numerous than the outer. The heads of the latter are variable in form. There is a rounded joint-surface which fits into the socket of the head of the inner pillar. From this it bends outward and forms a flattened oar-shaped process, which enters between the upper free end surfaces of the outer hair cells, which will be described later (Figs. 271 and 272). The thin

FIG. 272.



Piece of the organ of Corti of a rabbit, seen from above. × 470.

head-plates of the inner pillars cover the heads of the outer pillars and a part of the oar-like process. That these structures are differentiated from the cells by a kind of cuticular formation is shown by their connection with nucleated masses of protoplasm. On the inner surface of the outer pillar, in the angle between the foot-plate and the membrana basilaris, we find such a collection of protoplasm. The inner pillar, on the contrary, possesses two similar accumulations of protoplasm, one at the base and the other on the outer surface of the body of the pillar.

External to the outer pillars we find the *outer hair cells.* These are like the inner hair cells, with the exception that each contains in the upper half in the neighborhood of the cuticular border a dark round body which is known as *Hensen's spiral body.*

Their hairs are somewhat shorter than those of the inner hair cells. They are arranged in three or four rows, which are

separated from one another by rows of *Deiters' cells* (supporting cells). The latter are flask-shaped cells, each of which rests on the membrana basilaris by a narrow base. The middle thicker part of the cell contains a large nucleus, and becomes much smaller above to form a process which widens out at the end into a cuticular structure, the so-called *phalanx*. In the axis of each Deiters' cell there is a thin firm fibre which passes above into the phalanx and acts as a supporting mechanism for these cells. It is a cuticular differentiation of the cell protoplasm.

The phalanges are related to one another in such a way that they form a delicate network (*membrana reticularis*, Fig. 271). The spaces are filled by the cuticular borders of the outer hair cells.

Between the cells of this outer segment of Corti's organ is a whole system of intercellular spaces, which in the upper half separate the supporting and auditory cells from one another; while in the lower half, where the hair cells are not present, they separate only the supporting cells (Fig. 270). This whole system of spaces, together with the spaces which are left between the outer pillars and the inner row of outer hair cells, is known as *Nuel's space*. It communicates with the canal of Corti by means of narrow spaces between the thin bodies of the outer pillars. This entire canal system is filled with endolymph.

Fastened to the last row of Deiters' supporting cells there are many (five to eight) rows of cylindrical cells, the so-called *Henle's cells*. These become cubical toward the outside, and form about ten rows on the membrana basilaris of the so-called *cells of Claudius*. In man both kinds of cells may contain pigment granules.

Mention must still be made of a cuticular structure which is called the *membrana tectoria* (Cortii) (Fig. 270). It is a very thin membrane of cells adhering to the limbus spiralis. At the border of the labium vestibulare it becomes free, covers over the sulcus spiralis internus, and lies on the organ of Corti. The free thin border reaches up to the outermost row of outer hair cells. The structure of this membrane is purely fibrillar.

Into the organ of Corti the *ramus cochlearis* of the n. acusticus sends its end ramifications. It passes up in the axis of the cochlea and gives off branches which run toward the lamina spiralis ossea. Here at its base the cochlear nerve possesses a ganglion which follows the spiral windings of the cochlea, and is therefore known as the *ganglion spirale*. Each medullated nerve fibre passes over into a bipolar ganglion cell. The second process originating in the opposite pole of the cell becomes a medullated fibre. This enters the lamina spiralis ossea, and takes part in the formation of a nervous plexus. In passing through the foramina nervina these fibres lose their medullary sheaths and enter the organ of Corti as naked axis cylinders. Here they lie in many bundles, which in part run spirally in the cochlea, and in part proceed directly to the bases of the inner and outer hair cells, passing through the canal of Corti and the space of Nuel. The terminal branches of the fibres surround the lower parts of the hair cells and end on their surface. These cells are sense cells, which take up auditory impressions and pass them on to the first peripheral neurones, whose cell bodies lie in the ganglion spirale.

(*3*) *Blood-vessels of the Membranous Labyrinth.*

The branch of the arteria auditiva which supplies the membranous labyrinth breaks up into three twigs, namely, the art. vestibularis, the art. cochlearis, and the art. vestibulocochlearis (Siebenmenn).

(*a*) The *arteria vestibularis* supplies the n. vestibularis, the upper and lateral parts of the sacculus and utriculus, and the ampullæ of the upper and lateral semicircular canals.

(*b*) The *arteria vestibulocochlearis* supplies, by its vestibular branch, the lower median half of the sacculus and utriculus, the posterior ampulla, the lower end of the cochlea; and by its cochlear branch the first third of the first coil of the cochlea.

(*c*) The rest of the cochlea is supplied with blood by the *arteria cochlearis*. This breaks up in the axis of the cochlea into three or four branches, which run spirally and give off numerous twigs in a radial direction. Some of these are for the

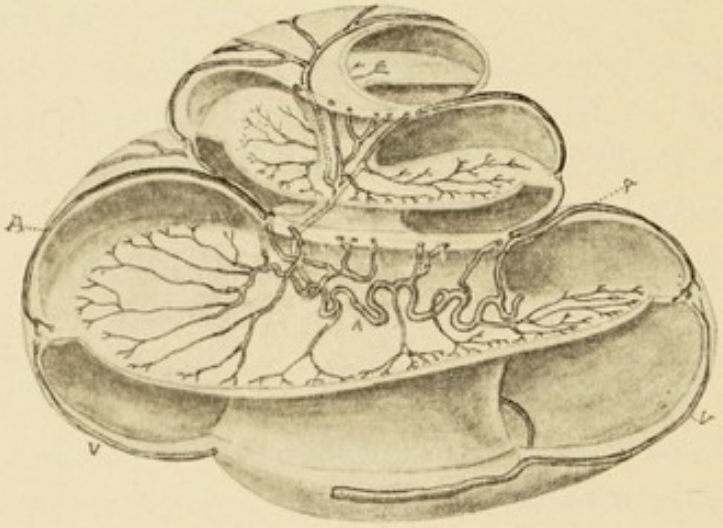
ganglion spirale, some for the lamina spiralis, and some for the walls between the scalæ. The last branches mentioned run to the stria vascularis, where they form a rich network of capillaries.

Of the capillary networks which arise from these arteries of the membranous labyrinth, those of the maculæ and cristæ are the densest.

The venous blood escapes from the membranous labyrinth by three separate venous trunks:

(*a*) The *vena aquæductus vestibuli* collects the blood from the semicircular canals and partly from the utriculus.

FIG. 273.



Cochlea of human adult, showing blood-vessels. × 12. (After Eichler.) *A*, arteries; *V*, veins.

(*b*) The *vena aquæductus cochleæ* carries the blood from a part of the utriculus, the sacculus, and the cochlea. The veins of the cochlea run mainly in the walls of the scala tympani. They unite to form the *venæ spirales*, which lie under the spiral ganglion. We distinguish two spiral veins: the lower (posterior) collects the blood from the first and part of the second coil of the cochlea; the upper (anterior) drains the upper segments of the cochlea.

The above-mentioned *vas prominens*, as well as the *vas spirale* which runs in the tympanal layer of the membrana

basilaris, opens into the vena spiralis, which at the same time carries a part of the blood from the ganglion spirale.

(*c*) The *central cochlear vein* drains the blood from the lamina spiralis and partly from the spiral ganglion. It opens into the *vena auditiva interna.*

The general relations of the arteries and veins of the cochlea are shown in Fig. 273, taken from Eichler's work.

(*4*) *Lymph Paths in the Labyrinth.*

The *ductus endolymphaticus* widens out to form a flat sac (*saccus endolymphaticus*), which lies at the posterior surface of the bone, between two folds of the dura mater. It communicates with the subdural lymph spaces by means of fine canals.

The perilymphatic spaces are placed in communication with the subarachnoideal space mainly by means of the *ductus perilymphaticus.* Besides the lymph spaces, the blood-vessels are surrounded by perivascular spaces.

(*b*) The Middle Ear.

The *tympanic cavity* lies in the temporal bone, bounded on the outside by the membrana tympani. It contains three small bones or ossicles, the stapes, malleus, and incus. The entire lining membrane consists of a single layer of flat cells. In the region of the opening of the Eustachian tube it possesses more than one layer of ciliated cells. Small alveolar glands, such as have been described by some authors, occur here only exceptionally.

The mucous membrane of the *Eustachian tube* is covered throughout its whole length with ciliated epithelial cells, which are arranged in a double layer. In the cartilaginous parts these cells are higher, and among them are found goblet cells. The ciliary movement is directed toward the pharynx. The stratum proprium, which consists of a fibrillar connective tissue, is united with the periosteum in the bony parts. In the cartilaginous parts, on the contrary—*i. e.*, in the region of the ostium pharyngeum—there are mucous glands and collections of leucocytes to form adenoid tissue. There are formed here

lymph follicles, which taken together are called *tubal tonsils.* The cartilage of the tube presents the structure of fibrous cartilage in the pharyngeal section. Sometimes elastic tissue also is present in this cartilage. In the upper parts of the tube the cartilage is hyaline.

(*c*) The Outer Ear.

The *tympanic membrane* (drum) forms the boundary between the middle and the outer ear. It is made up of three layers: the innermost or a continuation of the mucous membrane of the tympanic cavity; the outermost, on the contrary, is connected with the covering of the external meatus. From within outward the layers are:

(1) The mucous layer (stratum mucosum);
(2) The fibrous layer (lamina propria); and
(3) The cutaneous layer (stratum cutaneum).

(1) The *stratum mucosum* consists of a single layer of flat epithelial cells and a thin connective-tissue sheath which is intimately connected with the fibrous layer.

(2) The *lamina propria* is made up of two layers of connective-tissue fibres, the inner circular and the outer radial. The two layers are bound together by a little loose connective tissue.

(3) The *stratum cutaneum* consists of stratified epithelium and a thin connective-tissue corium in which no papillæ are present. The epithelium is made up of a Malpighian layer of one or two rows of cells and many layers of corneous non-nucleated epithelial cells.

The skin of the external meatus has a different structure in its various parts. The subcutaneous tissue is firm and the corium shows only very poorly developed papillæ. Numerous hairs and sebaceous glands occur here. Large coil glands (glandulæ ceruminosæ), whose structure resembles that of large sweat glands, are also found. Two parts can be recognized in these glands: the secreting body of the gland and the duct. The first consists of a layer of cubical gland cells, a layer of smooth muscle cells, and a homogeneous membrana propria. The

ducts are lined with a double layer of epithelial cells. The cells throughout the whole gland show a cuticular border on the side toward the lumen. These glandular tubules are distinguished from sweat glands by their wide lumena, and by the fact that the gland cells contain granules of different kinds. Of these, the most numerous are yellowish-brown pigment granules. Other granules resemble fat in their action toward osmic acid, although their other properties do not correspond with this (Schwalbe). These coil glands open in the newborn into the hair follicles. In the adult, on the contrary, their orifices are on the free skin surface near the hair follicles (Alzheimer).

The *cerumen* or wax consists of a secretion of the coil glands (fat droplets and pigment granules), together with hairs and desquamated epithelial cells.

The cartilage of the external meatus is elastic like that of the auricle.

The *blood-vessels* of the ear drum are derived partly from the vessels of the tympanic cavity, and partly from those of the external meatus. Here two vascular networks can be distinguished, the inner of which lies under the stratum mucosum, while the outer is situated between the epidermis and the lamina propria. Each of these networks surrounds the handle of the malleus, and forms a ridge around the border of the tympanic membrane. The vessels of the central part and those of the edge of the membrane are thus connected. Venous vessels of both plexuses anastomose with one another by means of perforating branches (Moos). The lymph-vessels of the ear drum have an arrangement similar to that of the blood-vessels. Fine networks of nerves have been found in this region.

4. OLFACTORY ORGAN.

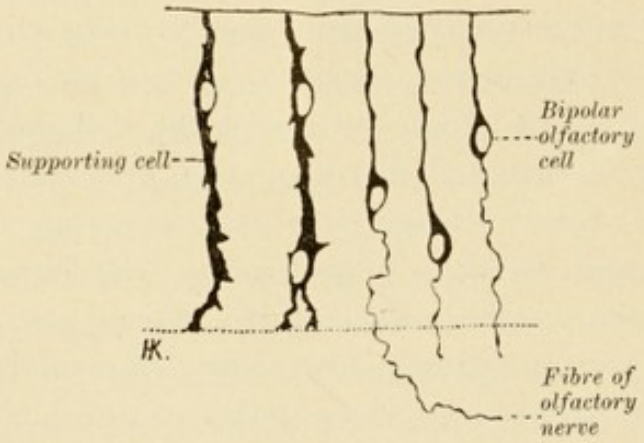
Having in view the structure of the nasal mucous membrane, the nasal cavity may be divided into three regions:

(1) The regio vestibularis;
(2) The regio respiratoria; and
(3) The regio olfactoria.

(1) The *regio vestibularis* is covered with a continuation of the outer skin, which gradually takes on the character of a mucous membrane. The outer layer is a stratified pavement epithelium which contains hairs, sebaceous glands, and sweat glands. A short distance from the outside, however, the hairs and glands disappear, the epithelium becomes like that of a mucous membrane, and mucous glands are found.

(2) The transition from this region to the *regio respiratoria* varies in different individuals. Usually it is marked by the appearance of a layer of ciliated epithelial cells, the nuclei of which are at various levels. Goblet cells are present in varying number. The connective-tissue tunica propria is thinner in the accessory nasal cavities than elsewhere. It contains usually a great many leucocytes, which wander through the epithelium into the nasal cavity. Branched tubular glands—mucous, serous, and mixed—are present.

FIG. 274.



From a vertical section through the mucous membrane of the regio olfactoria of a quite young dog. (Golgi's method.) × 450.

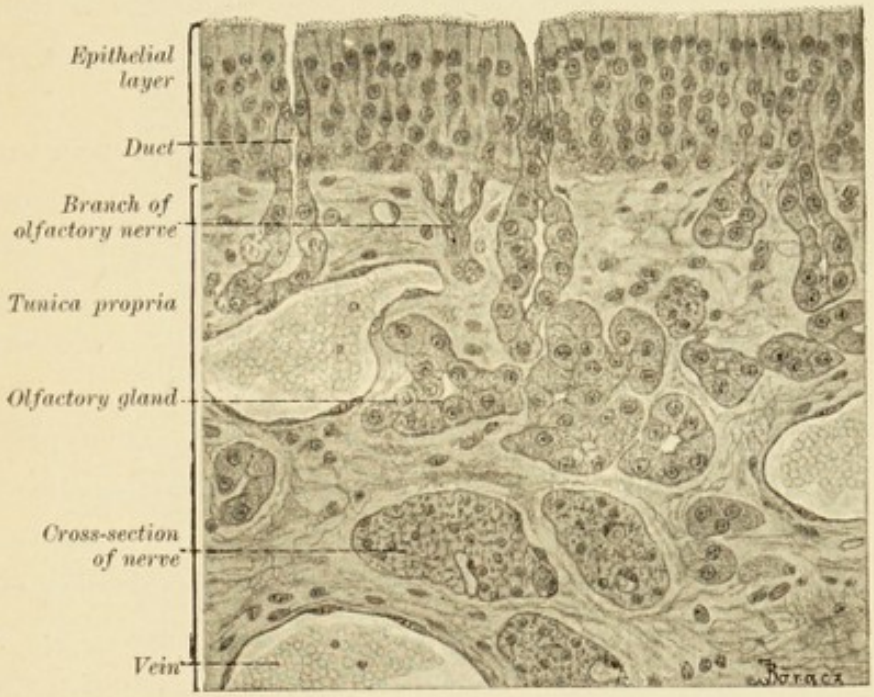
(3) The *regio olfactoria* is distinguished from its surroundings by its yellow coloration. The olfactory epithelium characteristic of this region is made up of a single layer of cylindrical cells whose nuclei lie at different levels. Two kinds of cells can be distinguished: the olfactory cells, and the supporting cells (Fig. 274).

The *olfactory cells* are peripherally placed, bipolar ganglion cells, the bodies of which lie in the epithelial layer. The

nucleus is round, with a distinct nucleolus, and the protoplasm forms a spindle-shaped cell sending out two processes. The upper one, which reaches to the free surface of the epithelial layer, is very short. It bears on its free end a number (six to eight) of firm short hairs. The lower thinner process passes over to form the axis cylinder of a centripetal nerve fibre, which runs to the bulbus olfactorius (Fig. 274).

The *supporting cells* (Fig. 274) are in many ways comparable with the Müller's fibres of the retina. They are epithelial cells of a cylindrical form, which become smaller at the

FIG. 275.



Vertical section through the mucous membrane of the regio olfactoria of a rabbit. × 360.

lower end. Small depressions in the lateral surfaces are often seen. These are filled up by the bodies of the olfactory cells. The basal ends of these cells are often forked, so that they touch the basal membrane with two or more parts. The oval nuclei lie at the same level in the thicker part of the cell. The protoplasm contains yellowish pigment, which gives to this part of the mucous membrane a characteristic color. The supporting cells possess a fine cuticular border. The borders of all the cells stand in such close connection with one another that they form a membrane, the *membrana limitans olfactoria*,

which allows of the passage of the peripheral hair-bearing ends of the olfactory cells through small spaces. At the lower edge of the epithelium in the region of the forked basal ends of the supporting cells there lie the so-called *basal cells*. These are conical cells arranged in a row and joined together by processes. Their nuclei form the lowest row in the whole epithelial layer.

The connective-tissue *tunica propria* forms a compact layer under the epithelium. It contains a fine network of elastic fibres, a large number of leucocytes, and a few pigment cells. Numerous glands are also present (Fig. 275). These *glandulæ olfactoriæ* (Bowmann) are simple or branched tubular serous glands. They open on the surface of epithelium by means of narrow ducts lined with flat epithelium.

The non-medullated fibres of the olfactory nerve passing through the tunica propria toward the bulbus olfactorius are derived from the lower processes of the olfactory cells. On the other hand, there are branches of the trigeminal nerve which end freely in the tunica propria and epithelial layer, and also in the respiratory region.

The arteries running in the deeper parts of the tunica propria break up into fine branches, which form three capillary systems (Zuckerkandl). One lies deep down in the periosteum, one surrounds the glands, and the third forms a network immediately under the epithelium. The veins make up a strongly developed plexus in the deeper parts of the tunica propria. This takes part in the formation of the erectile bodies.

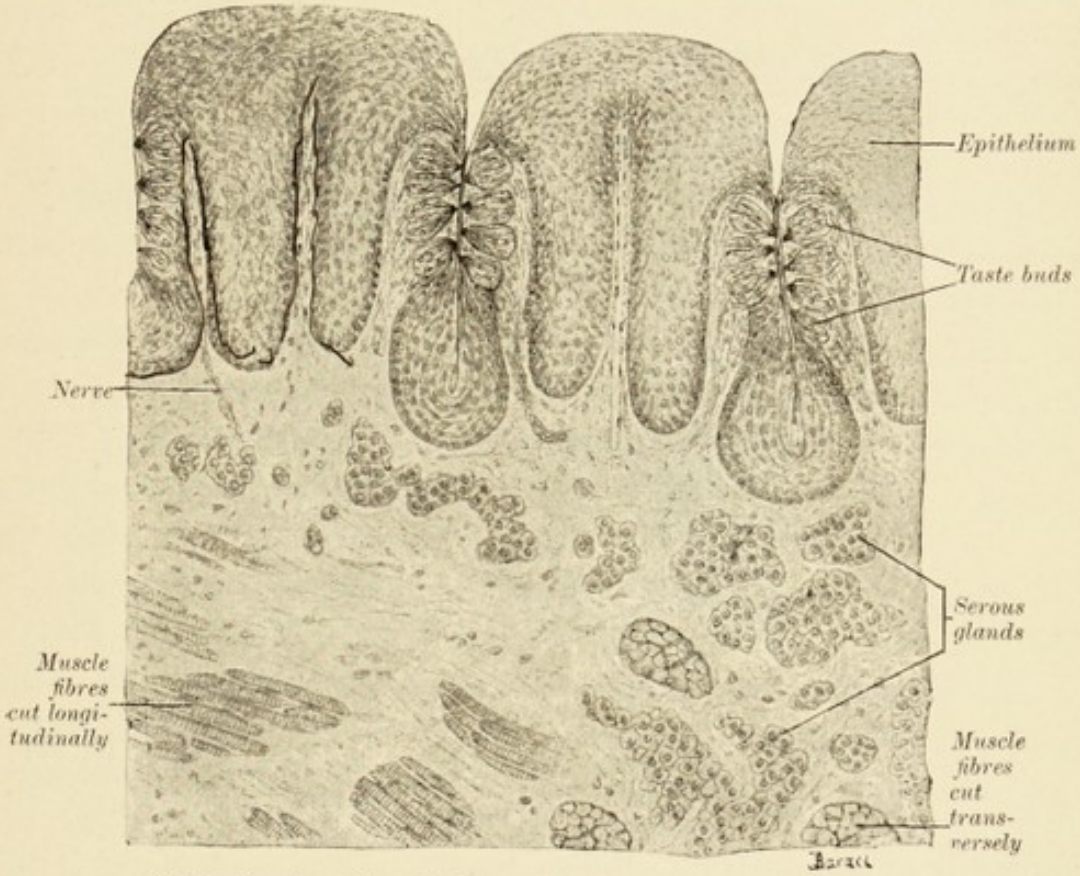
The lymph-vessels are arranged in a network in the tunica propria. Those of the olfactory region may be injected from the subarachnoideal space; for the olfactory nerve is surrounded by a continuation of the membranes of the brain.

Jacobson's organ is to be regarded in man as a rudimentary structure. It contains no sensory cells. In the lower animals, on the contrary, it is functional, and has the same structure as the olfactory mucous membrane.

5. ORGAN OF TASTE.

The true organs of taste are the so-called *taste buds*. These are present especially on the upper surface of the tongue in the circumvallate papillæ. They are found in some animals (rabbit) in the papilla foliata (Figs. 122 and 276). They are met with also in the fungiform papillæ, in the soft palate, the uvula, and the posterior surface of the epiglottis.

Fig. 276.



Vertical section through the papilla foliata of a rabbit. × 100.

Taste buds are spherical or oval masses of cells which occupy the whole thickness of the epithelial layer in which they lie. At the peripheral end there is an opening in the epithelium called the *taste pore*, or gustatory pore.

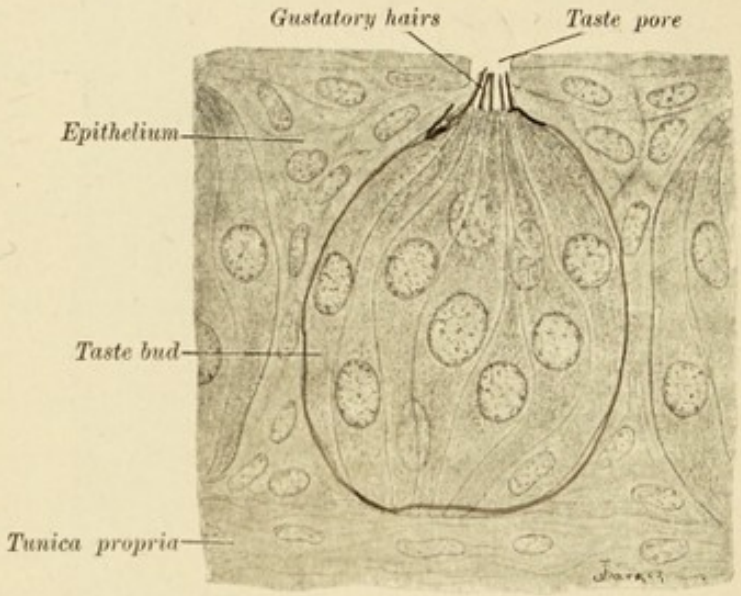
In each taste bud there can be distinguished two kinds of epithelial cells: the supporting cells, and the gustatory cells (neuro-epithelial cells).

1. The *supporting cells* are situated especially on the surface of the taste bud, but are present also in its interior. They are

elongated cells, the peripheral ends of which usually are drawn out into points which project into the gustatory pore. The nucleus lies in the thickened part of the cell, and may be at either end.

2. The *gustatory cells* are much like the supporting cells in appearance. They are long spindle-shaped cells, which are thickened in the region of the nucleus. At the peripheral free end each possesses a refractive hair-like structure which projects into the gustatory pore.

FIG. 277.



Taste buds from the papilla foliata of a rabbit. × 850.

Flat branched *basal cells* have been described by F. Hermann at the base of the taste buds. These have probably the function of supporting cells.

According to newer investigations (Retzius, Arnstein, v. Lenhossék), the gustatory cells are connected with the glossopharyngeal nerve only by contact. The branches of this nerve form a network in the tunica propria, from which fine bundles of fibres proceed to make up a subepithelial plexus. Some of the nerve fibres, which are both medullated and non-medullated, enter the taste buds, while others end between these structures. The *intragemmal* nerve fibres—*i. e.*, those entering the bud—give off numerous branches which surround the cells of the buds, particularly the gustatory cells.

and run almost up to the gustatory pore. They end by means of minute swellings which lie on the gustatory cells. The *intergemmal* fibres which end between the taste buds do not differ in their termination from other free nerve-endings in stratified pavement epithelium. Their dendritic end branches run to the most superficial layers of corneous epithelium, where they terminate in fine end bulbs.

GENERAL MICROSCOPIC TECHNIQUE.

1. THE MICROSCOPE.

Although it is impossible here to enter into a detailed discussion of the theory of the microscope, it is nevertheless necessary to give an outline of its main parts. Two kinds of microscopes may be spoken of: the *simple microscope*, which contains only simple lenses, and the *compound microscope*, in which there are many lens systems. The latter instrument is much more powerful than the former. It consists of two parts, the *stand* and the *lenses*.

The *stand* consists of an upright column which rests on a wide base. Fastened to this is a hollow cylinder, in which fits the *tube* which contains the lenses. There is also a platform or *stage* for the object examined, and a *mirror*. The stage, which is situated between the tube and the mirror, has at the point opposite the end of the tube a round hole through which the light rays are reflected from the mirror to the object. The intensity of this light is regulated by a diaphragm, which is placed under the opening in the stage. This may be the so-called *iris diaphragm*, which can be controlled by the hand, so that the opening may be made any size that is wished. The mirror usually possesses a flat surface on one side, which is used with low magnifications; and a concave surface on the other side, to be used when higher magnifications are employed. With the concave mirror the light rays are converged on the object. In order to concentrate the light rays still more, the

so-called Abbé's *condenser* is used. This is of especial service when very high powers are used.

The tube of the microscope can in most instruments be moved up and down by two mechanisms, the *coarse adjustment*, which consists of a rack and pinion; and the *fine adjustment*, which is made up of a *micrometer screw* at the upper end of the upright column. By turning this to the right or left, the tube may be lowered or raised by a fraction of a millimetre.

The essential part of the microscope is the lens system. There are two parts of this, the *ocular* (eye piece) and the *objective*. The ocular fits in the upper end of the tube, while the objective screws into its lower end. The ocular is a hollow cylinder with a lens at each end. The upper lens is the *ocular lens*, the lower one, the *collective lens*. The objective consists of a whole series of convex lenses (three or four), of which the smallest one lying next the object to be examined is called the front lens. We distinguish two kinds of objectives, the *dry lens* and the *oil-immersion lens*. The first serves all ordinary purposes; while the latter is used in the study of finer cellular and nuclear structure, as well as in bacteriological study. The difference between these two kinds of lenses consists in the presence of a layer of air between the dry lens and the object; while with the immersion lens there is interposed a medium between the lens and the object, which has a refractive index nearly equal to that of glass. This is of importance, because the rays of light from the object must pass through the cover glass into the air before they reach the objective. In passing over from the glass to the air the rays are bent outward, and a part of them thus do not enter the objective. By using a denser medium than air this difficulty is obviated. For this purpose cedar oil generally is used—a drop is placed on the cover glass over the object, and the tube lowered until the front lens enters the oil.

In recent years Karl Zeiss in Jena has devised the so-called *apochromatic objective*, by which the chromatic and spherical aberration is overcome.

A convenient but unessential addition to the stand is the

so-called *nose-piece*. This is a revolving objective holder, by which the objectives may easily be changed. The nose-piece may be arranged for the reception of two to five lenses—usually three.

Finally, some practical points in the use of the microscope may be mentioned:

(*a*) The lenses and mirror should be cleaned only with fine, soft cloths. Xylol and other fluids which dissolve Canada balsam should not be used.

(*b*) The best light is obtained from a sky covered with white clouds. Direct sunlight is usually not good. Artificial light never gives as good results as indirect sunlight. The Auer light and the incandescent electric light are the best artificial sources, if used with a blue glass over the diaphragm.

(*c*) Strong objectives need a strong light. With weak magnifications the flat mirror can be used; with higher powers, the concave mirror; and with the highest enlargement a condenser is necessary.

(*d*) With strong magnification the diaphragm may be enlarged; with low powers a small opening is used.

(*e*) The focal distance of weak lenses is great. The stronger the lens the shorter the focal distance.

(*f*) Every object should be examined first with weak magnification, and afterward with higher powers.

(*g*) Objectives with weak oculars give clearer pictures than with strong ones. It is better to use a strong objective with a weak ocular than a weak objective with a strong ocular.

(*h*) By means of the micrometer screw different levels of the same preparation may be studied.

2. THE PREPARATION OF SPECIMENS FOR MICROSCOPIC STUDY.

The elements of the animal organism may be investigated, either in the living condition, or after having been prepared by special methods.

Only a few things can be studied under the microscope without preparation. Among these, may be mentioned fluids such as blood, urine, spermatic fluid, etc. A drop is placed on a

glass slide and is covered over with a cover glass and examined. Thin membranes also (*e. g.*, omentum, mesentery, fasciæ) may be examined in the fresh condition by spreading them out over a glass side and keeping them moist by means of an indifferent fluid, such as blood serum, physiological salt solution, etc. In investigating larger organs we must separate the morphological units from one another or cut the tissue into thin sections.

(*a*) Isolation and Teasing of Tissues.

By means of two sharp needles fresh tissue may be torn apart so that its elements are isolated. It is best to have the tissue immersed in a drop or two of normal salt solution. Such tissues as tendon, muscle, and nerves can be studied in this way to advantage. The elements of many tissues, however, cannot be isolated so easily. In such instances the cement substance which binds the elements together should be dissolved out by means of *maceration*. The most useful fluids for this purpose are the following:

(*a*) *Ranvier's Dilute Alcohol* (*33 per cent.*).—This may be made by adding 65 cc. of distilled water to 35 cc. of 96 per cent. alcohol. This is a specially good fluid for isolating epithelial cells. Small pieces of tissue which have been left in the alcohol from six to twenty-four hours may easily be teased out.

(*b*) *Potassium* or *sodium hydrate* is most useful in a solution of 33 per cent., for the isolation of muscle elements (twenty minutes) and the elements of nails (three to five hours). For the study of hairs a 4.6 per cent. solution is used for three or four days. The elements should be examined in a solution of the same strength as that in which they have been macerated. Water should not be added. Care should be taken not to let the lens of the objective touch the fluids.

(*c*) Very dilute *formalin* (0.25 per cent.) or potassium bichromate (0.1 per cent.) may be used for the isolation of epithelial cells. Tissues should be left in these fluids one to two days.

(*d*) *Hydrochloric acid* is useful in isolating the kidney tubules. It should act for from ten to twenty-four hours.

Many other fluids may be used for special preparations (*e. g.*, nitric acid (5 per cent.) for the isolation of muscle elements, sodium bicarbonate for the demonstration of basement membranes, pancreatin in the study of connective tissue, and the various destructive methods in the isolation of the frameworks of organs).

(*b*) Sectioning of Tissues.

Another method of demonstrating the finer structure of tissues is by means of *sections*. These are thin slices of the tissue (1–50 μ thick), which are cut with a sharp knife either free hand or with the help of an apparatus known as the *microtome*. Free-hand sections have the advantage of being obtained more quickly and of not requiring such elaborate preparation. On the other hand, they cannot be cut sufficiently thin for all purposes; they are not of uniform thickness throughout; and it is impossible to cut two successive sections exactly the same thickness. The microtome is an instrument which is so arranged that the object to be cut is fixed on a stand which may be raised one or more micromillimetres at a time. The knife is fastened to a sliding stand, so that a section is cut each time it is drawn back, and the object stand raised. Other instruments have the knife stationary, and the object stand connected with a wheel which on each revolution advances the object toward the knife a certain number of micromillimetres. There is an apparatus attached to the instrument by which the thickness of the sections may be regulated. By means of this the micrometer screw which raises the object may be set so that the sections are all cut 5, 10, or 15, etc., micromillimetres thick.

In order to obtain sections of this kind, the tissues should be prepared by hardening and fixing them, so that they are firm. This may be done by freezing. Various freezing mixtures have been employed, but the best results can be obtained with the carbon dioxide apparatus. Several instruments have been devised for the use of this, but by far the best is that invented by Bardeen. Frozen sections cannot be cut with regularity thinner than 15 μ. They are mainly useful where it is neces-

sary to save time (*e. g.*, in diagnosis during a surgical operation), and where methods of maceration or digestion are to be employed in the study of the sections.

Where finer and more minute study is necessary, the sections must be fixed and hardened in various fluids, and impregnated with paraffin or celloidin.

(*c*) Fixation of Tissues.

By this term we mean the killing and fixing of the fresh tissue by means of various *fixing fluids* in such a way that the structure remains unchanged. The object of this is to prevent subsequent shrinkage of the tissue.

Certain general rules with regard to the use of fixing fluids may be mentioned:

(*a*) Fixing fluids should always be used in large quantities —a volume fifty to a hundred times as great as that of the tissue. This is to prevent its being too much diluted by the fluids of the tissue.

(*b*) The pieces of tissue used should be as small as possible. Where a large section is necessary, the piece of tissue can be made thin and the section cut from its flat surface.

(*c*) The tissue should be taken perfectly fresh from the animal's body.

(*d*) Fixing fluids should be prepared freshly.

(*e*) In the bottom of the flask in which the tissues are fixed, a small amount of cotton wool should be placed, to prevent the soft tissue being distorted by lying against the bottom.

The most useful fixing agents are the following:

(1) *Absolute alcohol* is a good fixing medium for very small pieces of tissue. It should be changed often, and should be allowed to act for six to twenty-four hours.

(2) *Perosmic acid* (0.5–1 per cent. solution) can be used only for very small pieces of tissue. It has small powers of penetration. Its maximum action is obtained in six to twenty-four hours. It should be kept in the dark in a glass-stoppered bottle. It is sometimes better to add a drop of nitric acid to the fluid, to prevent its reduction. The vapor of osmic acid is

very irritating to the mucous membranes, and the eyes should be protected in using it. Osmic acid forms a part of many fixing mixtures. Tissues fixed thus should be washed for from twenty-four to forty-eight hours in running water.

(3) *Flemming's fluid* (chrom-osmium-acetic acid) has the following constitution: 1 per cent. chromic acid, 15 parts; 2 per cent. osmic acid, 4 parts; glacial acetic acid, 1 part. The tissue is left in this from three hours to three days, and then washed one day in running water.

(4) *Hermann's fluid* (platinum-osmium-acetic acid) consists of 15 cc. of 1 per cent. aqueous platinum chloride solution; 4 cc. of 2 per cent. osmic acid; 1 cc. of glacial acetic acid. This is used in the same way as Flemming's fluid. It has the disadvantage of being expensive.

The last three fluids can be used in relatively small quantities.

(5) *Müller's fluid* consists of 2–2½ grammes of potassium bichromate, 1 gramme of sodium sulphate, and 100 cc. of water. A large quantity of this fluid should be used. It should be kept in the dark when used, and the tissues are left in it, according to their size, for from six weeks to three months. In the first weeks the fluid should be changed every day or two, and after that twice a week. Müller's fluid is especially useful in fixing the central nervous system. Fairly large pieces of tissue can be used.

(6) *Erlicki's fluid* consists of 2½ grammes of potassium bichromate, 1 gramme of copper sulphate, and 100 cc. of water. It resembles Müller's fluid in its action, but fixes the tissue in one-third of the time.

(7) *Corrosive sublimate* (bichloride of mercury) acts best as a warm saturated solution in physiological salt solution, with the addition of 1–5 cc. of glacial acetic acid to 100 cc. of the fluid. The duration of its action varies according to the size and density of the tissue, for from one to twenty-four hours. With fluids containing corrosive sublimate, no metal instruments should be used. Tissues so fixed should be washed carefully in running water for from twenty-four to forty-eight hours.

(8) *Zenker's fluid* has the following composition: potassium bichromate, 2.5 grammes; sodium sulphate, 1 gramme; corrosive sublimate, 5 grammes; glacial acetic acid, 5 cc.; water, 100 cc. Pieces of tissue are fixed in this for from twelve to twenty-four hours, and then washed in running water for from twenty-four to forty-eight hours. This is a particularly useful fluid. It may also be used as a decalcifying fluid.

(*d*) Hardening of Tissues.

Hardening is brought about best by the use of alcohol. The tissue should be taken from the fixing fluid, washed in running water, and transferred to 40–55 per cent. alcohol. From here it is put successively into 70 per cent., 85 per cent., and 96 per cent. alcohol. In each of these alcohols it is left for from twelve to twenty-four hours. In 96 per cent. alcohol it is left longest, the fluid being changed several times. All objects fixed in corrosive sublimate should be washed in running water for from twenty-four to forty-eight hours before being transferred to alcohol. If this is not done, tincture of iodine may be added to the 70 per cent. alcohol and the tissue left for some hours in this. The object of this procedure is to get rid of the sublimate crystals in the tissue.

All tissues, with the exception of bone and some hard connective tissues (*e. g.*, in sclerotic coat of eye, in penis), may be cut into sections after being imbedded in paraffin or celloidin. Bone should first be deprived of its inorganic material, and resistant connective tissues should be treated with a dilute solution of nitric acid.

(*e*) Decalcification of Bone.

Only tissues which have been fixed and hardened should be decalcified. Fresh tissues placed in decalcifying fluids lose the structure of their soft parts.

Pieces of bone are placed in a large quantity of the decalcifying fluid, which is changed occasionally. By means of a sharp needle it is possible to determine when the decalcification is complete. Some bones are decalcified much more easily than

others. The portion of the temporal bone containing the internal ear is especially resistant to these fluids. The following fluids are the most useful :

(*a*) *Nitric Acid.*—Aqueous solutions should have a strength of from 1 to 9 per cent. The time required varies considerably. Fœtal or very small bones are decalcified in a 1 per cent. solution in from three to ten days. For large pieces of adult bone and for teeth, it is necessary to use a 3 to 9 per cent. solution for many days. After decalcification the tissue should be washed for twelve to twenty-four hours in running water.

(*b*) *Hydrochloric Acid.*—This is more generally useful than nitric acid. It should be used in a 0.5 to 1 per cent. aqueous solution. In order to prevent a swelling of the tissues, normal salt solution may be used instead of water. Ebner's hydrochloric-acid-salt solution is made up of a cold saturated solution of salt diluted with 2 volumes of water, together with from 2 to 5 per cent. hydrochloric acid. This fluid acts slowly and should be changed often.

(*c*) *Zenker's fluid* is useful in decalcifying small pieces of bone. It should be allowed to act for from two to three days.

(*d*) A mixture of: chromic acid, 1 part; picric acid, 1 part; glacial acetic acid, 5 parts: is a good decalcifying fluid for small bones.

(*f*) Infiltration of Tissue with Celloidin and Paraffin.

In order to cut fixed and hardened objects into sections, it is necessary to infiltrate them with a substance of even and firm consistency. The substances commonly used are celloidin, paraffin, and photoxylin. The tissue should be entirely dehydrated by means of absolute alcohol. For infiltration with *celloidin*, this substance should be dissolved in a mixture of equal parts of absolute alcohol and ether. This takes two or three days, and a thick homogeneous fluid results. Three different thicknesses of this should be prepared in closely stoppered jars. Photoxylin is dissolved similarly. It is more expensive than celloidin, but has the advantage of being more transparent. After being dehydrated in absolute alcohol, the

tissues to be infiltrated are transferred to a mixture of equal parts of absolute alcohol and ether. After remaining in this for twenty-four hours they are transferred to the thinnest of the three celloidin solutions, and left for forty-eight hours. From this they are put into medium thick celloidin and left for twenty-four hours; then into thick celloidin for from twenty-four to forty-eight hours. Large pieces of tissue should be left in the celloidin solutions a longer time. After becoming thoroughly saturated with celloidin the object is lifted out and placed on a block of wood, or pressed wood fibre cut in a size to fit the microtome. The object is put in the position desired for sectioning, and a few drops of thick celloidin allowed to harden over it. This fixes it firmly on the block, and surrounds it with a layer of celloidin, which on evaporation becomes firm. When the surface of the celloidin is somewhat hardened, the block is placed in 70 per cent. alcohol until the whole object is firm and hard. This usually requires from twelve to forty-eight hours. With large pieces of tissue it is better to place the object in a glass dish and cover it with thick celloidin. This is allowed to evaporate slowly until the whole dish of celloidin is firm and hard. The tissue is then cut out together with a small quantity of the celloidin and fastened to a block.

For *infiltration with paraffin*, one requires pure paraffin, which melts at various temperatures. Two kinds are commonly used, a soft paraffin, melting at 45° C., and a hard paraffin, melting at 56°–57° C. There is needed also a thermostat, or a paraffin oven, which is so arranged that the temperature can be kept constant.

The piece of tissue which is to be infiltrated with paraffin should be entirely dehydrated in absolute alcohol. From this it should be put into some fluid in which paraffin can be dissolved. For this purpose xylol may be used. Tissues are left in this for from ten to thirty minutes. Instead of this, a mixture of 2 parts of absolute alcohol and 1 part of chloroform may be employed for from two to twelve hours. Pure chloroform may be used for from two to six hours. If

xylol is used, the tissues are transferred to a saturated solution of paraffin in xylol for two hours, and from this to melted soft paraffin. If a chloroform solution is used, the tissues are placed for twelve hours in a saturated solution of paraffin in chloroform, and from this to soft paraffin. In the latter substance the tissues are left for from one-quarter to two hours, and then transferred to melted hard paraffin, and left in this for from one-quarter to two hours. They should be allowed to remain in the hot paraffin as short a time as is possible for their complete infiltration. For small pieces, fifteen minutes are sufficient. In cold weather hard paraffin is difficult to cut, although thinner sections can be made with hard than with soft paraffin. When the tissues have become thoroughly infiltrated with the paraffin, they are placed together with a quantity of paraffin in a small paper box, which may be made by folding ordinary paper to the required shape; or they may be placed in a watch glass the bottom of which has been covered with a little glycerin. The pieces of tissue are placed in their proper position, and the whole is cooled quickly in cold water.

The method of cutting sections with the microtome differs somewhat according to the way in which the object has been imbedded. Tissue imbedded in celloidin is fastened, as described, to a block of wood or wood fibre, and fixed firmly in the microtome. The knife is placed in the knife-holder of the microtome, so that it is drawn through the tissue very obliquely. It should be slanted so much that nearly the whole edge of the knife passes through the piece of tissue. The surface of the knife should be kept flooded with 70 per cent. alcohol, and the object also should be kept moist. The sections which are cut are floated out in the alcohol on the knife, and are removed by means of a camel's hair brush to a vessel of 70 per cent. alcohol, where they may be kept for a considerable time without being injured.

Tissues imbedded in paraffin should be fastened to a block by melting the lower surface of the mass of paraffin. The knife should be placed with the edge at right angles to the long axis

of the microtome. Whereas in cutting celloidin sections nearly the whole edge of the knife is used, in paraffin sections only a small part of the edge is used. With large objects, however, the knife is placed obliquely in cutting paraffin sections also. The temperature of the room has an important influence on the cutting of paraffin sections. If the paraffin is of the right consistency, the sections should be quite flat, and should adhere to one another at the edge, so that what is known as a "ribbon" of sections is obtained—*i. e.*, they are fastened together in perfect sequence. Such ribbons may sometimes be obtained a foot or more in length, consisting of what are called serial sections.

If the paraffin sections do not flatten as they should, they may be made to do so by floating them on warm 30 per cent. alcohol, or on warm water. This should not be hot enough to melt the paraffin. From this they may be lifted out on a glass slide and allowed to dry in a thermostat (at 35° C.) for from twelve to forty-eight hours. This treatment causes the sections to adhere firmly to the slide, so that they may be stained and mounted. In order to be successful in this method, the slides which are used should be entirely free from fat or dirt of any sort. Simple washing with soap or alcohol is not sufficient. They should be washed with soap and water, boiled in a solution of potassium hydroxide, and allowed to remain several days in concentrated sulphuric acid. They are then washed in distilled water and kept until used in a mixture of alcohol and ether. They should be handled only with clean instruments, and not with the fingers.

Instead of this method, many so-called fixatives may be used. These are by no means so good. A common method is to coat the slide with a thin layer of albumin. The sections are pressed down on this and the albumin coagulated by heat. This solution of albumin is made as follows: egg albumin, glycerin, āā 50 grammes; sodium salicylate, 1 gramme.

Paraffin sections, after they have been fastened firmly to the slide by one of these methods, should be placed in xylol for five minutes. This dissolves the paraffin out of the tissue. The xylol should be changed once. If the tissue has already

been stained, the sections may be mounted directly in Canada balsam. If it is necessary to stain the sections, they should be transferred from xylol to absolute alcohol. Since most of the stains are aqueous solutions, the sections should be passed through 95 per cent. and 45 per cent. alcohol before being washed with water and placed in the staining fluid. If they are transferred directly from absolute alcohol to water, there is danger of their being loosened from the slide.

(*g*) Staining.

The object of staining tissues is to bring out more clearly the details of their structure. As has been explained in the section on the Blood, many stains can be divided into three groups: the acid, the basic, and the neutral stains. The acid stains color in general the protoplasm of the cells, while basic dyes stain the nuclei. This affinity of special parts of the cell for certain stains is the basis of what is known as *differential staining*. In the commoner examples of this, the nucleus is stained one color, and the protoplasm another. Other stains have a special affinity for tissues or parts of tissues. These are called specific stains (*e. g.*, neuroglia stain, elastic tissue stain, etc.). Tissues may be stained before they are sectioned, or the sections themselves may be stained.

The most useful stains in general laboratory work are mentioned briefly here, while the stains used for special purposes are spoken of in the section on Special Technique.

Carmine.—This serves well for staining tissues before they are cut. The *alcoholic borax carmine* of Grenacher is one of the best solutions. It is made as follows: In 100 cc. of a 4 per cent. aqueous borax solution there are dissolved by boiling 2–3 grammes of carmine; 100 grammes of 70 per cent. alcohol are added, and after standing for a considerable time the solution is filtered. The already hardened pieces of tissue are placed in this filtered solution for from one to three days. From this they are transferred to acid alcohol (4–6 drops of HCl in 100 cc. of 70 per cent. alcohol), in which a differentiation takes place. The stain remains in the nuclei, and is

washed out of the protoplasm. This usually takes twenty-four hours or longer, and the acid alcohol should be changed often.

Alum carmine of Grenacher is a pure nuclear stain. It is prepared as follows: 2 grammes of carmine are boiled in 5 per cent. aqueous alum solution for from ten to twenty minutes. On cooling, it is filtered, and 2 drops of carbolic acid added. Sections are stained in this for five minutes or longer. There is no danger of overstaining. Very small pieces of tissue may also be stained in this fluid.

Delafield's Hæmatoxylin.—Two grammes of crystallized hæmatoxylin are dissolved in 12.5 cc. of absolute alcohol; this solution is poured into 200 cc. of concentrated aqueous ammonium-alum solution. It is left for from three to four days in an open vessel in the light, and then filtered and mixed with 50 cc. of pure glycerin and 50 cc. of methyl alcohol. It is then filtered a second time, and after standing for several weeks is ready to use. It is best to use this stain very dilute; 1 or 2 drops in 20–50 cc. of distilled water make a solution which gives a good nuclear stain in from twelve to twenty-four hours. Mucus and the ground substance of hyaline cartilage are also stained blue by this method.

Hæmalum (P. Mayer) is prepared from crystallized hæmatein, 1 gramme of which is dissolved either in 50 cc. of 90 per cent. alcohol (with warming), or in a small quantity of glycerin, and mixed with 1 litre of 5 per cent. alum solution. This is filtered, and is ready for use at once. It may be used for sections or pieces of tissue. Sections are stained almost immediately, while pieces of tissue require from twenty-four to forty-eight hours. For washing out the tissues or sections, it is best to use 1–2 per cent. solution of alum. This gives a pure nuclear stain.

Hæmatoxylin-iron-alum (Heidenhain) is used for thin sections of tissue which has been hardened in corrosive sublimate. These are immersed in a 1.5–4 per cent. (for centrosomes, 2.5 per cent.) solution of iron alum for from one-half to three hours (for centrosomes, six to twelve hours). They are washed

carefully in tap water and transferred to 0.5 per cent. aqueous solution of hæmatoxylin and left for from twenty-four to thirty-six hours. After being washed in water they are differentiated in the iron-alum solution. They are then washed for one-fourth to one hour in running tap water, dehydrated, cleared, and mounted in balsam. This method demonstrates the centrosomes, chromatin, secretory capillaries (bile capillaries), and microsomes. The protoplasm may be counterstained in a dilute solution of acid rubin.

Anilin dyes (for classification, see section on Blood).

Safranin is an excellent nuclear stain. One way of preparing it is to dissolve 1 gramme of safranin in 100 grammes of absolute alcohol, and after several days to add 200 cc. of distilled water. Sections stained for twenty-four hours in this solution should be differentiated in absolute alcohol. Sections of tissues fixed in Flemming's fluid may be differentiated in absolute alcohol which contains 1 gramme of HCl to 1000 grammes of alcohol. The chromatin of the nucleus is colored a bright red.

Thionin is a valuable anilin dye. In 1 per cent. aqueous solutions it colors nuclei (chromatin) blue in a few minutes, and mucus red.

Vesuvin in 2 per cent. aqueous solutions is a brown nuclear stain. About five minutes are required for its action.

The most common *double stains* or multiple stains in use are the following:

Hæmatoxylin-eosin and Hæmalum-eosin.—Sections stained in hæmatoxylin or hæmalum are washed in water, and stained in a weak aqueous solution of eosin (1 part of eosin to 1000 parts of water). After washing in water, and for from three to five minutes in 96 per cent. alcohol the sections are cleared in creosote and mounted in balsam. This method stains the nuclei blue and the protoplasm pink. Congo-red may be used instead of eosin. The hæmatoxylin is used often in stronger solutions for five minutes, and then the sections should be decolorized in acid alcohol, and made blue again in ammonia-water.

Picro-carmine (Weigert).—Two grammes of carmine mixed with 4 cc. of ammonia are allowed to stand in a tightly closed vessel for twenty-four hours; 200 grammes of aqueous solution of picric acid are added. After twenty-four hours the addition of a few drops of concentrated acetic acid is made. This produces a precipitate, which after twenty-four hours is filtered out.

Picric acid also may be used as a counter-stain with sections which previously have been stained with carmine, hæmatoxylin, safranin, or acid fuchsin. For this a dilute alcoholic solution is employed.

Biondi-Ehrlich's Triple Stain (Methyl-green, Acid Fuchsin, Orange-G).—Heidenhain's modification of this stain is made as follows: Saturated aqueous solutions of the three stains are prepared—*i. e.*, 20 grammes of acid rubin in 100 cc. of water; 8 grammes of orange-G in 100 cc. of water; 8 grammes of methyl-green 00 in 100 cc. of water. Of these solutions, one mixes 4 cc. of the first with 7 cc. of the second, and then adds 8 cc. of the third. They should be added in this order, or a precipitate will result. For staining, 1 cc. of this mixture is diluted with 100 cc. of water. According to Heidenhain, it is of advantage to add the stain drop by drop to very dilute acetic acid (1 : 500 water), stirring constantly until the color is bright red. With this stain, it is best to use thin sections of tissue which have been hardened in corrosive sublimate. After being stained for twenty-four hours the sections should be washed in 90 per cent. alcohol or a mixture of 100 cc. of alcohol and from 2 to 4 drops of acetic acid.

Many other stains can be used with good results (*e. g.*, van Gieson's fluid (acid fuchsin and picric acid), methylene-blue, nigrosin, orcein, etc.).

After being stained, sections, whether cut in celloidin or paraffin, are submitted to a treatment which allows them to be mounted on a slide in a medium which is transparent and has a refractive index approaching that of glass (*e. g.*, Canada balsam). The sections are transferred from the staining fluids to water or a differentiating fluid, in which all excess of stain is washed

out. Then they are dehydrated in 96 per cent. alcohol, and transferred to a clearing fluid (*e. g.*, carbol-xylol (1 part of carbolic acid; 3 parts of xylol), creosote, bergamot oil, oil of cloves, etc.). The most generally useful clearing fluid is creosote. Carbol-xylol cannot be used with sections stained in anilin dyes. Sections are left in the clearing fluid for about five minutes, until they have become transparent. If they remain opaque in places, they have not been entirely dehydrated, and should be returned to the alcohol. From the clearing fluid the sections are lifted on to a slide by means of a section-lifter or spatula. The excess of clearing fluid is drained off, or, in the case of creosote, removed with a blotting-paper. A drop of Canada balsam is added, and a clean cover glass placed over each section. This is left until the balsam is hardened.

In some cases it is of advantage to mount celloidin sections in glycerin. For this, it is not necessary to pass the sections through alcohol. The glycerin, which is added to sections placed directly on the slide from water, does not dry. In order to make the specimen permanent, therefore, it is necessary to put a rim of cement around the edge of the cover glass. For this purpose, a mixture is made of 2 parts of paraffin and 8 parts of colophonium, which are melted carefully. This is placed around the cover glass and dried by means of a hot wire or needle.

(*h*) Injecting.

This is an art which is learned better through practice than by means of descriptions. It is necessary to use organs from animals which are freshly killed. Certain injection fluids or masses colored with various pigments must be prepared; and an apparatus must be arranged to supply a constant pressure. This apparatus is connected by means of a system of tubing with a cannula which is inserted in the blood-vessel or duct which is to be injected. The injection fluid is forced in this way into the vessels.

Certain general points in connection with injecting may be

mentioned. Blood-vessels should usually be washed out with salt solution before being filled with the injection mass. Fluids containing alcohol (*e. g.*, celloidin) cannot be injected until the vessels have been washed out first with salt solution and then with absolute alcohol. In using the gelatin masses, the body or organ to be injected should be kept at a temperature of 38°–40° C. Constant pressure can easily be obtained by means of a pressure bottle connected with a vessel of water which may be raised to any given height.

Some of the more useful injection masses are the following:

(1) *Berlin-blue.*—Saturated aqueous solution of Berlin-blue. This should be made with distilled water. It forms one of the most generally useful fluids we have.

(2) *Berlin-blue Gelatin.*—A saturated aqueous solution of Berlin-blue is added to a gelatin solution heated to 60° C., and filtered through flannel.

(3) *Carmine gelatin* (Ranvier): 10 grammes of gelatin are allowed to swell up in distilled water for from twelve to twenty-four hours. After it has been squeezed out with the hands the gelatin is melted in a water-bath (60° C.) and a carmine solution added. The latter is prepared by mixing 5 grains of carmine with 10 cc. of water, and adding drop by drop a solution of ammonia until the fluid is a dark cherry red. A solution of 30 per cent. acetic acid is then added carefully until the mixture is exactly neutral, If it is at all alkaline, the fluid will extravasate from the vessels. If, on the other hand, it is acid, granules will be present, which will interfere with its free passage through the capillaries. This is not an easy fluid to prepare. It is possible to titrate the ammonia and acetic acid, and, after thoroughly washing the gelatin to free it from acid, corresponding quantities of the two solutions can be added.

(4) *Lampblack gelatin, cinnabar gelatin, ultramarine-blue gelatin*, etc., can be prepared by adding the pigment granules to a gelatin solution. Lampblack should be freed from the fat which usually accompanies it.

(5) *Celloidin* injection masses are made with a solution of

celloidin in absolute alcohol and ether thin enough to flow easily into the vessels. Various granular pigments can be added.

(6) *Agar-agar* is used in the same way as celloidin. A very dilute solution (2–5 per cent.) in water is best.

(7) *Wood's metal* is a composition which has a very low melting-point and can be injected into the blood-vessels. By dissolving away the tissue from these, a cast of the vessels can be obtained.

(8) Methylene-blue, hæmatoxylin, silver nitrate, osmic acid, and other fluids are used for special purposes.

Tissues which have been injected should be hardened immediately. Thick sections (50 μ +) are the most instructive in the majority of cases. Celloidin and agar injections can be digested with hydrochloric acid and pepsin and a complete model of the blood-vessels obtained.

SPECIAL MICROSCOPIC TECHNIQUE.

1. THE CELL.

1. For the study of *protoplasmic movements*, one may use the fine hairs of *Tradescantia virginica*, which can be obtained from the freshly opened flower. These should be examined in water with high powers.

2. *Amœboid movements* may be observed in the amœba or in the living white blood-corpuscles of cold-blooded animals.

3. The *inner structure of cells* should be studied in fixed specimens. Flemming's, Hermann's, and Zenker's fluids are the most useful. Osmic acid is also of use, especially in Kolossow's method (see Epithelium). Cells are stained best with safranin, Heidenhain's hæmatoxylin-iron-alum, Ehrlich-Biondi's triple stain, nigrosin, methylene-blue, etc.

4. A classical object for the demonstration of *mitosis* can be obtained in June and July from frog, triton, and salamander larvæ. The outer skin, ova, etc., are sectioned and stained with safranin or iron hæmatoxylin. Excellent specimens can be gained from sections of a young growing onion top, or the growing point of any young plant (*e. g.*, lily).

5. For investigating *fertilization*, one may use the eggs of *Ascaris megalocephala*. The whole egg is fixed in Zenker's fluid, sectioned, and stained with iron hæmatoxylin.

2. EPITHELIAL TISSUE.

6. Epithelium may be studied advantageously in the fresh state by scraping the cells from mucous surfaces, etc. In a drop of the saliva placed on a slide, large flat epithelial cells are found. They may be stained in methylene-blue and mounted in glycerin.

7. By the methods of maceration, epithelial cells can be isolated. These may be studied unstained or colored by methylene-blue. Picro-carmine may be used with cells which have been fixed or hardened. A drop can be drawn under the cover glass by placing a piece of filter-paper on the opposite side; and the coloring material may be washed out in the same way.

Goblet cells may be obtained from the bronchus or intestine; ciliated epithelium, from the bronchus, nasal mucous membrane, etc. An excellent method of isolating the cells of the nasal mucous membrane consists in exposing it to the vapors of osmic acid for from six to eight hours, and then macerating in dilute alcohol. These cells may be stained in picro-carmine.

8. The *cement lines* are demonstrated best by the silver nitrate method. A membrane covered with endothelium, such as the mesentery, is stretched over a cork or cover glass and placed in a 0.1–1 per cent. aqueous silver nitrate solution. After from one to ten minutes to one hour the object becomes somewhat opaque. It is then placed in a large quantity of water and exposed to direct sunlight. Reduction usually occurs in from five to fifteen minutes. After this, it may be treated as an ordinary section and mounted in glycerin or Canada balsam. Many modifications of this method have been employed.

9. A special method for the demonstration of *protoplasmic bridges* has been suggested by Kolossow. This consists in fix-

ing the tissue for from one to six hours in 1 per cent. osmic acid. From this it is transferred to 5 per cent. tannic acid, or to a mixture of tannic and pyrogallic acids, and left for from eighteen to twenty-four hours. This gives a very clear picture of all protoplasmic structures. A counter-stain of safranin may be used. A useful modification of this method can be employed on sections (MacCallum). These are placed for one minute in the osmic acid mixture, washed in water, and transferred for two minutes to the reducing fluid. If this stain is not sufficiently intense, the sections may be washed in water, and the process repeated.

3. CONNECTIVE TISSUE, CARTILAGE, AND BONE.

10. For *gelatinous connective tissue*, the umbilical cord of a three to four months human fœtus, fixed in Zenker's fluid and stained in hæmatoxylin, may be employed. The subcutaneous tissue of very young pig's embryos can also be studied.

11. *Areolar connective tissue* may be obtained by producing artificial œdema in the subcutaneous tissue or in the intermuscular septa. This is done by injecting physiological salt solution by means of a hypodermic syringe into the loose tissue under the skin of a rabbit or rat. From the swollen tissue thus produced a small piece is cut and spread out under a cover glass. Various chemical tests may be made with such preparations. Magenta, acid fuchsin, and methylene-blue give good results in staining areolar tissue.

12. *White Fibrous Tissue.*—The tendons from the tail of a rat, or from the ankle of a pig, are the most available source from which to obtain this tissue. This may be studied fresh, or after having been acted on for twenty-four hours by a saturated solution of picric acid. In ordinary sections, white fibrous tissue is colored red in Van Gieson's fluid (acid fuchsin, picric acid), while elastic fibres are stained yellow and muscle brown.

13. *Tendon Cells.*—A small piece of the tail of a rat is placed in alum carmine solution for several days. It is then teased out and examined in glycerin.

14. Orcein is to be considered as a specific stain for *elastic tissue.* According to Unna's new method, the following fluid is used: 1 part of orcein; 100 parts of absolute alcohol; 1 part of HCl. Sections are placed in this fluid at 30° C. for from ten to fifteen minutes, and then washed in alcohol. Elastic fibres are stained dark brown.

Isolated elastic fibrils can be obtained by macerating a piece of the ligamentum nuchæ of an ox in a solution of pancreatin. If a piece 1 cm. in size be used, fibrils can be obtained in all stages of disintegration, depending on how near the centre of the piece they are situated. Specimens showing the membranes can be obtained by boiling ligamentum nuchæ in concentrated HCl, and pouring the whole out into a large quantity of cold water just before disintegration takes place (Mall).

Magenta is used to stain fresh specimens of elastic tissue.

Mallory's Elastic Tissue Stain.—Sections of tissue hardened in corrosive sublimate or Zenker's fluid are stained for from one to three minutes in aqueous acid fuchsin ($\frac{1}{20}$–$\frac{1}{10}$ per cent.). After washing in water, they are transferred for one minute to 1 per cent. phosphomolybdic acid, and again washed in water. After this they are placed for from two to twenty minutes in the following mixture: anilin-blue in water, 0.5 part; orange-G, 2 parts; oxalic acid, 2 parts; water, 100 parts. They are then washed, dehydrated, and cleared.

15. *Reticulum* is obtained best by digesting frozen sections of lymph gland, kidney, spleen, etc., in pancreatin. After twenty-four hours the sections are placed in a test-tube of water and shaken until the cells are displaced. They are then spread out on a slide, allowed to dry, and stained with acid fuchsin and picric acid (Mall).

16. *Fat* is stained by osmic acid, or Sudan III. It may be counterstained with safranin.

17. *Hyaline cartilage* may be obtained from the costal cartilages of young individuals; elastic cartilage, from the outer ear or epiglottis; fibrous cartilage, from the intervertebral ligaments or the point of insertion of the ligamentum teres femoris.

18. For decalcification of bone, see above.

19. Bones and teeth may be ground down to make dry sections. A well-macerated and fat-free bone is cut into sections 1–1½ mm. thick. These are rubbed first on emery paper and then on a glass plate with pumice on it. This can be accomplished best with the end of the fingers. A drop of water occasionally is added. When the section becomes very thin, it is washed in water, and polished on both sides on a hone and dried. It should be mounted in balsam which is so thick that it will not enter the air spaces.

20. In order to render the various canals and spaces of bones and teeth more distinct, they must be filled with a colored fluid. The best results are obtained in the following way: a dried and fat-free bone or tooth which has been macerated is cut into sections. These are boiled on a sand-bath for at least an hour in a mixture of equal parts of saturated solution of acid fuchsin and methyl-violet in absolute alcohol, until the remaining fluid is thick. The sections are then dried for twenty-four hours or longer in a thermostat (40° C.), and afterward ground down and polished as described before, xylol being used, however, instead of water.

4. MUSCLE.

21. Muscle may be studied in the fresh condition, by teasing out the fibrils in glycerin and staining with methylene-blue. Acetic acid brings out the nuclei.

22. The fibrils may be isolated by macerating the muscle in 0.1 per cent. chromic acid, or 33 per cent. alcohol for twenty-four hours.

23. The muscle of *Hydrophilus* hardened for twenty-four hours in 93 per cent. alcohol shows the fibrillar structure on teasing.

24. For the isolation of heart muscle, and smooth muscle elements, potassium hydroxide (33 per cent.), is used. In order to obtain permanent preparations of these elements Schieffer-decker suggests allowing the hydroxide to act for twenty minutes, and then adding 50 per cent. acetic acid to neutralize the

alkali completely. After washing in water the pieces of tissue are stained in alum carmine for some hours, and mounted in glycerin.

25. Sections of fixed and hardened muscle may be stained in various ways. The most useful are the following: Heidenhain's iron-hæmatoxylin, Ehrlich's triple stain, Kolossow's osmic acid treatment, etc.

5. NERVOUS TISSUE.

26. Isolated multipolar ganglion cells from the spinal cord are obtained as follows: small pieces of gray matter of the anterior horn are placed for from thirty-six to forty-eight hours in 33 per cent. alcohol. They are then stained in picrocarmine for twenty-four hours and examined in glycerin.

27. *Nissl's* method for staining nerve cells: material fixed in alcohol and imbedded in paraffin is cut into thin sections, which are fixed on slides by the water method. They are then placed in a solution of 15 parts of methylene-blue and 7 parts of Venetian soap in 4000 parts of water, at a temperature of 65°–70° C. until steam arises, or, according to van Gehuchten, at a temperature of 35°–40° C. for from five to six hours. They are then differentiated in a mixture of 1 part of anilin oil and 9 parts of 96 per cent. alcohol. If the white matter is decolorized, while the gray matter is still blue, the sections are passed through xylol into xylol-dammar.

28. Medullated nerve fibres may be studied in the fresh condition, and stained with methylene-blue.

29. Medullated nerve fibres may be fixed in the following way: a piece of fresh nerve is fixed for from three to six hours in 0.5 per cent. osmic acid solution or in Flemming's fluid. It is then washed in water, hardened in alcohol, and stained for twenty-four hours in safranin. After being differentiated in alcohol the nerve is dehydrated and cleared in oil of cloves. The nuclei of Schwann's and Henle's sheaths are colored red, while the nodes of Ranvier and the Schmidt-Lantermann's lines are plainly visible. Such nerves may also be sectioned.

30. Non-medullated nerves, which are to be treated in the

same way as medullated fibres, can be obtained from the vagus of a dog or an ox.

31. The crosses of Ranvier can be demonstrated by treating the fibres for from one-half to one hour with 0.5 per cent. silver nitrate solution (in the dark), and then exposing them, after washing in water for some hours, to the sunlight in a little glycerin.

6. BLOOD.

32. A drop of fresh blood placed under a cover glass will show rouleaux. On such specimens various chemical tests may be made (*e. g.*, the influence of water, strong salt solution, tannic acid, potassium hydroxide, etc.). Blood may be obtained by pricking the tip of the finger after washing it thoroughly with soap and water and then with ether. The first drop of blood should be removed, and specimens made from subsequent drops. The finger should not be squeezed. Cover glasses should be absolutely clean (see technique for mounting paraffin sections).

33. For the preparation of so-called *dried blood specimens*, thin smears of blood are made on cover glasses. A small drop of blood is placed on a clean cover glass and another is placed over it. The two are then drawn apart in such a way that their surfaces are always parallel. In this way two smears of blood are obtained, which should consist of a single layer of red blood-cells, etc. These are allowed to dry in the air for fifteen minutes, and then heated on a copper bar at a temperature of 120° C. for two hours (Ehrlich); or they may be left in a mixture of equal parts of absolute alcohol and ether for two hours (Nikiforoff). They are then dried and stained. Another method of fixing the blood cells is to immerse the slide in Zenker's fluid for fifteen minutes, and wash in running water for from one to two hours.

The various kinds of granules contained in leucocytes may be stained in the following ways:

α-granulations, in acidophilic or eosinophilic cells, are well stained in eosin (aqueous solution for twenty-four hours, or saturated glycerin solution for twelve hours); or in a saturated

aqueous solution of orange-G for twelve hours. A counterstain in hæmatoxylin or methylene-blue may be used, giving a preparation in which the nuclei are blue, and the red blood-corpuscles and α-granulations are red.

γ-granulations, basophilic granules (mast cells), are stained violet blue in dahlia (saturated solution in glacial acetic acid, 12.5 parts; absolute alcohol, 50 parts; distilled water, 100 parts).

δ-granulations are stained in a saturated aqueous methylene-blue solution. The staining requires from five to ten minutes.

ε-granulations, neutrophile cells, are stained best by Ehrlich's triple stain. This is a saturated aqueous solution of orange-G, 120 parts; acid fuchsin, 80 parts; methyl-green, 100 parts; to which are added water, 300 parts; absolute alcohol, 80 parts; and glycerin, 50 parts. This stain is used for from five to ten minutes, and then washed off with water. The red corpuscles are stained yellow, the neutrophile granules violet, the nuclei bluish green, and the eosinophile granules bright red.

In all these dried specimens the staining fluid is washed off with water and the specimens dried in the air. They are then mounted in balsam.

34. *Blood platelets* are obtained by pricking the finger through a drop of 1 per cent. osmic acid. The blood mixes with the acid and is fixed. Instead of osmic acid, one may use methyl-violet (1:10,000) in physiological salt solution, in which the platelets are stained blue.

7. CIRCULATORY SYSTEM.

35. *Small Blood-vessels and Capillaries.*—A piece of pia mater from the base of the human brain is washed in distilled water and fixed for from one to two hours in Zenker's fluid. Various stains may be used.

36. The *vascular epithelium* in capillaries and small vessels is demonstrated by injecting the vessels of a freshly killed frog with 1.5 per cent. silver nitrate solution. In the

mesentery, urinary bladder, and lung the vessels can best be observed.

37. *New Formation of Capillaries.*—A rabbit, cat, or dog about five days old is killed with chloroform, and the abdominal cavity opened. The mesentery or omentum majus is stretched over a cork or cover glass, and fixed for from one to two hours in Zenker's or Flemming's fluid. It is then stained with hæmatoxylin and eosin, or the Biondi-Ehrlich mixture.

38. *Elastic Tissue of Blood-vessels.*—Tissues fixed in absolute alcohol are stained in orcein or by Mallory's method. Henle's fenestrated membrane may be isolated by dissecting the muscle coats away from a medium-sized artery (femoral of dog). Pieces of the membrane may be obtained and stained with magenta. The membrane may also be isolated by treatment with potassium hydroxide.

39. The epithelium of the lymph sinuses can be demonstrated by injecting a 0.1 per cent. silver nitrate solution with a hypodermic syringe into the substance of the lymph gland. After half an hour the gland is fixed in alcohol, and thick sections are cut.

40. The *framework* of the lymph gland, spleen, thyroid, and adrenal may be isolated by digestion of frozen sections with pancreatin (see Reticulum).

41. It is instructive to study the elements of the lymph gland, spleen, etc., in the fresh condition or by stains such as methylene-blue.

8. DIGESTIVE SYSTEM.

42. *Goblet cells* may be well demonstrated by staining with thionin.

43. *Auerbach's* and *Meissner's* plexuses are stained by the gold chloride method (59).

44. The *zymogen granules* of the pancreas are colored red in safranin or the Biondi-Ehrlich stain.

45. *Bile capillaries* may be recognized by the following methods:

(*a*) Physiological self-injection of Chrzonszczewski consists in injecting the external jugular vein with a saturated aqueous solution of indigo-carmine. It is injected three times in one and one-half hours; 25–50 cc. for a dog, 20–30 cc. for a cat, and 15–20 cc. for a rabbit. At the end of this time the animal is killed, and small pieces of the liver are hardened in absolute alcohol. In frogs it is possible to place a piece of indigo-carmine the size of a pea in the large dorsal lymph sac. After twenty-four hours the animal is killed and the liver examined.

(*b*) Bile capillaries are demonstrated also by means of the chrom-silver methods of Golgi (58). Small pieces of fresh liver are placed for three days in osmium bichromate mixture and then transferred to 0.75 per cent. aqueous silver nitrate solution and left for from two to three days. After being washed for a short time in water the tissue is hardened in alcohol and cut into thick sections.

9. ORGANS OF RESPIRATION.

46. In order to demonstrate the *respiratory epithelium*, a young cat is killed by decapitation and the lungs filled through the trachea with a 0.05 per cent. silver nitrate solution. The trachea is then tied off and the whole organ immersed in a 0.5 per cent. silver nitrate solution and left in the dark. After an hour the lung is cut into pieces, which are hardened in the dark in alcohol of increasing strength. The reduction may be accomplished by exposing the pieces as a whole to sunlight or by cutting sections and exposing them.

47. Elastic tissue in the lung may be demonstrated by the orcein stain or by Mallory's method. By maceration in 35 per cent. potassium hydroxide solution the fibres can be isolated. Beautiful specimens showing the framework of the lung can be obtained by macerating pieces of lung in $\frac{1}{20}$ per cent. potassium bichromate for from one to three days.

10. URINARY AND REPRODUCTIVE SYSTEMS.

48. Kidney tubules may be isolated by treatment with HCl for from ten to twelve hours.

49. Kidney tubules may be filled with indigo-carmine by the method of Chrzonozczewski (45).

50. Fresh semen may be obtained from the epididymis of a rat, and studied in a drop of physiological salt solution.

51. Ova may be studied in the fresh condition from the ovary of a pig or cow. The liquor folliculi is allowed to escape, and with it often comes the ovum surrounded by some cells of the cumulus oöphorus.

52. Specimens of an injected placenta are instructive when teased out to isolate the villi.

11. SKELETAL SYSTEM.

53. *Red bone-marrow* should be studied in the fresh condition in a drop of physiological salt solution. Fixed specimens can also be made by the same methods as those employed in the study of blood. In such slides stained in eosin and methylene-blue, or with Ehrlich's triple stain, the various cellular elements can be made out. Bone-marrow may also be fixed in Zenker's fluid and paraffin sections stained by one of the above methods.

54. For the study of the *development of bone*, the finger of a human embryo three and one-half to five months old, or the leg of a pig's embryo 10–15 cm. in length, is decalcified by one of the methods described above after being fixed in Zenker's fluid. Paraffin or celloidin sections are cut and stained in hæmatoxylin and eosin, or in picro-carmine. For the development of connective-tissue bones the parietal bone of an embryo should be used.

12. NERVOUS SYSTEM.

55. To preserve the brain or spinal cord *in toto*, the most useful agent is formol in 10 per cent. solution. Tissue fixed in this may be used afterward for histological purposes, and may be hardened in Müller's fluid, etc. The tendency of formol to cause tissues to swell may be counteracted by adding an equal amount of 60 per cent. alcohol.

56. For the fixation of nerve tissue for histological study,

Müller's fluid is the most generally useful. Relatively large quantities of this must be used. Marina's fluid consists of 100 cc. of 90 per cent. alcohol, 5 cc. of 40 per cent. formol, and 10 grammes of chromic acid. Tissues hardened in this fluid may be used for Weigert's or Nissl's method. Osmic acid, Flemming's fluid, and absolute alcohol are used also for nervous tissues.

57. Staining of medullated fibres according to the *Pal-Weigert method* is as follows: Tissue fixed in Müller's fluid is transferred without washing in water to alcohol, in which it is hardened in the dark. Celloidin sections (40–50 μ) are cut, and if not brown are allowed to stand for a few hours in Müller's fluid. They are then stained for from twenty-four to forty-eight hours in the following solution: hæmatoxylin, 1 gramme; absolute alcohol, 10 cc.; distilled water, 90 cc.; saturated aqueous solution of lithium carbonate, 1cc. From this the sections are transferred to a 1–3 per cent. solution of lithium carbonate. When they are decolorized (after about one-half hour) they are placed for one-half to one minute in a freshly prepared 0.25 per cent. solution of potassium permanganate. The sections are now washed in distilled water and placed in the differentiating fluid, which consists of equal parts of 1 per cent. solution of potassium sulphite and 1 per cent. oxalic acid. The differentiation often takes an hour or more. The medullary sheaths are colored dark blue, while the gray substance is almost colorless. The sections should now be washed in water, dehydrated, and mounted in balsam. They may be counterstained in carmine, eosin, etc.

58. *Golgi's methods* are uncertain, and are liable to produce artifacts; but a successful impregnation gives a specimen of great value. The so-called *rapid method* is as follows: Small pieces, 3–4 mm. thick, are immersed in a mixture of 1 volume of 1 per cent. osmic acid, and 4 volumes of 3.5 per cent. potassium bichromate solution. About 10 cc. of this mixture are used for each piece of tissue. Hardening should take place in the dark and at a temperature of 25° C. The time required differs with the tissue used (*e. g.*, two to three days with

neuroglia cells; three to five days for nerve cells; five to seven days for collaterals). The pieces of tissue are transferred to 0.75 per cent. silver nitrate solution after having being washed in water and dried with filter-paper. They are left at ordinary room temperature in the silver nitrate for from two to three days. At this point a precipitate of silver chromate often forms, in which case the whole proceeding must be repeated. The pieces are then transferred to absolute alcohol for from one-half to one hour and imbedded quickly in celloidin—*i. e.*, thirty minutes. Comparatively thick sections are cut, dehydrated in absolute alcohol (two minutes), cleared in oil of bergamot, and mounted without a cover glass in balsam. The best results with the nervous system are obtained with embryonic tissues.

59. For all kinds of *nerve-endings* the gold chloride method of Ranvier and its many modifications may be used. Tissue is placed in a mixture made by boiling 8 parts of 1 per cent. gold chloride solution with 2 parts of formic acid. After an hour's action in the dark the tissue is washed in distilled water and allowed to remain in 20 per cent. formic acid in daylight for from twenty-four to forty-eight hours. It is then hardened in alcohol and imbedded in celloidin. Many other methods have been employed with success (*e. g.*, filtered lemon-juice five minutes, 1 per cent. gold chloride 1 hour, lemon-juice twenty-four hours; or formic acid 1 per cent. for one hour, gold chloride 1 per cent. two hours, formic acid 10 per cent. twenty-four hours). In none of these methods should metallic instruments be used. Instead of being sectioned, the tissue may sometimes (*e. g.*, muscle) be teased out in glycerin.

60. Nerves and nerve-endings may also be demonstrated by staining them with *methylene-blue* (Ehrlich), in one of the following ways: 0.33–4 per cent. solution of methylene-blue in warm physiological salt solution is injected into the veins (external jugular) of an animal. After a few hours the sympathetic ganglion cells, muscles, etc., are examined. Another method is to cut thin sections ($\frac{1}{2}$–1 mm. thick) of tissue from an animal which has just been killed, and stain this fresh tissue

with a weak solution of methylene-blue (1 per cent. in physiological salt solution) for from three-quarters to one and one-half hours. This stain is not permanent, but may be made so by treatment with the following fixing fluid of Bethe: ammonium molybdate, 1 gramme; distilled water, 10 cc. There may also be added hydrogen peroxide 1 cc. and hydrochloric acid 4 drops.

Tissues remaining in this fluid for from six to twenty hours should be kept on ice. They are then washed in running water and transferred to absolute alcohol for about one-half hour.

13. SKIN.

61. The stratum spinosum is seen plainly in tissue hardened in osmic acid. The stratum lucidum is yellow in sections stained in picro-carmine. The granules of the stratum granulosum are stained with carmine or hæmalum.

62. The mammary gland is studied best after fixation in Flemming's fluid and staining in safranin. The elements of the colostrum can be studied directly on the slide.

14. EYE.

63. A negative picture of the spaces and canals of the cornea may be obtained in the following way: The cornea of a fresh eye is deprived of its epithelium and allowed to remain in a 1 per cent. silver nitrate solution for from three to six hours in the dark. It is then placed in water in the sunlight, and after reduction has taken place is hardened in alcohol of increasing strengths. Sections parallel to the surface are made and mounted in balsam. The system of canals is colored white on a brown background.

64. The impregnation of the corneal cells and canals with gold may be accomplished by the gold chloride method (59).

65. For the study of the finer structure of the retina, the tissue is hardened in Flemming's fluid and thin paraffin sections are stained in safranin.

66. The nervous elements of the retina may be demonstrated by Ehrlich's methylene-blue method, or by Ramón y Cajal's

modification of Golgi's method. The latter staining is performed as follows: A piece of retina is dipped into celloidin for a moment, so that a thin layer hardens on the surface. The retina is then placed in the following solution for from twenty-four to forty-eight hours: 3 per cent. potassium bichromate solution, 20 cc.; 1 per cent. osmic acid, 5–6 cc. The tissue is dried on filter-paper and left in a 0.75 per cent. silver nitrate solution for twenty-four hours. It is then transferred directly to a mixture of 20 cc. of potassium bichromate solution and 2–3 cc. of 1 per cent. osmic acid. After from twenty-four to thirty-six hours it is placed again in the 0.75 per cent. silver nitrate solution, where it is allowed to remain for from one to two days. The tissue is now quickly dehydrated and imbedded in celloidin.

67. Nerves of the cornea can be demonstrated by the gold chloride method.

15. EAR AND NOSE.

68. The *cochlea* is opened at the apex under 0.5 per cent. osmic acid solution and allowed to remain for twelve hours in this solution. After washing the organ in water and hardening it in alcohol, the cochlea is decalcified in 2 per cent. chromic acid or 3 per cent. nitric acid. This takes a week or more, usually. Sections are cut in celloidin and stained in safranin.

69. Epithelial cells of the olfactory region of the nasal mucous membrane may be isolated by maceration in 33 per cent. alcohol for from two to three hours, and then transferred for ten minutes to 1 per cent. osmic acid.

70. The olfactory cells may be stained by Golgi's method.

INDEX OF AUTHORS.

AFANASSIEW, 144
Altmann, 21
Alzheimer, 377
Amici, 91
Apáthy, 101, 102, 103, 104
Arnold, 43
Arnstein, 382
Azoulay, 220

BAER, v., 243
Ballowitz, 58, 60
Bardeen, 94, 95, 96, 276, 387
Barfurth, 82
Barker, 110, 111, 286
Benda, 229
Bergh, 20
Berkley, 176, 202, 212, 220
Bethe, 103
Bizzozero, 117, 186
Blandin, 177
Bochenek, 99
Boveri, 32
Brödel, M., 217, 218, 219, 220
Browicz, 196, 199
Bubnoff, 63
Budge, 71
Bütschli, 21

CALVERT, 136, 137
Cattaneo, 307
Clark, J. G., 244
Cohnheim, 298
Cullen, T. S., 252

DANSKY, 247
Disse, 217
Dogiel, 204, 302, 309, 351, 360
Doyère, 313

EBERTH, 58
Ebner, v., 61, 217, 229, 230
Edinger, 286
Ehrlich, 59, 116
Eichler, 374
Ercolani, 261
Ewald, 106

FLEMMING, 20, 28, 32, 61, 135, 246
Flint, J. M., 146, 148, 149, 150, 175, 176, 194, 196
Frommann, 20

GOLGI, 100, 307, 315
Greef, 351
Gunge, 58

HAYEM, 117
Heape, 254
Heidenhain, M., 32, 40, 174, 181
Heitzmann, 201
Held, 102
Hendrickson, W. F., 202, 205
Hensen, 247
Hermann, 229, 382
Hewlett, A. W., 179
His, 110, 111, 112, 143, 170, 247
Hofmeyer, 261
Hozer, 220
Huber, 204, 315, 316

INABA, 151

JACOBSON, 247
Janosik, 151
Johnston, W. B., 213

KADY, H., 298
Kallius, 347, 350
Keibel, 261
Kerschner, 314
Kölliker, v., 62, 66, 84, 88, 106, 210, 247, 261, 286, 294, 314
Kolossow, 84, 205, 402
Kostanecki, v., 32, 33
Kowalewsky, 247
Krause, R., 173, 174, 176, 286
Krause, W., 309, 339, 360
Kuhne, 106, 314
Kultchitsky, 82
Kupffer, v., 200
Kurkow, 63
Kyes, P., 142

LANGERHANS, 193
Langhans, 261
La Valette, v., 229
Lebert, 61
Lenhossék, v., 39, 102, 229, 382
Leopold, 257, 261
Lepkowski, 161
Leydig, 20, 58
Littré, 223
Lugaro, 103
Luschka, 297

MACCALLUM, J. B., 84, 85, 86, 87, 95, 96, 97, 130, 248, 249, 276
Mall, F. P., 61, 62, 64, 65, 66, 125, 133, 140, 141, 142, 197, 201, 213, 217, 341, 404
Mandl, 255
Marinesco, 103
Maro, 258
Marpurgo, 276
Maurer, 43, 143
Mayer, 123
Meek, 276
Merkel, 61
Metchnikow, 60, 116
Meves, 228, 229, 230
Meyer, S., 102
Miller, W. S., 207, 209, 211
Minot, 151, 257, 261
Mitzukuri, 151
Mohl, 28
Moos, 377
Müller, H., 62
Müller, H. F., 118
Müller, Joh., 248
Müller, W., 350

NAGEL, 241
Nägele, 28
Nansen, 100
Nikiforoff, 407
Nissl, 103
Nuhn, 177
Nussbaum, M., 193

OPIE, E. L., 194
Oppel, 66, 197
Osler, W., 117

PALADINO, 242
Peter, K., 229
Pfitzner, 362
Pflüger, 240
Plato, 227, 229
Przewoski, 85, 86

RABL, C., 32
Raymón y Cajal, 101, 106, 286, 296, 302, 317, 347, 350, 351, 366

Ranvier, 60, 62, 123, 275, 307
Rathke, 247
Remak, 247
Rensen, 247
Retzius, 43, 101, 109, 161, 228, 242, 246, 306, 351, 366, 382
Riese, 246
Robin, 61
Rollet, 91, 93, 182
Rüdinger, 179
Ruffini, 314, 316
Rühle, 217

SABIN, F. R., 133, 286
Schaffer, J., 82, 177, 179
Schaper, 153
Schiefferdecker, 405
Schleiden, M., 17, 18
Schottländer, 246
Schulze, F., 61, 186, 210
Sherrington, 314, 315, 316
Siedlecki, 24
Smyrnow, v., 307
Sobotta, 242
Spalteholz, 336
Spee, v., 247
Spina, 71
Spuler, 61
Steinach, 220
Stieda, 143
Stöhr, 169
Sudler, M. T., 203
Szymonowicz, 158, 307, 309

TEICHMANN, 363
Toldt, 66, 363
Turner, 261

UNNA, 59
Uskow, 119

VALENTINE, 276
Van Beneden, 32
Van Gehuchten, 101, 286
Verheyn, 219
Verworn, 25
Virchow, 28, 61, 261

WALDEYER, 97, 247, 261, 363
Walker, G., 235
Weidenreich, 142
Weigert, 279
Wierzejski, 33
Wolff, 247
Wolters, 71

ZIMMERMANN, 216
Zuckerkandl, 380

INDEX.

ABBE'S condenser, 384
Absolute alcohol, 388
Absorption in intestine, 187
Accessory glands of male sexual organs, 234
line in muscle, 91
Acid, chrom-osmium-acetic, 389
dyes, 116
osmic, 388
Acidophile granulations, 116
Adelomorphous cells, 182
Adenoid tissue, 133
Adrenal, blood-vessels of, 150
development of, 150
gland, 147
Adventitia, 126, 127
Afferent lymph-vessels, 135
vessels of the kidney, 218
Agar-agar, 401
Agminated follicles, 188
Air cells, 208
sac, 208
passage, 208
Alcohol, absolute, 388
Ranvier's, 386
Alimentary tract, 154
Alum carmine, 396
Alveolar glands, 47, 49
sac, 210
Alveoli of lung, 207
of thyroid, 145
Amitosis, 28
Amnion, 257
Amœboid movement, 25
Amphipyrenin, 23
Amphophile granulations, 117
Ampulla of Thoma, 141
of vas deferens, 233
Anaphase, 29, 31
Anilin dyes, 116, 397
Anisotropic bands in muscle, 90, 91
Annuli fibrosi, 131
Anterior basal membrane, 341
horn. *See* Ventral horn.
median fissure. *See* Ventral median fissure.
pyramidal tract. *See* Ventral pyramidal tract.
root. *See* Ventral root.
Antrum folliculi, 241
Apáthy, theories of, 101
Apochromatic objective, 384
Appendix epididymis, 234
testis, 234
Appositional growth of bone, 271
of cartilage, 70
Aqueous humor, 340
Arachnoidea, 297
Arborescent cells, 293
Archoplasm, 25
Arcuate arteries, 218
fibres, internal, 287
veins, 219
Arcus tarseus, 363
Area cribrosa, 213
Areas of calcification, 268
of ossification, 268
Areolar connective tissue, 54
glands, 339
Arrectores pilorum, 327
Arteria hyaloidea, 357
corticis (adrenal), 150
capsulæ (adrenal), 150
medullæ (adrenal), 150
Arteries, 123
large, 127
medium sized, 126
precapillary, 122
of skull cavity, 127
Arteriolæ rectæ, 220
Articular ends of bones, 267
Asbestos change in cartilage, 72
Ascending arm of Henle's loop, 213, 215
Association centres of the brain, 291
paths of the brain, 291
Astrocytes, 285
Atresia, follicular, 245
Atrium, 208
Attraction sphere, 25
Auditory organ, 364
Auerbach's plexus, 191
Axial sheath of muscle-spindle, 315
Axis of spermatozoön, 228
Axis-cylinder process, 97, 98
of nerve-fibre, 104
Axone, 97, 98
hillock, 98

BAILLARGER, fibre-tract of, 293
Basal cells of taste-buds, 382
granules, 39
membrane of intestine, 185
of skin, 320
Basement membrane, 45
in thyroid, 147
Basic dyes, 116
granulations in leucocytes, 117
Basichromatin, 23

Basket cells, 50, 172
of mammary gland, 338
Basophile granulation, 117
Berlin blue, 400
gelatin, 400
Bile capillaries, 195
development of, 205
Bile ducts, 202
Bioblast, 21
Biondi-Ehrlich, triple stain, 398
Bipolar cells, 100
transition to unipolar, 101
Bladder, urinary, 221
Blood, 112
cells of lower vertebrates, 113
corpuscles, 112
intracellular development of, 123
nucleated red, 265
white, 114
dust, 118
function of, 119
histogenesis, 118
platelets, 117
shadows, 113
specimens, preparation of, 407
supply of muscles, 275
vascular system, 122
units of fat, 68
of kidney, 217
of liver, 200
Blood-vessels of adrenal, 150
of bone, 266
of central nervous system, 298
of cochlea, 373
of eyeball, 357
of intestine, 190
of kidney, 217
of liver, 197
of lung, 210
of lymph gland, 136
of membranous labyrinth, 373
of oral mucous membrane, 155
of ovary, 246
of penis, 237
of prostate, 235
of skin, 335
of spleen, 140
of stomach, 190
of testis, 227
of uterus, 254
of Wolffian body, 248
Body of gastric gland, 181
of nerve-cell, 102
of spermatozoa, 228
Bone, 74
blood-vessels of, 266
canaliculi, 78
cavities, 78
cells, 75, 79
compact and spongy, 74
connective tissue, 278
decalcification of, 390
destruction, 272
development of, 268
Bone formation, endochondral, 268
ground substance, 76
joining together of, 267
lacunæ, 75, 78
Bone-marrow, 265
Bones, 264
Bony labyrinth, 365
Borax carmine, 395
Bowman's capsule, 212
discs, 93
membrane, 341
Brachium conjunctivum. *See* Superior cerebellar peduncle.
pontis. *See* Middle cerebellar peduncle.
Branched alveolar gland, 49
tubular gland, 49
Bridges, intercellular 43
Bronchial arteries, 211
Bronchioli, respiratory, 207
Bronchiolus, 207
Bronchus, 207
Brownian molecular movement, 27
Bruch's membrane, 345
Brücke's line, 84, 90
Brunner's glands, 189
Buccal glands, 177
Buds, periosteal, 269
Bulbus oculi, 340
Burdach's column, 281

CAJAL, cells of, 291
Calcification, areas of, 268
of cartilage, 72
Calyces of kidney, 221
Canal, central, 279
Canaliculi, dental, 158
of bone, 78
Canalis hyaloideus, 357
Canalized fibrin, 260
Canals in dentine, 157
of cornea, 341
of Corti, 370
of Petit, 356
secretory, 174
system in cartilage, 71
Capillaries, 122
bile, 195
formation of, 122
secretory, 174
of oxyntic cells, 183
Capillary buds, 123
Capsula fibrosa of joints, 267
synovialis, 267
Capsule, internal, 288
of adrenal, 148
of Bowman, 212
of Glisson, 194
of joints, 267
of lymph gland, 133
of spermatozoön, 228
of spleen, 138
Cardiac glands, 184
Carmine, 395
gelatin, 400

Carotid gland, 153
Cartilage, 68
calcification of, 72
canal system, 71
capsule, 70
cells, 69
elastic, 72
ground substance, 69
growth of, 70
marrow, 71
of Santorini, 206
of Wrisberg, 206
ossification of, 72
senile (asbestos) change in, 72
spaces, 69
white fibrous, 73
Cartilages, 273
Cartilaginous framework of trachea, 206
Caruncula lachrymalis, 363
Cavernous part of urethra, 223
Cell, 18
balls of carotid gland, 153
membrane, 23
nodes, 260
Celloidin, 391
injection mass, 400
Cells of Cajal, 291
of Martinotti, 292
of Purkinji, 295
of Sertoli, 229
of the columns, 281
Cellular inclusions, 21
Cellulifugal conduction, 101
Cellulipetal conduction, 101
Cement, 161
development of, 164
lines, demonstration of, 402
of v. Ebner, 76
Central canal, 279
chyle vessel, 187, 191
glia mass, 286
gray matter, 280
lymph space, 187, 191
nervous system, 278
blood-vessels of, 298
spindle, 29
veins of liver, 198
Centrifugal cells, 282
Centripetal cells, 282
Centro-acinar cells, 193
Centrosome, 24
Cerebellar peduncles, 288
tract, 283
Cerebellum, 288, 293
granular cells of, 294
medulla, 296
neuroglia of, 296
Purkinji cells, 100
Cerebral cortex, 291
nerves, motor, 289
sensory, 289
Cerebrospinal nerves, 299
Cerumen, 377
Cervical glands of uterus, 253
Cervix uteri, 253
Checker-board nucleus, 115
Chemotaxis, 27
Chemotropism, 27
Chief cells, 182
Chloride of gold methods, 413
Chorda dorsalis, 51
Chorioid plexus, 298
Chorioidea, 343
Chorion, 258
frondosum, 257
Chorionic membrane, 257
villi, 257
Chromatin, 22
Chromatolysis, 32, 246
Chromatophile granules, 102, 103
Chromophile cells, 152
Chrom-osmium-acetic acid, 389
Chromosomes, 29
Chyle vessels, central, 187, 191
Cilia, 26
Ciliary body, 344
movement, 26
muscle, 344
Ciliated epithelium, 39
Cinnabar gelatin, 400
Circular sheath of hair, 325
Circulation in protoplasm, 26
of placenta, 262
Circulatory system, 121
Clarke's column, 279
Clasmatocytes, 60
Claudius, cells of, 372
Clitoris, 263
Cloquet's canal, 357
Club hair, 328
Coagulation phenomena, 104
Coccygeal gland, 154
Cochlea, 365, 367
vessels of, 373
Cochlear nerve, 290
nuclei, 290
Cohnheim's fields, 88
Coil gland, 48, 333
Collaterals, 98
Collecting tubules of kidney, 213, 216
Colloid substance in thyroid, 145
Colorless blood corpuscles, 114
Colostrum, 339
corpuscles, 338
Column of Burdach, 281
of Goll, 281
of Gowers, 283
of Stilling-Clarke, 279
Commissural cells, 282
Commissure, dorsal and ventral gray, 280
gray, 279
white, 280
Common bile duct, 202
Compound alveolar gland, 49
tubular gland, 49
Concentric corpuscles of Hassal, 143
Condenser, Abbe's, 384
Conduction of nervous impulses, 101

Cone fibre, 348
Cones, 348
Congo red, 397
Coni vasculosi Halleri, 231
Conjunctiva, 361
palpebralis, 362
scleræ, 362
Connecting tubules of kidney, 213, 216
Connective tissue, 53
bones, development of, 273
cells, 56
classification of, 53
histogenesis of, 61
nerve-endings in, 307
of kidney, 217
Contact relation of neurones, 101
Contraction bands, 92
of muscle, 92
Convoluted tubules of kidney, 213
Corium, 319
Cornea, 340
Corneal canals, 341
cells, 341
endothelium, 342
Cornification, 42
Corona ciliaris, 344
radiata, 242
Corpora lutea spuria, 244
vera, 244
Corpus albicans, 244
cavernosum urethræ, 235
ciliare, 344
fibrosa, 244
hæmorrhagicum, 243
Highmori, 224
luteum, 244
restiforme. *See* Inferior cerebellar peduncle.
spongiosum, 235
uteri, 253
Corpuscles of blood, 112
of Grandry, 308
of Herbst, 310
of Hassal, concentric, 143
of Meissner, 310
of Ruffini, 310
of Vater-Pacini, 311
Corrosive sublimate, 389
Cortex, cerebellar, 294
cerebral, 291
of adrenal, 148
of hairs. 323
of kidney, 212
of lymph gland, 134
pyramidal cells of, 100
representation of senses in, 291
Cortical sheath of glia fibres, 293
Corti's canal, 370
organ, 369
Cotyledons, 257
Cowper's glands, 235
Crenation of blood cells, 113
Crista acustica, 365
basilaris, 368
Cross of Ranvier, 106
Crossed pyramidal tract, 283
Crusta, 24
Crypt of tonsil, 168
Cubical epithelial cells, 38, 41
Cumulus oöphorus, 242
Cupola, 366
Cutaneous vessels, 335
Cuticle of hair, 323
of root sheath, 324
Cuticula, 24
dentis, 161
vaginæ pili, 324
Cuticular border in epithelium, 40
Cutis, 318
plate of myotome, 94
Cylindrical epithelium, 38, 41
Cystic duct, 202
Cytoblastema, 28

DECALCIFICATION of bone, 390
Decidua, basalis, 255
capsularis, 255
graviditatis, 255
menstrualis, 255
reflexa, 255
serotina, 255
vera, 255
Decidual cells, 256
Degenerations in epithelial cells, 44
Dehiscent gland, 49
Deiter's cells, 100, 285, 372
process, 97, 98
Delafield's hæmatoxylin, 396
Delomorphous cells, 182
Demilunes of Gianuzzi, 174
Dendrite, 97, 99
Dense connective tissue, 63
Dental canals, 157
canaliculi, 158
fibres, 157
germ, 161
papilla, 161
ridge, 161
sac, 162
sheath of Neumann, 159
Dentine, 157
cell bodies, 157
ground substance, 159
origin of, 163
Derma, 318
Descemet's membrane, 341
Descending arm of Henle's loop, 213, 215
Destruction of bone, 272
Deutoplasm, 24, 241
Development of adrenal, 150
of bile capillaries, 205
of bone from cartilage, 268
of bones, 268
of capillaries, 122
of cement, 164
of dentine, 163
of elastic tissue, 62
of enamel, 163

Development of fibrillar connective tissue, 61
of liver, 204
of lymphatics, 133
of muscle cells, 95
of muscles, 276
of spermatozoa, 229
of submaxillary, 175
of teeth, 161
of tonsils, 169
Diapedesis, 60, 115
Diarthrosis, 267
Diaster, 31
Differential staining, 395
Differentiation of cells, 36
Digestion leucocytosis, 114
of fat, 187
Digestive system, 154
Diploë, 273
Direct division, 28
Disc, tactile, 308
Discus proligerus, 242
Division of labor in cells, 36
Dorsal column, 280, 283
gray commissure, 280
horn, 279
median septum, 280
root, 279
Dorsolateral group of motor cells, 281
Double stains, 397
Doyère's hillock, 93, 313
Drum of ear, 376
Duct of Santorini, 192
of Wirsung, 192
Ductless glands, 49
Ducts of liver, 202
of mammary gland, 339
of salivary gland, 171
Ductuli aberrantes, 234
efferentes testis, 231
Ductulus aberrans Halleri, 234
capitis epididymis, 234
retis testis, 234
Ductus cochlearis, 367
endolymphaticus, 375
ejaculatorius, 233
pancreaticus, 192
accessorious, 192
papillaris, 215
perilymphaticus, 375
reuniens (Henseni), 365
utriculo-sacculari s, 365
Dura mater, 296
cerebralis, nerves of, 297

EAR, 364
wax, 377
Ebner's, v., cement lines, 76
glands, 167, 177
hydrochloric acid, 391
Ectoderm layer, 259
Ectoplasm, 19, 24
Efferent lymph-vessel, 136
Egg balls, 240
Egg cells of ovary, 238
nests, 240
Ehrlich's methylene-blue method, 415
Eimer's organ, 307
Ejaculatory duct, 233
Elastic cartilage, 72
connective tissue, 56, 64
fibres, 55
origin of, 62
fibrils, structure of, 64
granules of Ranvier, 63
limiting layer of pharynx, 177
membrane of Henle, 124
tissue stains, 404
Elastica externa, 127
interna, 126
Eleidin, 321
Ellipsoid of Krause, 348
Ellipsoids of the spleen, 140
Embryonic connective tissue, 53
Enamel, 160
cells, 162
fibres, 160
organ, 161
origin of, 163
prisms, 160, 164
pulp, 162
End-bulbs of nervous system, 309
Endocardium, 130
Endochondral ossification, 268
Endogenous cell formation, 70
Endolemma, 89
Endolymph, 365
Endometrium, 251
in menstruation, 254
in pregnancy, 255
Endoneural sheath, 109, 300
Endoneurium, 300
Endoplasm, 19
Endosteum, 266
Endothelium, 45
End-piece of tail of spermatozoön, 229
End-plate, 314
Endscheibe, 91
Eosinophile granulation, 116
Ependyma, 111
cells, 285
fibres, 285
Epicardium, 131
Epidermis, 320
Epididymis, 231, 232
Epilemma, 89
Epineurium, 299
Epiphyseal line, 272
Epithelium, 37, 40
classification of, 40
glandular, 46
histogenesis, 44
Epithelial cells of mesoblastic origin, 45
lamella of myotome, 94
Eponychium, 330
Epoöphoron, 246, 248
Erectile tissue of penis, 236
Erlicki's fluid, 389

Erythroblasts, 118, 265
Erythrocytes, 112
Essential gland cells of the testis, 229
Eustachian tube, 375
Eye, 340
  blood-vessels of, 357
Eyeball, 340
  lymph paths, 359
  nerves of, 360
Eyelashes, 361
Eyelids, 361
Excretion, 46
External female genitals, 262
Extrusion of polar bodies, 33

FALLOPIAN tube, 250
  False interstitial lamellæ, 75
Fasciæ, 278
Fasciculus cerebellospinalis dorsalis, 283
  cerebrospinalis lateralis, 283
    ventralis, 283
  longitudinalis medialis. *See* Posterior longitudinal bundle.
  ventrolateralis Gowersi, 283
Fastening villi, 257
Fat, 66
  cells, 58
  development of, 66
  digestion, 187
  germinal layer, 66
  lobule, 66, 67
  staining of, 66
  tissue, 58
Female genitals, external, 262
  sexual organs, 237
  urethra, 223
Fenestrated membrane of Henle, 64, 124
Fertilization, 32
Fibræ arcuatæ corneæ, 341
  zonulares, 356
Fibre baskets of retina, 352
  layer of Henle, 349
Fibres, dental, 157
Fibril bundles of muscle, 84
Fibrillar theory of protoplasmic structure, 20
  connective tissue, 54
Fibrin, 119
  canalized, 260
Fibro-muscular coat of gall-bladder, 203
Fibrous cartilage, 73
Filar-mass, 20
Fissura mediana ventralis, 280
Fixation of tissues, 388
Fixed connective-tissue cells, 57
Fixing agents, 388
Flagella, 26
Flagellated epithelium, 39
Flat epithelium, 37, 41
Flemming's fluid, 389
Foam theory of protoplasmic structure, 21
Follicle, Graafian, 242
  of lymph gland, 134
  of ovary, 238
Follicle of tonsil, 169
  primordial or primary, 240
  solitary, 138
Follicular atresia, 245
  cells, 240
Folliculi linguales, 167
Folliculus oöphorus vesiculosus, 242
Fontana, spaces of, 346
Foramina nervina, 368
Formation of elastic fibres, 62
Formed connective tissue, 63
Formatio reticularis, 279, 289
Fossa navicularis, 223
Fourth ventricle, 287
Fovea centralis, 353
Foveolæ gastricæ, 180
Framework of adrenal, 150
  of kidney, 217
  of pancreas, 194
  of spleen, 140, 142
  of thyroid, 146
Free nerve-endings, 304
    in connective tissue, 307
Freezing of tissues, 387
Frommann's silver line, 105
Fundus glands, 181
Funiculus cuneatus, 281
  dorsalis, 283
  gracilis, 281
  lateralis, 283
  ventralis, 282
Funnels of Schmidt-Lantermann, 105

GALL BLADDER, 203
  Galvanotaxis, 27
Ganglia, 301
Ganglion, 98
  spirale, 373
Ganglionic layer of cerebellum, 295
Gärtner's duct, 248
Gastric blood-vessels, 190
  glands, 181
  mucosa, 180
Gelatin, 400
Gelatinous bone-marrow, 266
  nucleus, 267
  substance of Rolando, 279
  tissue, 259
Generative system, 224
Genital corpuscles, 264, 309
Genito-urinary system of embryos, 247
Gennari, fibre tract of, 293
Germinal cells, 111
  centre, 119, 135
    in the spleen, 139
  epithelium, 239
  spot, 241
  vesicle, 241
Giant cells of bone-marrow, 265
    of placenta, 261
Gianuzzi, demilunes of, 174
Giraldé, organ of, 233, 248
Gitterfasern, 66, 197
Glands, 46

Gland body, 47
blood supply of, 51
classification of, 47, 49, 170
coil, 333
ducts, 47
fundus or peptic, 181
Krause's, 362
lachrymal, 364
mammary, 337
Meibomian, 362
of Brunner, 189
of Liberkühn, 185
of Montgomery, 339
of mouth cavity, 170
of œsophagus, 178, 179
of skin, 331
sebaceous, 331
sweat, 333
tarsal, 361
Glandulæ areolares, 33
Bartholini, 263
buccales, 176
bulbo-urethrales Cowperi, 235
ceruminosæ, 376
cervicales uteri, 253
ciliares, 361
gastricæ propriæ, 181
labiales, 176
linguales, 176
olfactoriæ (Bowmann), 380
palatinæ, 176
pyloricæ, 183
sudoriparæ, 333
urethrales (Littré), 223
vestibulares majores, 263
minores, 263
Glandular epithelium, 46
Glans clitoridis, 264
penis, 237
Glashaut, 242, 325
Glia cells, 285
fibres, 286
mass, central, 286
superficial, 286
Glisson's capsule, 194
Glomerulus of kidney, 212, 213
Glomus caroticum, 153
coccygeum, 154
Goblet cells, 39, 46, 186
Gold chloride methods, 413
Golgi cells, 109, 292
Golgi-Mazzoni corpuscles, 310
Golgi's method, 412
tendon spindles, 278
Goll's column, 281
Goose skin, 328
Gower's column, 283
Graafian follicle, 242
rupture of, 243
Grandry's corpuscles, 308
Granular cells, 58
of cerebellum, 294
sheath of Tomes, 159
Granulationes arachnoidales (Pacchioni), 297
Granulations, γ, 117
in leucocytes, 116
Granule theory of protoplasmic structure, 21
Granuloplasm, 19
Granulosa, 314
Gray commissure, 279
matter, 278
Ground bundles of lateral column, 283
of ventral column, 283
lamellæ, 76
substance of bone, 76
of dentine, 159
Growth of cartilage, 70
Gustatory cells, 382
organ, 381
pore, 381

HABENULA perforata, 369
Hæmalum, 396
Hæmalum-eosin, 397
Hæmatein, 396
Hæmatin, 120
Hæmatoidin, 120
Hæmatoxylin, 396
Hæmatoxylin-eosin, 397
Hæmatoxylin-iron-alum, 396
Hæmin, 120
Hæmoglobin, 112, 119
Hæmokonien, 118
Hairs, 322
Hair-bulb, 322
cells of auditory neuro-epithelium, 366
cuticle, 323
development of, 325
follicle, 323, 324
germ, 325
muscles of, 327
nerves of, 329
papilla, 322
root, 322
shaft, 322
sinus, 329
tactile, 329
Hardening of tissues, 390
Hassal's concentric corpuscles, 143
Haversian canals, 75
lamellæ, 75
Head of spermatozoön, 227
Heart, 130
layers of muscle in, 130
muscle, 83
histogenesis, 87
nerve-endings in, 312
of lower vertebrates, 86
protoplasmic bridges in, 86
nerves, 132
valves, 132
Hecateromeric cells, 282
Heidenhain's iron-hæmatoxylin, 396
Heisterian valve, 202
Heliotropism, 27

Henle, sheath of, 104, 109, 324
Henle's cells, 372
fenestrated membrane, 124
fibre layer, 349
loop, 213
Hensen's ductus reuniens, 365
line, 91
Hepatic duct, 202
Herbst's corpuscle, 310
Hermann's fluid, 389
Heteromeric cells, 282
Hilum of lymph gland, 136
stroma, 136
Histogenesis of blood, 118
of connective tissue, 61
of elastic tissue, 62
of epithelium, 44
of fat, 66
of heart muscle, 87
of the neurone, 110
of voluntary muscle, 94
Histology, 17
Histological units of spleen pulp, 141
Homomeric cells, 281
Horizontal cells of retina, 350
fibre tract of Gennari, 293
Horns, ventral and dorsal, 279
Horny layer of epidermis, 320
Howship's lacunæ, 272
Huschke's auditory teeth, 368
Huxley, sheath of, 324
Hyaline, 260
cartilage, 68
distribution of, 72
layer of hair, 325
Hyaloid artery, 357
canal, 357
membrane, 356
Hyaloplasm, 19
Hydatid of Morgagni, 234
Hydrotaxis, 27
Hydrotropism, 27
Hymen, 263
Hyponychium, 331
Hypophysis cerebri, 152

INCLUSIONS, cellular, 21
Indirect division, 28
Inferior cerebellar peduncle, 289
Injecting, 399
Injection masses, 400
Immersion lens, 384
Inner ear, 364
blood-vessels of, 373
lymph paths of, 375
enamel cells, 162
ground lamellæ, 76
Interannular segments, 105
Intercalary part of duct, 171
Intercellular bridges, 43
substance, 36
of bone, 76
of connective tissue, 54
Interfilar-mass, 20
Intergemmal nerve fibres, 383
Interglobular spaces, 159
Interlobar arteries of kidney, 218
Interlobular ducts, 171
trabeculæ of spleen, 140
veins of kidney, 219
of liver, 198
of spleen, 140
Intermediary lamellæ, 75
path for blood in spleen, 141
Intermediate bodies, 31
duct, 171
ducts of pancreas, 192
tubules of kidney, 213
zone of stomach, 184
Internal arcuate fibres, 287
capsule, 288
secretion, 49
Interolivary bundles of fibres, 287
Interradial bundles of fibres, 293
Interstitial cells of testis, 227
connective tissue of testis, 227
growth of cartilage, 70
lamellæ, 75
Intervillous spaces, 260
Intracellular development of blood corpuscles, 123
Intra-epithelial nerve-endings, 305
Intrafusal muscle-fibre, 315
Intragemmal nerve-fibres, 382
Intralobular ducts, 171
trabeculæ of spleen, 140
vein, 198
veins of spleen, 140
Intestine, 185
blood-vessels of, 190
lymph-vessels of, 191
mucosa of, 185
nerves of, 191
secretions of, 187
Intima, 129
pia, 298
Iris, 344
pigment layer of, 345
Iron-hæmatoxylin, 396
Irritability, 27
Islands of Langerhans, 194
proliferation, 260
Isolation of tissue elements, 386
Isotropic bands in muscle, 90, 91

JACOBSON'S organ, 380
Joining together of bones, 267
Joint capsules, 267
Joints, 267

KARYOLYSIS, 32, 246
Keimcentrum, 135
Keimzellen of His, 111
Keratin, 321
Keratohyalin granules, 321
Kidney, 212
blood-vessels of, 217
framework of, 217

Kidney, lobule of, 216
lymphatics of, 220
nerves of, 220
non-vascular zone of, 218
Kolossow's osmic-acid method, 402
Krause, ellipsoids of, 348
Krause's glands, 362
membrane, 84, 92
Kupffer's, v., stellate cells, 200

LABIA majora, 263
minora, 263
Labial glands, 177
Labium tympanicum, 367
vestibulare, 367
Labra glenoidalia, 267
Labyrinth, 364
of kidney, 213
Lacrymal canals, 364
gland, 364
Lacteal, 187, 191
Lacunæ, Howship's, 272
Lamellæ in bone, 75
Lamina basalis of chorioidea, 343
choriocapillaris, 343
cribrosa, 343, 354
elastica anterior, 341
posterior, 341
fusca scleræ, 342
spiralis membranacea, 367, 369
ossea, 367
suprachorioidea, 342
vasculosa chorioideæ, 343
Lampblack gelatin, 400
Langerhans, islands of, 194
Lange's spaces, 319
Lantanin, 23
Lantermann's lines, 105
Large granular cells of cerebellum, 295
mononuclear leucocytes, 115
pyramidal cells, 292
Larynx, 206
Lateral column, 280, 283
horn, 279
lemniscus, 290
pyramidal tract, 283
vestibular nucleus, 290
waves in muscle, 92
Lemniscus lateralis, 290
medialis, 287
Lens, 355
capsule, 356
fibres, 355
of microscope, 384
Leucoblast, 119
Leucocytes, 114
classification of, 115
distribution of, 114
Leucocytosis, 114
Lieberkühn's glands, 185
Ligamentum sacculorum 365
spirale, 367
Limbus spiralis, 367
Limiting capsule of myotome, 95
Lines of Schmidt-Lantermann, 105
Lingual tonsils, 167
Linin, 23
Liquor folliculi, 241
Lissauer's zone, 290
Liver, 194
blood-vessels, 197
cells, 195
development of, 204
lobule, 194
lymphatics, 201
Lobes and lobules of thymus, 143
Lobule of kidney, 216
of liver, 194
of spleen, 140
Lobuli epididymis, 231
testis, 224
Locomotor system, 264
Longitudinal bundle, posterior, 289
Long rayed cells, 293
Loop of Henle, 213
Loose connective tissue, 63
Lung, 207
blood-vessels of, 210
lymphatics of, 211
Lunula, 330
Lutein, 244
cells, 243
Lymph, 120
capillaries, 132
glands, 133
framework of, 133
nodules, peripheral, 138
in adrenal, 150
paths of eyeball, 359
of membranous labyrinth, 375
sinuses, 134
space of Tenon, 359
vessels, 132, 135
of intestine, 191
of kidney, 220
of ovary, 246
of stomach, 191
of uterus, 254
Lymphatic pharyngeal ring, 167
sheath of arteries of spleen, 140
Lymphatics, development of, 133
of liver, 201
of lung, 211
Lymphocytes, 115, 120
Lymphoid masses in intestine, 188

MACERATION, 386
Macula acustica, 365
germinativa, 241
lutea, 353
Magenta, 404
Male sexual organs, 224
accessory glands, 234
urethra, 223
Mallory's elastic tissue stain, 404
Malpighian corpuscle of kidney, 213
of spleen, 138
layer of skin, 320

Malpighian pyramids, 212
Mammary gland, 337
ducts of, 339
Mantle fibres, 30
Margarin crystals, 67
Marginal veil, 111
Marina's fluid, 412
Marrow cavity, primary, 269
of bones, 265
Martinotti, cells of, 292
Mast cells, 59
Matrix cells of hair, 326
unguis, 330
Maturation of the egg, 33
Mauthner's membrane, 107
Media, 126
Medial lemniscus, 287
Median fissure, ventral, 280
septum, dorsal, 280
vestibular nucleus, 290
Mediastinum testis, 224
Medulla, 287
of adrenal, 149
of cerebellum, 296
of hairs, 323
of kidney, 212
of lymph-gland, 134
sensory tract in, 288
Medullary cavity, primary, 269
cords, 134
plate, 110
rays, 212
sheath, 104
Megaloblasts, 265
Meibomian glands, 362
Meissner's plexus, 192
tactile corpuscles, 309
Membrana basilaris, 50, 369
chorii, 257
granulosa, 242
hyaloidea, 356
limitans externa, 349
interna, 352
olfactoria, 379
præformativa, 163
propria, 50
folliculi, 242
of glands, 172
reticularis, 372
tectoria, 372
tympani, 376
vestibuli (Reissneri), 367
Membrane of Henle, 124
of Schwalbe, 64
Membranes of central nervous system, 296
Membranous cochlea, 367
labyrinth, 365
urethra, 223
Meninges, 296
Menisci interarticulares, 267
tactile, 307
Menstruation, 254
Merkel's corpuscles, 306
tactile cells, 307
Mesentery, 205
Metakinesis, 29
Metaphase, 31
Metazoa, 18
Methylene-blue for nerve-endings, 413
Microblasts, 265
Micrometer screw, 384
Microscope, 383
Microscopic anatomy of organs, 121
Microsome, 19
Microtome, 387
Midbrain, 287
sensory tract in, 288
Middle cerebellar peduncle, 289
ear, 375
layer of cerebellum, 295
Milk line or ridge, 337
Mitome, 20
Mitosis, 28
Mixed glands, 173
muscles, 89
Molecular layer of cerebellum, 295
of cerebral cortex, 291
Moll's glands, 361
Monaster, 30
Mononuclear leucocytes, 115
Montgomery's glands, 339
Morgagni, hydatid of, 234
Mossy fibres, 296
Mother star, 30
Motility of cells, 25
Motor cells of cord, 281
cerebral nerves, nuclei of, 289
nerve-endings, 312
and sensory neurones, relation of, 317
Mouth cavity, 155
glands of, 170
Mucoid tissue, 53
Mucosa of gall-bladder, 203
of intestine, 185
of stomach, 180
Mucous cells, 172
of intestine, 186
glands, 174
membrane of larynx and trachea, 206
of mouth cavity, 155
Müllerian duct, 249
Müller's fibres, 352
fluid, 389, 412
Multicellular gland, 46
Multipolar cells, 100
Muscle, 80
bud, 314
cells, nuclei of developing, 96
changes during contraction, 92
development of, 94
fibre, intrafusal, 315
histogenesis of, 94
layers of heart, 130
nerve-endings in, 312
spindles, 314
striæ, 84, 90
Muscles, 274
blood-supply of, 275

Muscles, development of, 276
of the uterus, 253
Muscularis mucosæ of intestine, 188
of œsophagus, 178
of œsophagus, 179
Muscular system, 274
Musculus ciliaris, 344
Muskelsäulchen, 84
Myelocytes, 265
Myoblasts, 95
Myocardium, 130
Myometrium, 251
Myotome, 94

NAIL, 329
bed, 329
body, 329
groove, 329
leaves, 330
root, 329
wall, 329
Nasal duct, 364
Nasopharynx, 177
Nebenkern, 193
Nebenscheibe, 91
Neck of enamel organ, 162
of gastric gland, 181
Negative chemotaxis, 27
Nerve cell, body of, 102
cells, 98
corpuscles of Golgi-Mazzoni, 310
genital, 309
of Ruffini, 310
endings, 304
in connective tissue, 307
in muscle, 312
in nervous tissue, 316
motor, 312
sensory, 314
fibres, 103
process. *See* Axone.
Nerves, 299
cerebrospinal, 299
sympathetic, 300
of dura mater, 297
of eyeball, 360
of hairs, 329
of the heart, 132
of the intestine, 191
of the kidney, 220
of the liver, 201
of the lung, 211
of the ovary, 246
of the pancreas, 194
of the stomach, 191
of the submaxillary gland, 176
of the uterus, 254
Nervi nervorum, 301
Nervous system, 278
central blood-vessels of, 289
peripheral, 299
tissue, 97
Neumann's dental sheath, 159
Neural tube, 110
Neuraxone. *See* Axone
Neurilemma, 105
Neuroblast, 111
Neuro-epithelial cells, 307
Neurofibrils, 101, 104
Neuroglia, 285
of cerebellum, 296
of cerebral cortex, 293
Neurokeratin network, 106
Neurone, 97
contact relation of, 101
histogenesis, 110
theory, 101
Neuroplasm, 104
Neurospongium, 111
Neutral dyes, 116
Neutrophile granulation, 117
Nicol's prisms, in study of bone, 76
of muscle, 90
Nissl's bodies, 102, 103
method, 406
Nodes of Ranvier, 105
Nodules, lymph-, 138
Non-medullated nerve fibres, 109
Non-vascular zone of kidney, 218
Normoblasts, 265
Nose, 377
-piece, 385
Nuclear fluid, 23
Nucleated red blood corpuscles, 265
Nuclei of cerebral nerves, 289
of developing muscle cells, 96
Nuclein, 22
Nucleolus, 22
Nucleus, 19, 22
dorsalis, 279
olivaris inferior, 288
pulposus, 267
Nuel's space, 372
Nutrient arteries of bone, 266

OBJECTIVE ocular, 384
Odontoblasts, 156, 162
Œsophageal glands, 178, 179
Œsophagus, 178
Oil immersion lens, 384
Oken's body, 247
Olfactory cells, 378
glands, 380
nerve, 291
fibres, 109
organ, 377
Optic nerve, 291, 340, 354
Oral cavity, 155
mucous membrane, 155
Ora serrata, 235, 246
Orbicularis ciliaris, 244
Orcein, 403
Organ of Giraldé, 233
of Jacobson, 380
Organon spirale, 369
Organs, microscopic anatomy of, 121
Origin of blood cells, 118
of connective-tissue fibrils, 61

Origin of elastic tissue, 62
Osmic acid, 388
method of Kolossow, 403
Ossein, 74
Ossification, areas of, 268
of cartilage, 72, 268
Osteoblasts, 264, 270
Osteoclasts, 266, 272
Osteogenous tissue, 268
Otokonien crystals, 366
Otolith, 366
membrane, 366
Outer ear, 376
ground lamellæ, 76
Ovaries, 237
Ovary, blood-vessels of, 246
cortex of, 238
follicles of, 238
lymph-vessels of, 246
medulla of, 238
nerves of, 246
stroma of, 239
tunica albuginea of, 238
Ovula Nabothi, 253
Ovulation, 254
Ovum, primordial, 239
Oxychromatin, 23
Oxyntic cells, 182

PACCHIONIAN bodies, 297
Palatine glands, 177
tonsils, 169
Palpebral arteries, 363
Pal-Weigert method, 412
Pancreas, 192
framework of, 194
nerves of, 194
Panniculus adiposus, 320
Papillæ circumvallatæ, 166
dental, 161
filiformes, 165
fungiformes, 165
of oral mucous membrane, 155
of skin, 319
of tongue, 164
Papillary duct, 213, 215
Paradidymis, 233, 248
Paraffin, 392
Paramitome, 20
Paranuclein, 22
Paranucleus, 193
Parareticular cells, 350
Parathyroid gland, 147
Parenchyma of testis, 225
Parietal cells, 182
Paroöphoron, 246, 248
Parotid gland, 176
Parovarium, 246, 248
Pars cavernosa urethræ, 223
ciliaris retinæ, 346, 354
iridica retinæ, 345
membranacea urethræ, 223
optica retinæ, 346
papillaris of corium, 319
Pars prostatica urethræ, 223
reticularis of corium, 319
Pavement epithelium, 41
Peduncles, cerebellar, 288
Pellicula, 24
Pelvis of kidney, 221
Penicilli, 140
Penis, 235
blood-vessels of, 237
Pepsinogen, 182
Peptic glands, 181
Periaxial space of muscle spindle, 315
Pericardium, 132
Pericellular plexus, 302
Perichondral ossification, 268
Perichondrium, 68, 71
Perilobular space of liver, 201
Perilymph, 365
Perimetrium, 251
Perimysial sheath, 315
Perimysium externum, 274
internum, 274
Perineurium, 300
Periosteal buds, 269
Periosteum, 264
Peripheral lymph-nodule, 138
nervous system, 299
sensory neurones, origin of, 111
veil, 111
Peritenonium, 277
Peritoneum, 205
Perivascular lymph-spaces, 129, 201
spaces in nervous system, 299
Perivitelline space, 242
Permanent tooth, dental ridge, 162
Perosmic acid, 388
Petit's canal, 356
Peyer's patch, 188
Phagocytes, 60
Phagocytosis, 116
Phalanx, 372
Pharyngeal tonsils, 169
Pharynx, 177
Phototaxis, 27
Pia mater, 297
blood-vessels of, 298
Picric acid, 398
Picrocarmine, 398
Pigment cells, 58
epithelium, 44
in the skin, 322
layer of iris, 345
Pillars of organ of Corti, 370
Pituitary body, 152
Placenta, 257
circulation of blood in, 262
fœtalis, 257
uterina s. materna, 257
Placental villi, 257
Plain muscle fibres. *See* Smooth muscle.
Plana semilunata, 365
Plasma cells, 59
of blood, 112
Platelets of blood, 117

Platelets, preparation for study, 408
Platinum-osmium-acetic acid, 389
Pleuræ,, 210
Plexus annularis, 360
chorioideus, 298
myentericus, 191
of Auerbach, 191
of Meissner, 192
Plicæ conniventes Kerkringii, 185
palmatæ, 253
semilunares, 362
villosæ, 181
Polar bodies, extrusion of, 33
radiation, 31
Polymorphonuclear leucocytes, 115
Polymorphous cells, 292
Pons, 287
sensory tract in, 288
Porus lactiferus, 337
Positive chemotaxis, 27
Posterior basal membrane, 341
epithelial layer, 342
horn. *See* Dorsal horn.
longitudinal bundle, 289
median septum. *See* Dorsal median septum.
root. *See* Dorsal root.
Precapillary arteries and veins, 122
Pregnancy, 255
Preparation of specimens, 385
Prickle cells, 42
Primary bundles of muscle fibres, 274
follicles, 240
medullary cavity, 269
Primitive fibrils in muscles, 88
in nerves, 104
organ of the fat lobule, 66
ova, 239
Primordial follicles, 240
medullary cavity, 269
ova, 239
Processus ciliaris, 344
Proliferation islands, 260
Prominentia spiralis, 368
Prophase, 29
Prostate, 234
blood-vessels of, 235
interstitial tissue of, 234
nerves of, 235
Prostatic urethra, 223
Protoplasm, 18, 19
Protoplasmic bridges, 43
demonstration of, 402
in heart muscle, 86
in intestinal mucosa, 186
inclusions, 21
processes, 97, 99
Protozoa, 18
Pseudopodia, 25
Pulmonary artery, 210
vein, 210
Pulp cavity, 156
of spleen, 138, 139
of tooth, 156
Purkinje cells, 100, 295
Pyloric glands, 183
Pyramidal cells of cortex, 100, 292
tract, 288
crossed, 283
ventral, 283
Pyramids of Ferrein, 212
of Malpighi, 212

QUERSCHEIBE, 84

RADIAL bundles of nerve fibres, 293
Ramus ascendens of Henle's loop, 213, 215
Ramus descendens of Henle's loop, 213, 215
Ranvier's alcohol, 386
cross, 106
nodes, 105
segments, 105
Raphé of semicircular canals, 365
Rathke's duct, 249
Real interstitial lamellæ, 75
Red blood corpuscles, 112
nucleated, 265
number of, 114
bone marrow, 265
muscle, 89
Reduction of chromosomes, 33
Reflex arc, 317
Reissner's membrane, 367
Remak's fibres, 109
Renal artery, 217
Reproduction, 28
Reproductive system, 224
Respiratory bronchioli, 207
epithelium, 207
system, 206
Rete testis (Halleri), 225, 226
Reticular tubular gland, 49
Reticulin, 66
Reticulum, 65
Retina, 346
neuro-epithelial layer, 348
pigment sheath, 347
Retinal vessels, 357
Ripening of the egg, 33
Rod fibre, 348
Rods, 348
Rolando, gelatinous substance of, 279
Root canal, 156
of hair, 322
sheath, 324
Rosenmüller, organ of, 246, 248
Rotation in protoplasm, 26
Rouleaux, 114
Ruffini's corpuscles, 310
Rugæ of vagina, 263

SACCULUS, 364, 365
Saccus endolymphaticus, 375
Safranin, 397
Salivary corpuscles, 169
ducts, 171

Salivary glands, 170, 175
Sarcolemma, 89
Sarcoplasm, 81, 84, 88
function of, 94
Sarcoplasmic discs, 85
Scala tympani, 367
vestibuli, 367
Schläuche of Pflüger, 240
Schwann's corpuscles, 106
sheath, 104, 106
Sclera, 342
Sebaceous glands, 331
Secondary bundles of muscle fibres, 274
papillæ of tongue, 165
Secretion, 46
in intestine, 187
internal, 49
Secretory canals, 174
capillaries, 51, 174
in liver cells, 196
oxyntic cells, 183
unit of kidney, 216
of liver, 200
Sectioning of tissues, 387
Sections, 344
Segments of Ranvier, 105
Semen, 227
Semicircular canals, 365
Seminal vesicles, 233
Seminiferous tubules, 225
Sense cells, 307
organs, 318
representation in cortex, 291
Sensory cerebral nerves, nuclei of, 289
epithelium, 37
neurones, peripheral, origin of, 111
nerve-endings, 314
tract in midbrain, 287
Septa placentæ, 261
Septula testis, 224
Septum, dorsal median, 280
medianum dorsale, 280
ventral median, 280
Serial sections, 294
Serosa, 205
Serous glands, 174
tubules, 172
Sertoli cells, 229
Sexual organs, female, 237
male, 224
Shadows of blood cells, 113
Sharpey's fibres, 76, 264
Sheath of Henle, 324
of Huxley, 324
Sheaths of hair root, 323
Short rayed cells, 293
Signet ring cells, 58, 67
Silent area of the brain, 291
Silver line of Frommann, 105
nitrate staining, 402
Simple branched tubular gland, 48, 49
epithelium, 40
unbranched alveolar gland, 49
tubular gland, 49
Sinus of brain, 329
lactiferus, 337
prostaticus, 235
terminalis of lymph-gland, 136
Sinuses of lymph-gland, 134
Skeletal muscle, 88
system, 264
Skin, 318
blood-vessels, and nerves, 335
Small glands of mouth cavity, 176
granular cells of cerebellum, 294
mononuclear leucocytes, 115
pyramidal cells, 292
Smooth muscle, 81
nerve-endings in, 312
Solitary follicles, 138
of intestine, 188
Space of Fontana, 346
of Lange, 319
Spaces, intervillous, 260
Spatia zonularis, 356
Special microscopic technique, 401
Spermatic ducts, 231
Spermatids, 230
Spermatoblasts, 230
Spermatocytes, 230
Spermatogenesis, 229
Spermatogonia, 229
Spermatozoön, 227
development of, 229
Sphincter ani, 190
of common bile duct, 202
pylori, 184
Spider cells, 282
Spinal cord, 278
ganglia, 303
Spindle, Golgi tendon, 278
muscle, 314
nerve, 316
Spleen, 138
blood-vessels of, 140
capsule of, 138
framework of, 140
pulp of, 138
sinuses of, 142
Spongioblasts, 350
Spongy bone, 74
substance, 80
Staining of sections, 395
Stains, acid, basic, and neutral, 116
Statoliths, 366
Status mamillaris, 181
Stellate cells of v. Kupffer, 200
veins of Verheyn, 219
Stigmata, 43
Stilling-Clarke, column of, 279
Stomach, 180
blood-vessels of, 190
lymph-vessels of, 191
nerves of, 191
Stomata, 43
Stratified cylindrical epithelium, 42
epithelium, 41
flat epithelium, 42

Stratum corneum, 320, 321
cylindricum, 320
fibrosum of joint capsule, 267
germinativum, 320
granulosum, 242, 321
terminale, 85
lucidum, 321
Malpighii, 320
mucosum of uterine muscle, 253
spinosum, 321
subserosum of uterine muscle, 253
supravasculare of uterine muscle, 253
synoviale of joint capsule, 267
vasculare of uterine muscle, 253
zonale, 291
Stria vascularis, 368
Striæ acusticæ, 290
Striated muscle, 88
histogenesis, 94
nerve-endings in, 312
Striation of muscle, 84, 90
Stroma of blood cell, 113
of hilum of lymph-gland, 163
of ovary, 136
Subchorionic limiting ring, 262
Subcutaneous tissue, 320
Sublingual gland, 176
Submaxillary gland, 175
development of, 175
nerves of, 176
Submucosa of intestine, 189
of œsophagus, 178
of oral mucous membrane, 155
Subpapillary network of vessels, 335
Subserous connective tissue, 205
Substantia adamantia, 160
eburnea, 157
gelatinosa (Rolandi), 279
grisea centralis, 280
lentis, 355
ossea, 161
propria corneæ, 341
Succus entericus, 188
prostaticus, 234
Sulcus lateralis dorsalis, 280
ventralis, 367
spiralis externus, 368
internus, 367
Superficial glands of œsophagus, 179
glia mass, 286
Superior cells of auditory neuro-epithelium, 366
cerebellar peduncle, 289
Supporting cells of Müller, 352
of nasal mucous membrane, 379
of testis, 229
Supraradial network, 293
Suprarenal gland, 147
Sweat glands, 333
Sympathetic ganglia, 302
nerve fibres, 109
nerves, 300
Synarthrosis, 267
Synchondrosis, 267
Syncytium, 22, 88
of chorionic villus, 259
Syndesmosis, 267
Synovia, 268
Synovial fluid, 268
villi, 268

TACTILE cells of Merkel, 307
corpuscles of Meissner, 309
of Merkel, 306
disc of Grandry's corpuscle, 308
hairs, 329
menisci, 307
organ, 318
Tæniæ coli, 190
Tail of spermatozoön, 228
Tangential fibres in cortex, 291
Tarsal glands, 361
Tarsus, 361
Taste buds, 381
bulbs, 166
organ of, 381
pore, 381
Tear sac, 364
Teasing of tissues, 386
Technique, microscopic, 383
Teeth, 156
development of, 161
Teichmann's crystals, 120
Tela subcutanea, 319
Telæ chorioideæ, 298
Telodendria, 99
Telophase, 29, 32
Tendon cells, 57
fibres, 57
spindles, 278
Tendons, 277
Tenon's lymph-space, 359
Tensor chorioideæ, 344
Terminal bronchus, 208
Tertiary bundles of muscle fibres, 274
Testes, 224
blood-vessels of, 227
Theca folliculi, 242
Thermotaxis, 27
Thionin, 397
Thoma, ampulla of, 141
Thymus, 143
Thyroid, 144
framework of, 146
Tigroid bodies, 102, 103
Tissues, 35
definition and classification of, 36
Tome's granular sheath, 159
processes, 164
Tongue, 164
muscles of, 167
papillæ of, 164
Tonsils, 167
development of, 169
tubal, 376
Tooth cavity, 156
development of, 161

Tooth, papilla, 161
pulp, 156
sac, 162
Trabeculæ of lymph-gland, 133
of spleen, 138, 140
Trachea, 206
Tractus cerebello-spinalis dorsalis, 283
cerebro-spinalis lateralis, 283
ventralis, 283
intermedio-lateralis, 279
solitarius, 290
Transitional leucocytes, 115
Transition zone of stomach, 184
Trapezoid body, 290
Trigeminal nerve, 290
Triple stain of Biondi-Ehrlich, 398
True connective-tissue cells, 57
gastric glands, 181
glands, 46
Tuba uterina Fallopii, 250
Tubal tonsils, 376
Tubular glands, 47, 49
Tubuli contorti testis, 225
recti testis, 225, 226
seminiferi, 225
Tubulo-alveolar gland, 49
Tunica adnata, 224
albuginea of corpora cavernosa, 236
of ovary, 238
testis, 224
externa, 242
fibrosa testis, 224
interna, 242
serosa, 205
vaginalis communis, 224
propria, 224
vasculosa testis, 224
Tympanic cavity, 375
membrane, 376
Tyson's glands, 332

ULTRAMARINE blue, 400
Unbranched alveolar glands, 49
tubular glands, 49
Unformed connective tissue, 63
Unicellular glands, 46
Unipolar cells, 99
transition from bipolar cells, 101
Units of kidney structure, 216
of liver, 200
Unna's elastic tissue stain, 404
Unstriped muscle. *See* Smooth muscle.
Ureter, 221
Urethra, 223
Urinary bladder, 221
passages, 221
system, 212
Uterus, 251
blood-vessels of, 254
changes during menstruation, 254
pregnancy, 255
glands of, 253
lymph-vessels of, 254
Uterus masculinus, 235
muscle of, 253
nerves of, 254
Utriculus, 364, 365
prostaticus, 235

VACUOLES, 21
Vagina, 262
Valves of the heart, 132
of veins, 128
Valvulæ conniventes, 185
Varicosities of nerve fibres, 306
Vasa afferentia (kidney), 218
efferentia (kidney), 218
testis, 231
vasorum, 129
Vas deferens, 232
epididymis, 231, 232
prominens, 368
Vasoformative cells, 123
Vater-Pacini, corpuscles of, 311
Veins, 127
of adrenal, 150
of spleen, 140
precapillary, 122
Vena portæ, 198
Venæ emissariæ, 237
Ventral column, 280, 282, 283
gray commissure, 280
horn, 279
median fissure, 280
pyramidal tract, 283
root, 279
Ventro-lateral group of motor cells, 281
Ventro-median group of motor cells, 281
Venulæ rectæ, 220
Verheyn, stillate veins of, 219
Vesicula germinativa, 241
prostatica, 235
seminalis, 233
Vestibular glands, 263
nerve, 290
nuclei, 290
Vestibulum of lung, 208
Villi of intestine, 185
of placenta, 257
synovial, 268
Visual cells, 348
organ, 340
Vitreous body, 356
humor, 340, 356
Volkmann's canals, 76
Voluntary muscle, 88
histogenesis of, 94

WANDERING cells, 60
Wax of ear, 377
Weber's organ, 249
Weigert-Pal method, 412
White blood corpuscles, 114
commissure, 280
connective-tissue fibrils, 54
fibrous cartilage, 73

White fibrous connective tissue, 54, 63
matter, 278
muscle, 89
substance of cerebellum, 296
Wirsung's duct, 192
Wolffian body, 247
duct, 247
Wood's metal, 401

YELLOW bone marrow, 265
elastic connective tissue, 64
Yolk, 241

ZELLSCHICHT, 259
Zenker's fluid, 390
Zona fasciculata, 148
glomerulosa, 148
pectinata, 369
pellucida, 240
reticularis, 149
tecta, 369
vasculosa of ovary, 238
Zonula ciliaris, 356
Zwischenscheibe, 84, 91
Zymogen granules, 192

WELLCOME LIBRARY INSTITUTE

Catalogue of Books

PUBLISHED BY

Lea Brothers & Company,

706, 708 & 710 Sansom St., Philadelphia.
111 Fifth Avenue, New York.

Our publications can be purchased from any Bookseller in the United States or Canada, or they will be delivered by express or mail, carriage paid to any address on receipt of the printed price.

JULY, 1904.

STANDARD MEDICAL PERIODICALS.

Progressive Medicine.

A Quarterly Digest of New Methods, Discoveries and Improvements in the Medical and Surgical Sciences by Eminent Authorities. Edited by DR. HOBART AMORY HARE. In four illustrated octavo volumes of 300–400 pages each, issued quarterly, commencing with March each year. Per annum (4 volumes), in heavy paper covers, $6.00; in cloth binding, $9.00, delivered.

The Medical News.

WEEKLY, $4.00 PER ANNUM.

Each number contains 48 quarto pages, illustrated. A crisp, fresh weekly professional newspaper.

The American Journal of the Medical Sciences.

MONTHLY, $5.00 PER ANNUM.

Each issue contains 192 octavo pages, fully illustrated. The most advanced, practical, original and enterprising American exponent of scientific medicine.

The Medical News Visiting List for 1904.

Four styles, Weekly (dated for 30 patients); Monthly (undated, for 120 patients per month); Perpetual (undated, for 30 patients weekly per year); and Perpetual (undated, for 60 patients weekly per year). Each style in one wallet-shaped book, leather bound, with pocket, pencil and rubber. Price, each, $1.25. Thumb-letter index, 25 cents extra.

The Medical News Pocket Formulary.

New (5th) edition carefully revised to date. Containing 1700 prescriptions representing the latest and most approved methods of administering remedial agents. Strongly bound in leather, with pocket and pencil. Price, $1.50, *net*.

COMBINATION RATES.

Progressive Medicine	per annum	$6.00
The American Journal of the Medical Sciences	"	5.00
The Medical News	"	4.00
Progressive Medicine and The American Journal	"	10.00
Progressive Medicine and The Medical News	"	9.00
The American Journal and The Medical News	"	8.00
Progressive Medicine, The American Journal, and The Medical News	'	13.50
The Medical News Visiting List in combination with any of the above Periodicals		75
The Medical News Pocket Formulary in combination with any of the above Periodicals		75

Fine descriptive circulars of any of the above mailed on request.

ABBOTT (**A. C.**). *PRINCIPLES OF BACTERIOLOGY:* a Practical Manual for Students and Physicians. Sixth edition enlarged and thoroughly revised. 12mo., 636 pages, with 111 engravings, of which 26 are colored. Cloth, $2.75, *net.*

ALLEN (**CHARLES W.**). *RADIOTHERAPY AND PHOTOTHERAPY, INCLUDING RADIUM AND HIGH-FREQUENCY CURRENTS.* Their Medical and Surgical Applications in Diagnosis and Treatment. Octavo, 618 pages, with 131 engravings and 27 plates in colors and monochrome. Cloth, $4.50, *net. Just ready.*

ALLEN (**HARRISON**). *A SYSTEM OF HUMAN ANATOMY.* Comprising 813 quarto pages, with 380 engravings on stone and 241 woodcuts. Cloth, $23.

ALLING (**ARTHUR N.**) **AND GRIFFEN** (**O. A.**). *AN EPITOME OF DISEASES OF THE EYE AND EAR.* 12mo., about 225 pages, with 82 engravings. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

AMERICAN SYSTEM OF PRACTICAL MEDICINE. In Contributions by Eminent American Authors. Edited by ALFRED L. LOOMIS, M.D., LL.D., and W. GILMAN THOMPSON, M.D. In four octavo volumes of about 900 pages each, fully illustrated. Per volume, cloth, $5; leather, $6; half morocco, $7. *For sale by subscription only.* Prospectus free on application.

AMERICAN SYSTEM OF DENTISTRY. *IN TREATISES BY VARIOUS AUTHORS.* Edited by WILBUR F. LITCH, M.D., D.D.S. In three octavo volumes, containing about 3200 pages, with 1873 illustrations and many full-page plates. Per volume, cloth, $6; leather, $7. Prospectus free on application to the Publishers.

AMERICAN SYSTEMS OF GYNECOLOGY AND OBSTETRICS. Gynecology edited by MATTHEW D. MANN, A.M., M.D., and Obstetrics edited by BARTON C. HIRST, M.D. In four large octavo volumes comprising 3612 pages, with 1092 engravings, and 8 colored plates. Per volume, cloth, $5.

AMERICAN TEXT-BOOK OF ANATOMY. See *Gerrish*, page 7.

AMERICAN TEXT-BOOKS OF DENTISTRY. *IN CONTRIBUTIONS BY EMINENT AMERICAN AUTHORITIES.* In two octavo volumes of more than 800 pages each, richly illustrated:

—— *PROSTHETIC DENTISTRY.* Edited by CHARLES J. ESSIG, M.D., D.D.S., Professor of Mechanical Dentistry and Metallurgy, Department of Dentistry, University of Pennsylvania, Philadelphia. Second Edition, 807 pages, with 1089 engravings. Cloth, $6; leather, $7, *net.*

—— *OPERATIVE DENTISTRY.* Edited by EDWARD C. KIRK, D.D.S., Professor of Clinical Dentistry, Department of Dentistry, University of Pennsylvania. Second Edition, 857 pages, 897 engravings. Cloth, $6.00; leather, $7.00, *net.*

ARCHINARD (**P. E.**). *AN EPITOME OF BACTERIOLOGY AND MICROSCOPY.* 12mo., 210 pages, with 80 illustrations. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

ARNEILL'S *EPITOME OF CLINICAL DIAGNOSIS AND URINALYSIS. Lea's Series of Medical Epitomes.* See page 10.

ASHHURST (**JOHN, JR.**). *THE PRINCIPLES AND PRACTICE OF SURGERY.* For the use of Students and Practitioners. Sixth and revised edition. In one 8vo. volume of 1161 pages, with 656 engravings. Cloth, $6; leather, $7.

A TREATISE ON SURGERY BY AMERICAN AUTHORS. *FOR STUDENTS AND PRACTITIONERS OF SURGERY AND MEDICINE.* Edited by ROSWELL PARK, M.D. Third edition. Octavo, 1408 pages, with 692 engravings and 64 plates. Cloth, $7.00, *net;* leather, $8.00, *net.* ☞ Published also in 2 volumes: Vol. I., General Surgery; Vol. II., Special or Regional Surgery. Per volume, cloth, $3.75, *net;* leather, $4.75, *net.*

ATTFIELD (**JOHN**). *CHEMISTRY; GENERAL, MEDICAL AND PHARMACEUTICAL.* Sixteenth edition, specially revised by the Author for America. In one handsome 12mo. volume of 784 pages, with 88 illustrations. Cloth, $2.50, *net.*

BACON (GORHAM). *ON THE EAR.* Third Edition. One 12mo. volume, 430 pages, with 120 engravings and 7 colored plates. Cloth, $2.25, *net.*

BALLENGER (W. L.) AND WIPPERN (A. G.). *A POCKET TEXT-BOOK OF DISEASES OF THE EYE, EAR, NOSE AND THROAT.* 12mo., 525 pages, with 148 illustrations, and 6 colored plates. Cloth, $2, *net.* Flexible red leather, $2.50, *net.*

BARNES (ROBERT AND FANCOURT). *A SYSTEM OF OBSTETRIC MEDICINE AND SURGERY.* Octavo, 872 pages, 231 illustrations. Cloth, $5.

BARTHOLOW (ROBERTS). *CHOLERA; ITS CAUSATION, PREVENTION AND TREATMENT.* 12mo., 127 pages, with 9 illustrations. Cloth, $1.25.

BERGMANN'S *SURGERY.* See *Von Bergmann.*

BILLINGS (JOHN S.). *THE NATIONAL MEDICAL DICTIONARY.* Including in one alphabet English, French, German, Italian and Latin Technical Terms used in Medicine and the Collateral Sciences. In two imperial octavo volumes, containing 1574 pages and two colored plates. Per vol., leather, $7. Specimen pages on application.

BLACK (D. CAMPBELL). *THE URINE IN HEALTH AND DISEASE, AND URINARY ANALYSIS, PHYSIOLOGICALLY AND PATHOLOGICALLY CONSIDERED.* 12mo., 256 pages, 73 engravings. Cloth, $2.75.

BLOODGOOD (JOSEPH C.). *SURGICAL PATHOLOGY AND DIAGNOSIS.* Octavo about 1000 pages, with many engravings and plates in black and colors. *Preparing.*

BLOXAM (C. L.). *CHEMISTRY, INORGANIC AND ORGANIC.* With Experiments. New American from the fifth London edition. In one handsome octavo volume of 727 pages, with 292 illustrations. Cloth, $2; leather, $3.

BREWER (GEORGE E.) *A TEXT-BOOK OF THE PRINCIPLES AND PRACTICE OF SURGERY.* Octavo, 700 pages, with 280 engravings and 7 plates. Cloth, $4.00; leather, $5.00, *net;* half morocco, $5.50, *net.*

BRUCE (J. MITCHELL). *MATERIA MEDICA AND THERAPEUTICS.* Sixth edition. In one 12mo. volume of 600 pages. Cloth, $1.50, *net.*
Students' Series of Manuals. Page 15.

—— *PRINCIPLES OF TREATMENT.* In one octavo volume of 625 pages. Cloth, $3.75, *net.*

BRYANT (THOMAS). *THE PRACTICE OF SURGERY.* Fourth edition. Octavo, 1040 pages, with 727 illustrations. Cloth, $6.50; leather, $7.50.

BULL'S *SYSTEM OF SURGERY.* See *Von Bergmann.*

BURCHARD (HENRY H.). *DENTAL PATHOLOGY.* New (2d) edition, thoroughly revised by OTTO E. INGLIS, D.D.S. In one octavo volume of about 600 pages, with about 450 engravings. *Shortly.*

BURNETT (CHARLES H.). *A TREATISE ON THE EAR.* Second edition. 8vo., 580 pages, with 107 illustrations. Cloth, $4; leather, $5.

CARTER (R. BRUDENELL) AND FROST (W. ADAMS). *OPHTHALMIC SURGERY.* In one pocket-size 12mo. volume of 559 pages, with 91 engravings and one plate. Cloth, $2.25. See *Series of Clinical Manuals,* page 13.

CASPARI (CHARLES, JR.). *A TREATISE ON PHARMACY.* For Students and Pharmacists. Second edition. Revised and enlarged. Octavo, 774 pages, with 302 illustrations. Cloth, $4.25, *net.*

CHAPMAN (HENRY C.). *HUMAN PHYSIOLOGY.* Second edition. Octavo, 921 pages, with 595 illustrations. Cloth, $4.25; leather, $5.25, *net.*

CHARLES (T. CRANSTOUN). *PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY.* Octavo, 451 pages, with 38 engravings and 1 colored plate. Cloth, $3.50.

CHEYNE (W. WATSON) AND BURGHARD (F. F.). *SURGICAL TREATMENT.* In seven octavo cloth bound volumes, comprising 2883 pages, with 827 engravings. Volume I, $3.00, *net.* Volume II, $4.00, *net.* Volume III, $3.50, *net.* Volume IV., $3.75, *net.* Volume V, $5.00, *net.* Vol. VI, $5.00, *net.* Volume VII, $5.75, *net.* Complete work, $30.00, *net.*

CLELAND (JOHN). *A DIRECTORY FOR THE DISSECTION OF THE HUMAN BODY.* In one 12mo. volume of 178 pages. Cloth, $1.25.

CLOUSTON (THOMAS S.). *CLINICAL LECTURES ON MENTAL DISEASES.* New (6th) edition. Crown 8vo., of about 750 pages, with about 20 colored plates. *Ready Shortly.*

COAKLEY (CORNELIUS G.). *DISEASES OF THE NOSE, THROAT, NASO-PHARYNX AND TRACHEA.* Second edition. 12mo., 556 pages, with 103 engravings, and 4 colored plates. Cloth, $2.75, *net.*

COATS (JOSEPH). *A TREATISE ON PATHOLOGY.* Octavo, 829 pages, with 339 engravings. Cloth, $5.50; leather, $6.50.

COLEMAN (ALFRED). *A MANUAL OF DENTAL SURGERY AND PATHOLOGY.* Octavo, 412 pages, with 331 engravings. Cloth, $3.25.

COLLINS (C. F.) AND (DAVIS F.). *POCKET TEXT-BOOK OF DIAGNOSIS.* 12mo., about 350 pages. *Shortly. Lea's Series of Pocket Text-Books.* See page 12.

COLLINS (H. D.) AND ROCKWELL (W. H., JR.). *A POCKET TEXT-BOOK OF PHYSIOLOGY.* 12mo., of 316 pages, with 153 illustrations. Cloth, $1.50, *net;* flexible leather, $2.00, *net. Lea's Series of Pocket Text-Books.* See page 12.

CONDIE (D. FRANCIS). *A PRACTICAL TREATISE ON THE DISEASES OF CHILDREN.* Sixth edition. 8vo. 719 pages. Cloth, $5.25; leather, $6.25.

CORNIL (V.). *SYPHILIS: ITS MORBID ANATOMY, DIAGNOSIS AND TREATMENT.* Translated, by J. HENRY C. SIMES, M.D., and J. WILLIAM WHITE, M.D. 8vo. 461 pages, with 84 illustrations. Cloth, $3.75.

CROCKETT (M. A.). *A POCKET TEXT-BOOK OF DISEASES OF WOMEN.* 12mo. of 368 pages, with 107 illustrations. Cloth, $1.50, *net.* Flexible Red Leather, $2.00, *net. Lea's Series of Pocket Text-Books.* Page 12.

CROOK (JAMES K.). *MINERAL WATERS OF UNITED STATES.* Octavo, 574 pages. Cloth, $3.50, *net.*

CULBRETH (DAVID M. R.). *MATERIA MEDICA AND PHARMACOLOGY.* Third edition. Octavo, 905 pages, with 473 engravings. Cloth, $4.75, *net.*

CUSHNY (ARTHUR R.) *PHARMACOLOGY AND THERAPEUTICS.* Third edition. Octavo of 750 pages, with 52 illustrations. Cloth, $3.75; leather, $4.75, *net.*

DALTON (JOHN C.). *A TREATISE ON HUMAN PHYSIOLOGY.* Seventh edition, thoroughly revised. Octavo of 722 pages, with 252 engravings. Cloth, $5; leather, $6.

DALTON (**JOHN C.**). *DOCTRINES OF THE CIRCULATION OF THE BLOOD.* In one handsome 12mo. volume of 293 pages. Cloth, $2.

DAVENPORT (**F. H.**). *DISEASES OF WOMEN.* Fourth edition. 12mo., 402 pages and 154 engravings. Cloth, $1.75, *net.*

DAVIS (**F. H.**). *LECTURES ON CLINICAL MEDICINE.* Second edition. In one 12mo. volume of 287 pages. Cloth, $1.75.

DAVIS (**EDWARD P.**). *A TREATISE ON OBSTETRICS.* New (2d) and thoroughly revised edition. Octavo, 800 pages, with 274 engravings, and 39 full-page plates in colors and monochrome. Cloth, $5.00, *net;* leather, $6.00, *net. Just ready.*

DAYTON'S *EPITOME OF THE PRACTICE OF MEDICINE. Lea's Series of Medical Epitomes.* See page 10.

DE LA BECHE'S *GEOLOGICAL OBSERVER.* In one large octavo volume of 700 pages, with 300 engravings. Cloth, $4.

DE SCHWEINITZ (**GEORGE E.**). *THE TOXIC AMBLYOPIAS.* Very handsome octavo, 240 pages, 46 engravings, and 9 full-page plates in colors. De luxe binding, $4, *net.*

DRAPER (**JOHN C.**). *MEDICAL PHYSICS.* A Text-book for Students and Practitioners of Medicine. Octavo of 734 pages, with 376 engravings. Cloth, $4.

DRUITT (**ROBERT**). *THE PRINCIPLES AND PRACTICE OF MODERN SURGERY.* From the twelfth London edition, edited by STANLEY BOYD, F.R.C.S. Large octavo, 965 pages, with 373 engravings. Cloth, $4; leather, $5.

DUANE (**ALEXANDER**). *A DICTIONARY OF MEDICINE AND THE ALLIED SCIENCES.* Comprising the Pronunciation, Derivation and Full Explanation of Medical, Dental, Pharmaceutical and Veterinary Terms. Together with much Collateral Descriptive Matter, Numerous Tables, etc. Fourth edition, with appendix. Square octavo volume of 688 pages with 8 colored plates and thumb index. Cloth, $3.00, *net;* limp leather, $4.00, *net.*

DUDLEY (**E. C.**). *PRINCIPLES AND PRACTICE OF GYNECOLOGY.* New (fourth) edition, thoroughly revised. Octavo, 770 pages, with 420 engravings, of which 50 are colored, and 16 full-page plates in colors and monochrome. Cloth, $5.00, *net;* leather, $6.00, *net;* half morocco, $6.50, *net.*

DUNGLISON (**ROBLEY**). *A DICTIONARY OF MEDICAL SCIENCE. ILLUSTRATED.* Containing a full Explanation of the Various Subjects and Terms of Anatomy, Physiology Medical Chemistry, Pharmacy, Pharmacology, Therapeutics, Medicine, Hygiene, Dietetics, Pathology, Surgery, Ophthalmology, Otology, Laryngology, Dermatology, Gynecology. Obstetrics, Pediatrics, Medical Jurisprudence, Dentistry, Veterinary Science, etc., etc. By ROBLEY DUNGLISON, M.D., LL.D., late Professor of Institutes of Medicine in the Jefferson Medical College of Philadelphia. New (twenty-third) edition, thoroughly revised by THOMAS L. STEDMAN, M.D., Member of the New York Academy of Medicine, etc. Imperial octavo of 1220 pages, with 577 illustrations, including 84 plates in colors and black. Thumb-letter index. Cloth, $8.00, *net;* leather, $9.00, *net;* half morocco, $9.50, *net. Just ready.*

DUNHAM (**EDWARD K.**). *MORBID AND NORMAL HISTOLOGY.* Octavo, 450 pages, with 360 illustrations. Cloth, $3.25, *net.*

DUNHAM (**EDWARD K.**). *NORMAL HISTOLOGY.* New (third) and revised edition. Octavo, 334 pages, with 260 illustrations. Cloth, $2.75, *net. Just ready.*

DWIGHT (E. W.). *AN EPITOME OF MEDICAL JURISPRUDENCE.* 12mo., 241 pages. Cloth, $1.00, *net.* *Lea's Series of Medical Epitomes.* See page 10.

—— *AN EPITOME OF TOXICOLOGY.* 12mo., about 225 pages. Cloth, $1.00, *net.* *Lea's Series of Medical Epitomes.* See page 10.

ECKLEY (WILLIAM T.). *A GUIDE TO DISSECTION OF THE HUMAN BODY.* Octavo, 400 pages, with 220 large engravings in black and colors. Cloth, $3.50, *net.*

—— *REGIONAL ANATOMY OF THE HEAD AND NECK FOR STUDENTS AND PRACTITIONERS.* Octavo, 240 pages, with 36 engravings and 20 plates in black and colors. Cloth, $2.50, *net.*

EDES (ROBERT T.). *TEXT-BOOK OF THERAPEUTICS AND MATERIA MEDICA.* In one 8vo. volume of 544 pages. Cloth, $3.50; leather, $4.50.

EDIS (ARTHUR W.). *DISEASES OF WOMEN.* 8vo., 576 pages, with 148 engravings. Cloth, $3; leather, $4.

EGBERT (SENECA). *HYGIENE AND SANITATION.* Third edition. In one 12mo. volume of 467 pages, with 86 illustrations. Cloth, $2.25, *net.*

ELLIS (GEORGE VINER). *DEMONSTRATIONS IN ANATOMY.* Eighth edition. Octavo, 716 pages, with 249 engravings. Cloth, $4.25; leather, $5.25.

EMMET (THOMAS ADDIS). *THE PRINCIPLES AND PRACTICE OF GYNÆCOLOGY.* For the use of Students and Practitioners. Third edition, enlarged and revised. 8vo. of 880 pages, with 150 original engravings. Cloth, $5; leather, $6.

ERICHSEN (JOHN E.). *THE SCIENCE AND ART OF SURGERY.* From the eighth enlarged and revised London edition. In two large octavo volumes containing 2316 pages, with 984 engravings. Cloth, $9; leather, $11.

ESSIG (CHARLES J.). *PROSTHETIC DENTISTRY.* Second edition. See *American Text-books of Dentistry*, page 2.

ESSIG (C. J.) AND KOENIG (AUGUSTUS). *DENTAL METALLURGY.* New (fifth) edition, thoroughly revised. 12mo., 318 pages with 76 engravings. Cloth, $2.00, *net.*

EVANS (DAVID J.). *A POCKET TEXT-BOOK OF OBSTETRICS.* 12mo. of 409 pages, with 148 illustrations. Cloth, $1.75, *net;* limp leather, $2.25, *net.* *Lea's Series of Pocket Text-Books.* Page 12.

EWING (JAMES). *A PRACTICAL TREATISE ON THE BLOOD.* Second edition. Octavo, 492 pages, with 43 engravings and 18 full-page colored plates. Cloth, $3.50, *net.*

FARQUHARSON (ROBERT). *A GUIDE TO THERAPEUTICS.* Fourth edition, revised by FRANK WOODBURY, M.D. 12mo., 581 pages. Cloth. $2.50.

FERGUSON'S *EPITOME OF THE NOSE AND THROAT.* *Lea's Series of Medical Epitomes.* See page 10.

FIELD (GEORGE P.). *A MANUAL OF DISEASES OF THE EAR.* Fourth edition. Octavo, 391 pages, with 73 engravings and 21 colored plates. Cloth, $3.75.

FINDLEY (PALMER D.). *A TREATISE ON GYNÆCOLOGICAL DIAGNOSIS.* Octavo, 493 pages, 210 engravings, 45 plates in black and colors Cloth, $4.50; leather, $5.50, *net.*

FLINT (AUSTIN). *A TREATISE ON THE PRINCIPLES AND PRACTICE OF MEDICINE.* Seventh edition, thoroughly revised by FREDERICK P. HENRY, M.D. In one large 8vo. volume of 1143 pages, with engravings. Cloth, $5; leather, $6.

FLINT (AUSTIN). *A PRACTICAL TREATISE ON THE HEART.* Second edition, enlarged. Octavo, 550 pages. Cloth, $4.

——— *MEDICAL ESSAYS.* In one 12mo. volume of 210 pages. Cloth, $1.38.

——— *ON PHTHISIS.* In one 8vo. volume of 442 pages. Cloth, $3.50.

FORMULARY, THE NATIONAL. See *National Dispensatory.* Page 14.

FORMULARY, POCKET. Fifth edition. See page 1. $1.50, *net.*

FOSTER (MICHAEL). *A TEXT-BOOK OF PHYSIOLOGY.* Sixth and revised edition. Octavo, 923 pages, with 257 illustrations. Cloth, $4.50; leather, $5.50.

FOTHERGILL (J. MILNER). *HAND-BOOK OF TREATMENT.* Third edition. Octavo, 664 pages. Cloth, $3.75; leather, $4.75.

FOWNES (GEORGE). *A MANUAL OF ELEMENTARY CHEMISTRY.* Twelfth edition. Embodying WATTS' *Physical and Inorganic Chemistry.* Royal 12mo., 1061 pages, with 168 engravings, and 1 colored plate. Cloth, $2.75.

FRANKLAND (E.) AND JAPP (F. R.). *INORGANIC CHEMISTRY.* Octavo, 677 pages, with 51 engravings and 2 plates. Cloth, $3.75; leather, $4.75.

FULLER (EUGENE). *DISORDERS OF THE SEXUAL ORGANS IN THE MALE.* Octavo, 238 pages, with 25 engravings and 8 plates. Cloth, $2.

GALLAUDET (BERN B.). *A POCKET TEXT-BOOK OF SURGERY.* 12mo. of about 500 pages, with many illustrations. *In Press. Lea's Series of Pocket Text-Books.* Page 12.

GANT (FREDERICK JAMES). *THE STUDENT'S SURGERY.* A Multum in Parvo. In one square octavo volume of 845 pages, with 159 engravings. Cloth, $3.75.

GAYLORD (HARVEY R.) AND ASCHOFF (LUDWIG). *PATHOLOGICAL HISTOLOGY.* With introductory note by WILLIAM H. WELCH, M.D. Quarto, 354 pages, with 81 engravings and 40 full-page plates. Cloth, $7.50, *net.*

GERRISH (FREDERIC H.). *A TEXT-BOOK OF ANATOMY.* By American Authors. Edited by FREDERIC H. GERRISH, M.D. Second edition. Imp. octavo, 937 pages, with 1003 illustrations in black and colors. Cloth, $6.50; sheep, $7.50, *net;* half morocco, $8.00, *net.*

GIBBES (HENEAGE). *PRACTICAL PATHOLOGY AND MORBID HISTOLOGY.* Octavo of 314 pages, with 60 illustrations, mostly photographic. Cloth, $2.75.

GRAY (HENRY). *ANATOMY, DESCRIPTIVE AND SURGICAL.* Fifteenth edition, thoroughly revised. In one imperial octavo volume of 1249 pages, with 780 large and elaborate engravings. Price with illustrations in colors, cloth, $6.25, *net*; leather, $7.25, *net.* Price, with illustrations in black, cloth, $5.50; leather, $6.50, *net.*

GRAYSON (CHARLES P.). *DISEASES OF THE THROAT, NOSE, AND ASSOCIATED AFFECTIONS OF THE EAR.* Octavo, 548 pages, with 129 engravings and 8 plates in colors and monochrome. Cloth, $3.50, *net.*

GREEN (T. HENRY). *PATHOLOGY AND MORBID ANATOMY.* Ninth revised edition. Octavo, 565 pages, with 339 engravings and 4 colored plates. Cloth, $3.25, *net.*

GREENE (WILLIAM H.). *MEDICAL CHEMISTRY.* 12mo., 310 pages, with 74 illustrations. Cloth, $1.75.

GRINDON (JOSEPH). *A POCKET TEXT-BOOK OF SKIN DISEASES.* 12mo. of 367 pages, with 39 illustrations. Cloth, $2.00; flexible leather, $2.50, *net. Lea's Series of Pocket Text-Books.* Page 12.

GROSS (SAMUEL D.). *THE URINARY BLADDER, THE PROSTATE GLAND AND THE URETHRA.* Third edition, revised by SAMUEL W. GROSS, M.D. Octavo of 574 pages, with 170 illustrations. Cloth, $4.50.

GUENTHER (A. E. AND T. C.). *AN EPITOME OF PHYSIOLOGY.* 12mo., 225 pages, illustrated. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

HABERSHON (S. O.). *DISEASES OF THE ABDOMEN.* Second American from the third English edition. Octavo, 554 pages, with 11 engravings. Cloth, $3.50.

HALE (HENRY E.). *AN EPITOME OF ANATOMY.* 12mo., 389 pages, 71 engravings. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

HALL (WINFIELD S.). *TEXT-BOOK OF PHYSIOLOGY.* Octavo, 672 pages, with 343 engravings and 6 colored plates. Cloth, $4.00, *net;* leather, $5.00, *net.*

HAMILTON (ALLAN McLANE). *NERVOUS DISEASES.* Second and revised edition. Octavo, 598 pages, with 72 engravings. Cloth, $4.

HAMILTON (MILDRED M.). *A POCKET TEXT-BOOK OF MASSAGE.* 12mo, about 400 pages, illustrated. *Preparing. Lea's Series of Pocket Text-Books.* See page 12.

HARDAWAY (W. A.). *MANUAL OF SKIN DISEASES.* Second edition. 12mo., 560 pages with 40 illustrations and 2 colored plates. Cloth, $2.25, *net.*

HARE (HOBART AMORY). *A TEXT-BOOK OF PRACTICAL THERAPEUTICS,* with Special Reference to the Application of Remedial Measures to Disease and their Employment upona Rational Basis. Ninth revised edition. Octavo, 851 pages, 105 engravings, 4 colored plates. Cloth, $4.00, *net;* leather, $5.00, *net;* half morocco, $5.50, *net.*

——— *PRACTICAL DIAGNOSIS.* The Use of Symptoms in the Diagnosis of Disease. Fifth edition, revised and enlarged. Octavo, 727 pages, with 236 engravings, and 25 full-page plates. Cloth, $5.00; leather, $6.00; half morocco, $6.50, *net.*

——— **Editor.** *A SYSTEM OF PRACTICAL THERAPEUTICS.* By American and Foreign Authors. Second edition. In three large octavo volumes containing 2593 pages, with 457 engravings and 26 full-page plates. Price per volume, cloth, $5.00, *net;* leather, $6.00, *net;* half morocco, $7.00, *net. For sale by subscription only.* Full prospectus free on application to the publishers.

——— *ON THE MEDICAL COMPLICATIONS AND SEQUELÆ OF TYPHOID FEVER.* Octavo, 276 pages, 21 engravings, and 2 full-page plates. Cloth, $2.40, *net.*

HARRINGTON (CHARLES). *A TREATISE ON PRACTICAL HYGIENE.* Second edition. Handsome octavo of 755 pages, with 113 engravings and 12 plates in colors and monochrome. Cloth, $4.25, *net.*

HARTSHORNE (HENRY). *A CONSPECTUS OF THE MEDICAL SCIENCES.* Comprising Manuals of Anatomy, Physiology, Chemistry, Materia Medica, Practice of Medicine, Surgery and Obstetrics. Second edition. 12mo., 1028 pages, with 477 illustrations. Cloth, $4.25; leather, $5.

HAYDEN (JAMES R.). *A POCKET TEXT-BOOK OF VENEREAL DISEASES.* Third edition. In one 12mo. volume of 304 pages, with 66 engravings. Cloth, $1.75, *net.*; Flexible red leather, $2.25, *net. Lea's Series of Pocket Text-Books.* See page 12.

HAYEM (GEORGES) AND HARE (H. A.). *PHYSICAL AND NATURAL THERAPEUTICS.* Heat, Electricity, Climate and Mineral Waters. Edited by H. A. HARE, M.D. Octavo, 414 pages, with 113 engravings. Cloth, $3.

HERMAN (G. ERNEST). *FIRST LINES IN MIDWIFERY.* 12mo., 198 pages, with 80 engravings. Cloth, $1.25. *Students' Series of Manuals.* See page 15.

HERMANN (L.). *EXPERIMENTAL PHARMACOLOGY.* A Hand-Book of the Methods for Determining the Physiological Actions of Drugs. Translated by ROBERT MEADE SMITH, M.D. 12mo., 199 pages, with 32 engravings. Cloth, $1.50.

HERRICK (JAMES B.). *A HANDBOOK OF DIAGNOSIS.* In one handsome 12mo. volume of 429 pages, with 80 engravings and 2 colored plates. Cloth, $2.50.

HERTER (C. A.). *LECTURES ON CHEMICAL PATHOLOGY.* In one 12 mo. volume of 454 pages. Cloth, $1.75, *net.*

HILL (BERKELEY). *SYPHILIS AND LOCAL CONTAGIOUS DISORDERS.* In one 8vo. volume of 479 pages. Cloth, $3.25.

HILLIER (THOMAS). *A HANDBOOK OF SKIN DISEASES.* Second edition. In one royal 12mo. volume of 353 pages, with two plates. Cloth, $2.25.

HIRST (BARTON C.) AND PIERSOL (GEORGE A.). *HUMAN MONSTROSITIES.* Magnificent folio, containing 220 pages of text and illustrated with 123 engravings and 39 large photographic plates from nature. In four parts, price each, $5.

HOBLYN (RICHARD D.). *A DICTIONARY OF THE TERMS USED IN MEDICINE AND THE COLLATERAL SCIENCES.* Thirteenth edition. In one 12mo. volume of 845 pages. Cloth, $3.00, *net.*

HOLLIS' *EPITOME OF MEDICAL DIAGNOSIS. Lea's Series of Medical Epitomes.* See page 10.

HOLMES (TIMOTHY). *A TREATISE ON SURGERY.* Fifth edition. Octavo, 1008 pages, with 428 engravings. Cloth, $6; leather, $7.

——— *A SYSTEM OF SURGERY.* Edited by JOHN H. PACKARD, M.D. In three 8vo. volumes, 3137 pages, 979 engravings, 13 plates. Per volume, Cloth, $6.

HUNTINGTON (GEORGE S.). *ABDOMINAL ANATOMY.* Imperial quarto, 590 pages, including 300 full-page plates. De luxe edition, $10.00, *net.*

HYDE (JAMES NEVINS) AND MONTGOMERY (FRANK H.). *A PRACTICAL TREATISE ON DISEASES OF THE SKIN.* Sixth edition, thoroughly revised. Octavo, 832 pages, with 107 engravings and 27 full-page plates, 9 of which are colored. Cloth, $4.50, *net;* leather, $5.50, *net;* half morocco, $6.00, *net.*

JACKSON (GEORGE THOMAS). *THE READY-REFERENCE HANDBOOK OF DISEASES OF THE SKIN.* Fourth edition. 12mo. volume of 617 pages, with 82 engravings, and 3 colored plates. Cloth, $2.75, *net.*

JAMIESON (W. ALLAN). *DISEASES OF THE SKIN.* Third edition. Octavo, 656 pages, with 1 engraving and 9 double-page chromo-lithographic plates. Cloth, $6.

JEWETT (CHARLES). *ESSENTIALS OF OBSTETRICS.* Second edition. 12mo., 385 pages, with 80 engravings and 5 colored plates. Cloth, $2.25, *net.*

——— *THE PRACTICE OF OBSTETRICS.* By American Authors. Second edition. One octavo volume of 775 pages, with 445 engravings in black and colors, and 35 full-page colored plates. Cloth, $5.00; leather, $6.00; half morocco, $6.50.

JULER (HENRY). *A HANDBOOK OF OPHTHALMIC SCIENCE AND PRACTICE.* Third edition. Octavo, 733 pages, with 190 engravings, 25 plates, Test-types and Color-Blindness Test. Cloth, $5.25, *net.*

KELLY (A. O. J.) *A MANUAL OF THE PRACTICE OF MEDICINE.* Octavo, about 600 pages, illustrated. *Preparing.*

KIEPE (EDWARD J.). *EPITOME OF MATERIA MEDICA AND THERAPEUTICS. Lea's Series of Medical Epitomes.* See page 10.

KING (A. F. A.). *A MANUAL OF OBSTETRICS.* Ninth edition. In one 12mo. volume of 629 pages, with 275 illustrations. Cloth, $2.50, *net.*

KIRK (EDWARD C.). *OPERATIVE DENTISTRY.* Second edition. See *American Text-books of Dentistry,* page 2.

KLEIN (E.). *ELEMENTS OF HISTOLOGY.* Fifth edition. In one pocket-size 12mo. volume of 506 pages, with 296 engravings. Cloth, $2.00, *net. Students' Series of Manuals.* Page 15.

KOPLIK (HENRY). *DISEASES OF INFANCY AND CHILDHOOD.* Octavo, 675 pages with 169 engravings and 32 plates in black and colors. Cloth, $5.00; leather, $6.00, *net.*

LANDIS (HENRY G.). *THE MANAGEMENT OF LABOR.* In one handsome 12mo. volume of 329 pages, with 28 illustrations. Cloth, $1.75.

LEA (HENRY C.). *CHAPTERS FROM THE RELIGIOUS HISTORY OF SPAIN; CENSORSHIP OF THE PRESS; MYSTICS AND ILLUMINATI; THE ENDEMONIADAS; EL SANTO NINO DE LA GUARDIA; BRIANDA DE BARDAXI.* In one 12mo. volume of 522 pages. Cloth. $2.50.

——— *A HISTORY OF AURICULAR CONFESSION AND INDULGENCES IN THE LATIN CHURCH.* In three octavo volumes of about 500 pages each. Per volume, cloth, $3.

——— *THE MORISCOS OF SPAIN: THEIR CONVERSION AND EXPULSION.* In one royal 12mo. volume of about 425 pages. Extra cloth, $2.25, *net.*

——— *STUDIES IN CHURCH HISTORY.* New edition. 12mo., 605 pages. Cloth, $2.50.

——— *SUPERSTITION AND FORCE; ESSAYS ON THE WAGER OF LAW, THE WAGER OF BATTLE, THE ORDEAL AND TORTURE.* Fourth edition, thoroughly revised. In one royal 12mo. volume of 629 pages. Cloth, $2.75.

LEA'S SERIES OF MEDICAL EPITOMES. Edited by V. C. PEDERSEN, M.D. Covering the entire field of medicine and surgery in twenty two convenient volumes of about 250 pages each, amply illustrated and written by prominent teachers and specialists. Compendious, authoritative and modern. Following each chapter is a series of questions which will be found convenient in quizzing. The Series is constituted as follows:

Hale's Anatomy. Guenther's Physiology. McGlannan's Inorganic Chemistry and Physics. McGlannan's Organic and Physiological Chemistry. Kiepe's Materia Medica and Therapeutics. Dayton's Practice of Medicine. Hollis's Medical Diagnosis. Arneill's Clinical Diagnosis and Urinalysis. Nagel's Nervous and Mental Diseases. Wathen's Histology. Stenhouse's Pathology. Archinard's Bacteriology and Microscopy. Magee and Johnson's Surgery. Alling and Griffen on the Eye and Ear. Ferguson on the Nose and Throat. Schmidt's Genito-Urinary and Venereal Diseases. Schalek's Dermatology. Pedersen and Parker's Gynæcology. Manton's Obstetrics. Tuley's Pediatrics. Dwight's Jurisprudence. Dwight's Toxicology. For separate notices see under various authors' names.

LEA'S SERIES OF POCKET TEXT-BOOKS. See page 12.

LE FEVRE (EGBERT). *A TEXT-BOOK OF PHYSICAL DIAGNOSIS.* 12mo., 450 pages, 74 engravings, 12 plates. Cloth, $2.25, *net.*

LONG (ELI H.). *DENTAL MATERIA MEDICA AND THERAPEUTICS.* 12mo., 321 pages, 6 engravings, 18 plates. Cloth, $3.00, *net.*

LOOMIS (ALFRED L.) AND THOMPSON (W. GILMAN), Editors. *A SYSTEM OF PRACTICAL MEDICINE.* In Contributions by Various American Authors. In four very handsome octavo volumes of about 900 pages each, fully illustrated in black and colors. Per volume, cloth, $5; leather, $6; half Morocco, $7. *For sale by subscription only.* Full prospectus free on application.

LYMAN (HENRY M.). *THE PRACTICE OF MEDICINE.* In one very handsome octavo volume of 925 pages with 170 engravings. Cloth, $4.75; leather, $5.75.

MAGEE (M. D.) AND JOHNSON (WALLACE). *AN EPITOME OF SURGERY.* 12mo., about 300 pages, with 130 engravings. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

MAISCH (JOHN M.). *A MANUAL OF ORGANIC MATERIA MEDICA.* Seventh edition, thoroughly revised by H. C. C. MAISCH, Ph.G., Ph.D. In one 12mo. of 512 pages, with 285 engravings. Cloth, $2.50, *net.*

MALSBARY (GEO. E.). *A POCKET TEXT-BOOK OF THEORY AND PRACTICE OF MEDICINE.* 12mo. 405 pages, with 45 illustrations. Cloth, $1.75, *net;* flexible red leather, $2.25, *net. Lea's Series of Pocket Text-Books.* Page 12.

MANTON (W. P.). *AN EPITOME OF OBSTETRICS.* 12mo., 265 pages, 82 illustrations. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

MANUALS. See *Medical Epitomes*, page 10; *Pocket Text-Books*, page 12.

MARSH (HOWARD). *DISEASES OF THE JOINTS.* In one 12mo. volume of 468 pages, with 64 engravings and a colored plate. Cloth, $2. See *Series of Clinical Manuals*, page 13.

MARTIN (EDWARD.) *SURGICAL DIAGNOSIS.* One 12mo. volume of 400 pages, richly illustrated. *Preparing.*

MARTIN (WALTON) AND ROCKWELL (W. H., JR.). *A POCKET TEXT-BOOK OF CHEMISTRY AND PHYSICS.* 12mo. 366 pages, with 137 illustrations. Cloth, $1.50, *net;* flexible leather, $2.00, *net. Lea's Series of Pocket Text-Books.* Page 12.

McGLANNAN (A.). *AN EPITOME OF INORGANIC CHEMISTRY AND PHYSICS.* 12mo, 216 pages, with 20 engravings. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

——— *AN EPITOME OF ORGANIC AND PHYSIOLOGICAL CHEMISTRY.* 12mo., 246 pages, with 9 engravings. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

MEDICAL EPITOME SERIES. See *Lea's Series of Medical Epitomes*, page 10.

MEDICAL NEWS POCKET FORMULARY. See page 1. $1.50, *net.*

MITCHELL (JOHN K.). *REMOTE CONSEQUENCES OF INJURIES OF NERVES AND THEIR TREATMENT.* 12mo., 239 pages, 12 illustrations. Cloth, $1.75.

MITCHELL (S. WEIR). *CLINICAL LESSONS ON NERVOUS DISEASES.* 12mo., 299 pages, with 17 engravings and 2 colored plates. Cloth, $2.50.

MORROW (PRINCE A.). *SOCIAL DISEASES AND MARRIAGE. SOCIAL PROPHYLAXIS.* Octavo, 390 pages. Cloth, $3.00, *net. Just ready.*

MUSSER (JOHN H.). *A TREATISE ON MEDICAL DIAGNOSIS,* for Students and Physicians. New (fifth) edition, thoroughly revised and rewritten. Octavo, 1205 pages, with 395 engravings, and 63 full-page colored plates. Cloth, $6.50, *net;* leather, $7.50, *net;* half morocco, $8.00, *net.*

NAGEL (J. D.) *AN EPITOME OF NERVOUS AND MENTAL DISEASES.* 12mo., about 250 pages, illustrated. *Shortly. Lea's Series of Medical Epitomes.* See page 10.

NATIONAL DISPENSATORY. See *Stillé, Maisch & Caspari*, page 14.

NATIONAL FORMULARY. See *National Dispensatory*, page 14.

NATIONAL MEDICAL DICTIONARY. See *Billings*, page 3.

NETTLESHIP (E.). *DISEASES OF THE EYE.* Sixth American from sixth English edition. Thoroughly revised. 12mo., 562 pages, with 192 engravings, 5 colored plates, Test-types, Formulæ and Color-blindness Test. Cloth, $2.25, *net.*

NICHOLS (JOHN B.) AND VALE (F. P.). *A POCKET TEXT-BOOK OF HISTOLOGY AND PATHOLOGY.* 12mo. of 459 pages, with 213 illustrations. Cloth, $1.75, *net;* flexible leather, $2.25, *net. Lea's Series of Pocket Text-Books.* Page 12.

NORRIS (WM. F.) AND OLIVER (CHAS. A.). *TEXT-BOOK OF OPHTHALMOLOGY.* In one octavo volume of 641 pages, with 357 engravings and 5 colored plates. Cloth, $5; leather, $6.

OWEN (EDMUND). *SURGICAL DISEASES OF CHILDREN.* In one 12mo. volume of 525 pages, with 85 engravings and 4 colored plates. Cloth, $2. See *Series of Clinical Manuals*, page 13.

PARK (WILLIAM H.). *BACTERIOLOGY IN MEDICINE AND SURGERY.* 12mo., 688 pages, 87 engravings in black and colors, 2 colored plates. Cloth, $3.00, *net.*

PARK (ROSWELL), Editor. *A TREATISE ON SURGERY*, by American Authors. For Students and Practitioners of Surgery and Medicine. Third edition. In one large octavo volume of 1408 pages, with 692 engravings and 64 plates. Cloth, $7.00; leather, $8.00, *net*. Published also in 2 volumes: Vol. I., General Surgery; Vol. II., Special or Regional Surgery. Per volume, cloth, $3.75, *net;* leather, $4.75, *net*.

PEDERSEN AND PARKER'S *EPITOME OF GYNECOLOGY*. *Lea's Series of Medical Epitomes*. See page 10.

PEPPER (A. J.). *SURGICAL PATHOLOGY*. In one 12mo volume of 511 pages, with 81 engravings. Cloth, $2. See *Students' Series of Manuals*, page 15.

PICK (T. PICKERING). *FRACTURES AND DISLOCATIONS*. In one 12mo. volume of 530 pages, with 93 engravings. Cloth, $2. See *Series of Clinical Manuals*, p. 13.

PLAYFAIR (W. S.). *THE SCIENCE AND PRACTICE OF MIDWIFERY*. Seventh American from the Ninth English edition. Octavo, 700 pages, with 207 engravings and 7 full page plates. Cloth, $3.75; leather, $4.75, *net*.

POCKET FORMULARY. Fifth edition. See page 1.

POCKET TEXT-BOOK SERIES covers the entire domain of medicine in eighteen volumes of 350 to 525 pages each, written by teachers in leading American medical colleges. Issued under the editorial supervision of BERN B. GALLAUDET, M.D., of the College of Physicians and Surgeons, New York. Thoroughly modern and authoritative, concise and clear, amply illustrated with engravings and plates, handsomely printed and bound. The series is constituted as follows: Rockwell's Anatomy; Collins & Rockwell's Physiology; Martin & Rockwell's Chemistry and Physics; Nichols & Vale's Histology and Pathology; Schleif's Materia Medica and Therapeutics; Malsbary's Practice; Collins & Davis' Diagnosis; Potts on Nervous and Mental Diseases; Gallaudet's Surgery; Hayden on Venereal Diseases; Grindon on the Skin; Ballenger & Wippern on Eye, Ear, Nose and Throat; Evans' Obstetrics; Crockett's Gynecology; Tuttle on Diseases of Children; Zapffe's Bacteriology; Wicks on Nursing; Hamilton on Massage. For separate notices see under various authors' names. Special circular free on application.

POLITZER (ADAM). *A TEXT-BOOK OF THE DISEASES OF THE EAR AND ADJACENT ORGANS*. Third American from the Fourth German edition. In one octavo volume of 896 pages, with 346 engravings. Cloth, $7.50, *net*.

POSEY (W. C.) AND WRIGHT (JONATHAN). *A TREATISE ON THE EYE, NOSE, THROAT AND EAR*. Octavo, 1251 pages, richly illustrated with 650 engravings and 35 plates in black and colors. Cloth, $7.00; leather, $8.00, *net*. Published also in two volumes. Vol. I., Posey on the Eye. Cloth, $4.00, *net*. Vol. II., Wright on the Nose, Throat and Ear. Cloth, $3.50, *net*.

POTTS (CHAS. S.). *A POCKET TEXT-BOOK OF NERVOUS AND MENTAL DISEASES*. 12mo. of 455 pages, with 88 illustrations. Cloth, $1.75, *net;* flexible leather, $2.25, *net*. *Lea's Series of Pocket Text-Books*, page 12.

—— *A TEXT-BOOK ON MEDICINE AND SURGICAL ELECTRICITY*. Octavo, about 350 pages, amply illustrated. *Shortly*.

PROGRESSIVE MEDICINE. See page 1. Per annum, $9.00, in cloth; $6.00 in paper.

PURDY (CHARLES W.). *BRIGHT'S DISEASE AND ALLIED AFFECTIONS OF THE KIDNEY*. In one octavo volume of 288 pages, with 18 engravings. Cloth, $2.

PYE-SMITH (PHILIP H.). *DISEASES OF THE SKIN*. In one 12mo. volume of 407 pages, with 28 illustrations, 18 of which are colored. Cloth, $2.

RALFE (CHARLES H.). *CLINICAL CHEMISTRY*. In one 12mo. volume of 314 pages, with 16 engravings. Cloth, $1.50. See *Students' Series of Manuals*, page 14.

REMSEN (IRA). *THE PRINCIPLES OF THEORETICAL CHEMISTRY*. Fifth edition thoroughly revised. In one 12mo. volume of 326 pages. Cloth, $2.

REYNOLDS (EDWARD) AND NEWELL (F. S.). *MANUAL OF PRACTICAL OBSTETRICS*. Octavo, 531 pages, 253 engravings and 3 plates. Cloth, $3.75, *net*.

RICHARDSON (MAURICE H.). *A PRACTICAL TREATISE ON ABDOMINAL SURGERY.* Octavo, about 800 pages, profusely illustrated with engravings and colored plates. *Preparing.*

RICHARDSON (BENJAMIN WARD). *PREVENTIVE MEDICINE.* In one octavo volume of 729 pages. Cloth, $4.

ROBERTS (JOHN B.). *THE PRINCIPLES AND PRACTICE OF MODERN SURGERY.* Second edition. In one octavo volume of 838 pages, with 474 engravings and 8 plates. Cloth, $4.25, *net;* leather, $5.25, *net.*

ROBERTS (SIR WILLIAM). *A PRACTICAL TREATISE ON URINARY AND RENAL DISEASES, INCLUDING URINARY DEPOSITS.* Fourth American from the fourth London edition. Octavo, 609 pages, 81 illustrations. Cloth, $3.50.

ROCKWELL (W. H., Jr.). *A POCKET TEXT-BOOK OF ANATOMY.* 12mo., 600 pages, illustrated. Cloth, $2.25; flexible leather, $2.75, *net. Lea's Series of Pocket Text-Books.* Page 12.

ROGER (G. H.). *INFECTIOUS DISEASES.* Translated by M. S. GABRIEL, M.D. Octavo, 864 pages, 41 illustrations. Cloth, $5.75, *net. Just ready.*

ROSS (JAMES). *THE DISEASES OF THE NERVOUS SYSTEM.* Octavo, 726 pages, with 184 engravings. Cloth, $4.50; leather, $5.50.

SCHAFER (EDWARD A.). *THE ESSENTIALS OF HISTOLOGY, DESCRIPTIVE AND PRACTICAL.* Sixth edition. Octavo, 426 pages, with 463 illustrations. Cloth, $3, *net.*

——— *A COURSE OF PRACTICAL HISTOLOGY.* Second edition. In one 12mo. volume of 307 pages, with 59 engravings. Cloth, $2.25.

SCHALEK (ALFRED). *AN EPITOME OF DERMATOLOGY.* 12mo., 225 pages, 34 illustrations. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

SCHLEIF (WM.). *A POCKET TEXT-BOOK OF MATERIA MEDICA, THERAPEUTICS, PRESCRIPTION WRITING, MEDICAL LATIN AND MEDICAL PHARMACY.* Second edition. 12mo., 380 pages. Cloth, $1.75; flexible leather, $2.25, *net. Lea's Series of Pocket Text-Books.* Page 12.

SCHMAUS (HANS.) AND EWING (JAMES). *PATHOLOGY AND PATHOLOGICAL ANATOMY.* Sixth edition. Octavo, 602 pages, with 351 illustrations, including 34 colored inset plates. Cloth, $4.00, *net.*

SCHMIDT (LOUIS E.). *AN EPITOME OF GENITO-URINARY AND VENEREAL DISEASES.* 12mo, 249 pages, 21 illustrations. Cloth, $1.00, *net. Lea's Series of Medical Epitomes.* See page 10.

SCOTT (R. J. E.). *See State Board License Examination Series.* Page 14.

SENN (NICHOLAS). *SURGICAL BACTERIOLOGY.* Second edition. In one octavo volume of 268 pages, with 13 plates, 10 of which are colored, and 9 engravings. Cloth, $2.

SERIES OF CLINICAL MANUALS. A Series of Authoritative Monographs on Important Clinical Subjects, in 12mo. volumes of about 550 pages, well illustrated. The following volumes are now ready: CARTER and FROST'S Ophthalmic Surgery, $2.25; MARSH on Diseases of the Joints, $2; OWEN on Surgical Diseases of Children, $2; PICK on Fractures and Dislocations, $2. For separate notices, see under various authors' names.

SERIES OF MEDICAL EPITOMES. See page 10.

SERIES OF POCKET TEXT-BOOKS. See page 12.

SERIES OF STATE BOARD LICENSE EXAMINATIONS. See page 14.

SERIES OF STUDENTS' MANUALS. See page 15.

SIMON (CHARLES E.). *CLINICAL DIAGNOSIS, BY MICROSCOPICAL AND CHEMICAL METHODS.* Fifth edition, thoroughly revised. Octavo, 695 pages, with 150 engravings and 22 full-page plates in colors. Cloth, $4.00, *net. Just ready.*

——— *PHYSIOLOGICAL CHEMISTRY.* In one octavo volume of 453 pages. Cloth, $3.25, *net.*

SIMON (W.). *MANUAL OF CHEMISTRY.* A Guide to Lectures and Laboratory Work. A Text-book specially adapted for Students of Medicine and Pharmacy. Seventh edition. In one 8vo. volume of 613 pages, with 64 engravings and 8 plates showing colors of 64 tests and a spectra plate. Cloth, $3.00, *net.*

SLADE (D. D.). *DIPHTHERIA; ITS NATURE AND TREATMENT.* Second edition. In one royal 12mo. volume, 158 pages. Cloth, $1.25.

SMITH (J. LEWIS). *THE DISEASES OF INFANCY AND CHILDHOOD.* Eighth edition, thoroughly revised and rewritten and greatly enlarged. 8vo., 983 pages, with 273 illustrations and 4 full-page plates. Cloth, $4.50; leather, $5.50.

SMITH (STEPHEN). *OPERATIVE SURGERY.* Second and thoroughly revised edition. In one octavo vol. of 892 pages, with 1005 engravings. Cloth, $4; leather, $5.

SOLLY (S. EDWIN). *A HANDBOOK OF MEDICAL CLIMATOLOGY.* Octavo, 462 pages, with engravings and 11 full-page plates. Cloth, $4.00.

STARR (M. ALLEN). *A TREATISE ON ORGANIC NERVOUS DISEASES.* Octavo, 740 pages, with 275 engravings and 26 plates. Cloth, $6.00, *net;* leather, $7.00, *net;* half morocco, $7.50, *net. Just ready.*

STATE BOARD LICENSE EXAMINATION SERIES. Classified and Edited by R. J. E. Scott, A.M., M.D. A series of handy, well arranged, 12mo. volumes of about 200 pages each, bound in flexible cloth and printed on paper suitable for either pen or pencil, every other page being left blank for memoranda. The respective volumes cover the subjects of (1) Anatomy; (2) Chemistry; (3) Obstetrics; (4) Surgery; (5) Practice, Materia Medica and Therapeutics; (6) Pathology and Diagnosis; (7) Physiology and Hygiene. Per volume, $1.50, *net.*

STENHOUSE'S *EPITOME OF PATHOLOGY. Lea's Series of Medical Epitomes.* See page 10.

STILLE (ALFRED). *CHOLERA; ITS ORIGIN, HISTORY, CAUSATION, SYMPTOMS, LESIONS, PREVENTION AND TREATMENT.* In one 12mo. volume of 163 pages, with a chart showing routes of previous epidemics. Cloth, $1.25.

——— *THERAPEUTICS AND MATERIA MEDICA.* Fourth and revised edition. In two octavo volumes, containing 1936 pages. Cloth, $10.

STILLE (ALFRED), MAISCH (JOHN M.) AND CASPARI (CHAS. JR.). *THE NATIONAL DISPENSATORY:* Containing the Natural History, Chemistry, Pharmacy, Actions and Uses of Medicines, including those recognized in the latest Pharmacopœias of the United States, Great Britian and Germany, with numerous references to the French Codex. Fifth edition, revised and enlarged in accordance with and embracing the new *U. S. Pharmacopœia*, Seventh Decennial Revision. With Supplement containing the new edition of the *National Formulary.* Imperial octavo, 2025 pages, with 320 engravings. Cloth, $7.25; leather, $8. With Thumb Index. Cloth, $7.75; leather, $8.50.

STIMSON (LEWIS A.). *A MANUAL OF OPERATIVE SURGERY.* Fourth edition. In one royal 12mo. volume of 581 pages, with 293 engravings. Cloth, $3.00, *net.*

——— *A TREATISE ON FRACTURES AND DISLOCATIONS.* Third edition. In one handsome octavo volume of 842 pages, with 336 engravings and 32 full-page plates. Cloth, $5 *net;* leather, $6, *net;* half morocco, $6.50, *net.*

STUDENTS' QUIZ SERIES. A Series of Manuals in question and answer form, for Students and Practitioners, covering the essentials of medical science. Thirteen volumes, pocket size, convenient, authoritative, well illustrated, handsomely bound in cloth, and issued at a low price. 1. Anatomy (double number); 2. Physiology; 3. Chemistry and Physics; 4. Histology, Pathology and Bacteriology; 5. Materia Medica and Therapeutics; 6. Practice of Medicine; 7. Surgery (double number); 8. Genito-Urinary and Venereal Diseases; 9. Diseases of the Skin; 10. Diseases of the Eye, Ear, Throat and Nose; 11. Obstetrics; 12. Gynecology; 13. Diseases of Children. Price, $1 each, except Nos. 1 and 7, *Anatomy and Surgery*, which being double numbers are priced at $1.75 each. Full specimen circular on application to publishers.

STUDENTS' SERIES OF MANUALS. A Series of Manuals by Eminent Teachers or Examiners. The volumes are pocket-size 12mos. of from 300–540 pages, profusely illustrated, and bound in red limp cloth. The following volumes may now be announced: HERMAN'S First Lines in Midwifery, $1.25; BRUCE'S Materia Medica and Therapeutics (sixth edition), $1.50, *net;* KLEIN'S Elements of Histology (5th edition), $2.00, *net;* PEPPER'S Surgical Pathology, $2; TREVES' Surgical Applied Anatomy, $2.00, *net;* RALFE'S Clinical Chemistry, $1.50.

For separate notices, see under various authors' names.

STURGES (OCTAVIUS). *AN INTRODUCTION TO THE STUDY OF CLINICAL MEDICINE.* In one 12mo. volume. Cloth, $1.25.

SUTER (W. NORWOOD). *A MANUAL OF REFRACTION AND MOTILITY.* 12mo., 382 pages, 101 engravings, 4 colored plates. Cloth, $2.00, *net.*

SUTTON (JOHN BLAND). *SURGICAL DISEASES OF THE OVARIES AND FALLOPIAN TUBES.* Including Abdominal Pregnancy. In one 12mo. volume of 513 pages, with 119 engravings and 5 colored plates. Cloth, $3.

SZYMONOWICZ (L.) AND MacCALLUM (J. BRUCE). *A TEXT-BOOK OF HISTOLOGY OF THE HUMAN BODY:* including Microscopical Technique. Octavo, 437 pages, with 277 original engravings and 57 inset plates in black and colors, containing 81 figures. Cloth, $4.75, *net.*

TAIT (LAWSON). *DISEASES OF WOMEN AND ABDOMINAL SURGERY.* Octavo, 554 pages, 62 engravings, and 3 plates. Cloth, $3.

TAYLOR (ALFRED S.). *MEDICAL JURISPRUDENCE.* From the twelfth English edition, revised by CLARK BELL, ESQ., of the N. Y. Bar. Octavo, 831 pages, with 54 engravings and 8 full-page plates. Cloth, $4.50; leather, $5.50.

TAYLOR (ROBERT W.). *GENITO-URINARY AND VENEREAL DISEASES AND SYPHILIS.* New (third) edition, thoroughly revised. Octavo, about 750 pages, with 153 engravings and 39 full-page colored plates. Cloth, $5.00, *net;* leather, $6.00, *net;* half morocco, $6.50, *net. Just ready.*

—— *A PRACTICAL TREATISE ON SEXUAL DISORDERS IN THE MALE AND FEMALE.* Second edition. Octavo, 434 pages, with 91 engravings and 13 plates. Cloth, $3.00, *net.*

—— *A CLINICAL ATLAS OF VENEREAL AND SKIN DISEASES.* Including Diagnosis, Prognosis and Treatment. In eight large folio parts, measuring 14 x 18 inches, and comprising 213 beautiful figures on 58 full-page chromo-lithographic plates, 85 fine engravings, and 425 pages of text. Bound in one volume, half Turkey Morocco, $28.

TAYLOR (SEYMOUR). *INDEX OF MEDICINE.* A Manual for the use of Senior Students and others. In one large 12mo. volume of 802 pages. Cloth, $3.75.

THOMAS (T. GAILLARD) AND MUNDE (PAUL F.). *A PRACTICAL TREATISE ON THE DISEASES OF WOMEN.* Sixth edition, thoroughly revised. Octavo 824, pages, with 347 engravings. Cloth, $5; leather, $6.

THOMPSON (W. GILMAN). *A TEXT-BOOK OF PRACTICAL MEDICINE.* For Students and Practitioners. Second edition. Octavo, 1014 pages, with 59 illustrations. Cloth, $5.00, leather, $6.00, half morocco, $6.50, *net.*

THOMPSON (SIR HENRY). *THE PATHOLOGY AND TREATMENT OF STRICTURE OF THE URETHRA AND URINARY FISTULÆ.* From the third English edition. Octavo, 359 pages, with 47 engravings and 3 plates. Cloth, $3.50.

THORNTON'S *FORMULARY. The Medical News Pocket Formulary.* See page 1.

TIRARD (NESTOR). *MEDICAL TREATMENT OF DISEASES AND SYMPTOMS.* Handsome octavo volume of 627 pages. Cloth, $4.00, *net.*

TREVES (SIR FREDERICK). *OPERATIVE SURGERY.* New (second) edition, revised by the author and JONATHAN HUTCHINSON, Jr., F.R.C.S. In two 8vo volumes containing 1574 pages, with 474 illustrations. De luxe edition, half morocco, $6.50, *net,* per volume. *Just ready.*

TREVES (FREDERICK). *A SYSTEM OF SURGERY.* In Contributions by Twenty-five English Surgeons. In two large octavo volumes, containing 2298 pages, with 950 engravings and 4 full-page plates. Per set, cloth, $16.

——— *SURGICAL APPLIED ANATOMY.* New edition. 12mo., 577 pages, 80 engravings. Cloth, $2.00, *net.* *See Students' Series of Manuals*, page 15.

TULEY (HENRY E.). *AN EPITOME OF PEDIATRICS.* 12mo, 266 pages, with 33 engravings. Cloth, $1.00, *net.* *Lea's Series of Medical Epitomes.* See page 10.

TUTTLE (GEO. M.). *A POCKET TEXT-BOOK OF DISEASES OF CHILDREN.* 12mo. 374 pages, with 5 plates. Cloth, $1.50, *net;* flexible leather, $2.00, *net.* *Lea's Series of Pocket Text-Books.* Page 12.

VAUGHAN (VICTOR C.) AND NOVY (FREDERICK G.). *CELLULAR TOXINS*, or the Chemical Factors in the Causation of Disease. New (4th) edition. 12mo., 480 pages with 6 engravings. Cloth, $3, *net.*

VEASEY (CLARENCE A.). *A MANUAL OF OPHTHALMOLOGY.* 12mo., 410 pages, 194 engravings, 10 colored plates. Cloth, $2.00, *net.*

VISITING LIST. *THE MEDICAL NEWS VISITING LIST* for 1904. Four styles: Weekly (dated for 30 patients); Monthly (undated for 120 patients per month); Perpetual (undated for 30 patients each week); and Perpetual (undated for 60 patients each week). The 60-patient book consists of 256 pages of assorted blanks. The first three styles contain 32 pages of important data, thoroughly revised, and 160 pages of assorted blanks. Each in one volume, price, $1.25. With thumb-letter index for quick use, 25 cents extra. For special combination rates see page 1.

VON BERGMANN (E.), VON BRUNS (P.), AND VON MIKULICZ (J.). *A SYSTEM OF PRACTICAL SURGERY.* Edited by WILLIAM T. BULL, M.D. In five imperial octavo volumes containing about 4000 pages, with about 1600 illustrations in the text and about 100 full-page colored plates. Per volume, cloth, $6.00; library binding, $7.00; half morocco, $8.50, *net.* For sale by subscription only. Full prospectus sent on request.

WATHEN (JOHN R.). *AN EPITOME OF HISTOLOGY.* 12mo, 229 pages, with 114 engravings. Cloth, $1.00, *net* *Lea's Series of Medical Epitomes.* See page 10.

WATSON (THOMAS). *LECTURES ON THE PRINCIPLES AND PRACTICE OF PHYSIC.* Fifth edition with additions by H. HARTSHORNE, M.D. In two 8vo. volumns of 1840 pages, with 190 engravings. Cloth, $9.

WHARTON (HENRY R.). *MINOR SURGERY AND BANDAGING.* Fifth edition. 12mo., 640 pages, with 509 engravings, many of which are photographic. Cloth, $3.00, *net.*

WHITLA (WILLIAM). *DICTIONARY OF TREATMENT.* Octavo of 917 pages. Cloth, $4.

WHITMAN (ROYAL). *ORTHOPEDIC SURGERY.* Second edition. One octavo volume of 843 pages, with 507 illustrations, mostly original. Cloth, $5.50, *net.* *Just ready.*

WICKS MAUD (A.). *A POCKET TEXT-BOOK OF NURSING.* 12mo., about 400 pages, illustrated. *Preparing.* *Lea's Series of Pocket Text-Books.* Page 12.

WILLIAMS (DAWSON). *MEDICAL DISEASES OF INFANCY AND CHILDHOOD.* Second edition specially revised for America by F. S. Churchill, A.M., M.D. Octavo, 538 pages, 52 engravings and 2 colored plates. Cloth, $3.50, *net.*

WILSON (ERASMUS). *A SYSTEM OF HUMAN ANATOMY.* Revised edition, octavo, 616 pages, with 397 engravings. Cloth, $4; leather, $5.

WOOLSEY (GEORGE). *APPLIED SURGICAL ANATOMY REGIONALLY PRESENTED.* Octavo, 511 pages, with 125 original illustrations in black and colors. Cloth, $5.00; leather, $6.00, *net.*

ZAPFFE (FRED. C.) *A POCKET TEXT-BOOK OF BACTERIOLOGY.* 12mo., 350 pages with 145 engravings and 7 colored plates. Cloth, $1.50; flexible leather, $2.00, *net.* *Lea's Series of Pocket Text-Books.* Page 12.

13 August 1968

$ 3.00.